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Dr. David Edwards
Director, Division of Animal Feeds
Center for Veterinary Medicine
Food and Drug Administration
MPN 4, Room 2658
12225 Wilkins Avenue
Rockville, MD 20852

November 25, 2019

GRAS Notification Marine Microalgae Oil by DSM Nutritional Products

Dear Dr. Edwards

DSM Nutritional Products is hereby submitting a Notification of the Generally Recognized As Safe use of Marine Microalgae Oil in food for dogs. This material functions as a source of omega-3 fatty acids, particularly EPA (Eicosapentaenoic Acid) and DHA (Docosahexaenoic Acid) in a ration similar to that of fish oil.

DSM Nutritional Products gathered the appropriate information on the safety and utility of the notified substance which was provided to an independent panel of experts in the field for their evaluation. The enclosed dossier contains the safety and efficacy study data that was provided to the panel. Information on the identity of the production organism, manufacture of the commercial forms, and the panel's signed conclusion statement. Also included are copies of the pertinent literature and the peer reviewed publications addressing the safety of Marine Microalgae Oil and its performance in food for dogs, indicative of those commercially fed in the United States.

DSM Nutritional Products has concluded that Marine Microalgae Oil is GRAS through scientific procedures and is therefore exempt from the requirement for premarket approval noted in Section 201 (s) of the Federal Food Drug and Cosmetic Act.

Sincerely DSM Nutritional Products,

James La Marta, Ph.D., CFS
Sr. Manager Regulatory Affairs North America

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SUMMARY OF DATA FOR A GRAS CONCLUSION

Algal Oil produced by *Schizochytrium* sp.

for use as a source of DHA and EPA in Food for Dogs

18 September 2019

By:

Veramaris USA, LLC

Blair, Nebraska

James La Marta

Parsippany, NJ

Contents

Part 1: Signed Statements and Certification 6
1.1 Submission of GRAS Notice 6
1.2 Name and Address of Notifier 6
1.3 Name and Address of Manufacturer 6
1.4 Name and Address of the Distributor 6
1.5 Name of the Notified Substance 7
1.6 Intended Conditions of Use 7
1.7 Statutory Basis for the GRAS Conclusion 7
1.8 Exemption from Premarket Approval Requirements 7
1.9 Availability of Information 7
1.10 Freedom of Information Act (FOIA) Exemptions 8
1.11 Certification 8
2: Identity of the Notified Substance 9
2.1 Common or usual name of the notified substance 9
2.2 Characterization of the product 9
2.2.1 Chemical Identity 9
2.2.2 Physical Properties 9
2.2.3 Composition of the commercial formulation 10
2.2.4 Chemical Composition 10
2.3 Description of the production organism 13
2.3.1 Classification of the organism: *Schizochytrium sp.* 13
2.3.3 Parental strain 13
2.3.4 Production strain 14
2.3.5 Absence of Toxins 14
2.4 Manufacturing process for Oil from *Schizochytrium* sp. Marine Microalgae 15
2.4.1 Overview of Manufacturing Method 15
2.4.2 Raw Materials 16
2.4.3 Fermentation Process 18
2.4.4 Recovery Process 19
2.4.6 Method to ensure stability of the production organism 20
2.5 Specifications 21
2.6 Comparison to Algal Oil used in Human Nutrition 22
2.7 Analytic Methods 22
2.8 Stability 22
2.8.1 Stability of AOCED 22
2.8.2 Stability of Algal Oil in Canned Dog Food 24
2.8.3 Storage Stability of AOCED in Dry Dog Food 28
2.8.4 Homogeneity 37
Part 3: Dietary Exposure 39
3.1 Dietary Exposure to the notified substance 39
3.1.1 Target Animal 39
3.2 Dietary Exposure to any other substance that is expected to be formed in or on food 39
3.3 Dietary Exposure to any other substance that is present with the notified substance either naturally or due to its manufacture (e.g.., contaminants or by-products) 39
Part 4: Self-limiting levels of use 41
Part 5 Common use in food prior to 1958 42
Part 6 Narrative of the basis for the GRAS conclusion 43

6.1 Long chain Polyunsaturated Fatty Acid Metabolism in Dogs....43
6.2 History of the Use of Algal Products in Animal Food....44
6.2 Literature....47
6.3 Safety of the proposed use of AOCED....47
6.4 Efficacy of the proposed use of AOCED....48
7 Supporting data and information....50
7.1 Canine Metabolism of n-3 Polyunsaturated Fatty Acids (PUFA) and Bioavailability from Dietary Sources....50
7.1.1 Studies during gestation, lactation, and puppy development: n-3 LCPUFA Synthesis from Dietary ALA....50
7.1.2 Studies in adult dogs: DHA Bioavailability from n-3 LCPUFA Sources....50
7.1.4 Adult dogs: Tissue EPA levels following n-3 LCPUFA supplementation....54
7.1.5 Adult dogs: Tissue ARA levels following n-3 LCPUFA Supplementation....54
7.1.6 Studies during Gestation, Lactation, and Puppy Development: DHA, EPA and ARA levels following DHA ethyl esters supplementation....55
7.1.7 Summary and Conclusions from the literature....55
7.2 Review of the Safety of *Schizochytrium sp*. in other species....55
7.2.1 Dried Whole Cell Biomass....55
7.2.2 Oil....58
7.3 Review of the Safety of DHA and EPA in Dogs....60
7.4 Target Animal Safety Studies....68
7.4.1 Objective of the study....68
7.4.2 Study design....68
7.4.3 Diets Offered Prior to the Initiation of the Treatment Period....69
7.4.4 Diet Offered During the Study....69
7.4.5 Animal Care....73
7.4.6 Housing....73
7.4.7 Clinical Observations....73
7.4.7.1. Mortality....74
7.4.7.2 Body Weights....74
7.4.7.3 Food Consumption....74
7.4.7.4 Parturition and litter observations....75
7.4.7.5 Clinical Pathology....75
7.4.7.6 Statistical Analysis....75
7.4.8 Results and Discussion....76
7.4.8.1 F_0 Generation....76
7.4.8.2 F_1 Generation....77
7.4.8.3 Effect of AOCED on blood levels of EPA and DHA....78
7.4.8.4 Statement of compliance with GLP....82
7.5 Information that may appear to be inconsistent with the GRAS....83
determination....83
7.6 Summary....83
8 Annexes....84
9 References....85
10 Expert Panel Statement....90

List of Figures

Figure 1 Structure of Docosahexaenoic Acid (DHA, C22:6*n*-3) 9
Figure 2 Structure of Eicosapentaenoic Acid (EPA, C20:5*n*-3) 9
Figure 3 Overview of the manufacturing process 16
Figure 5 Stability of ACED in canned dog food at 25° C 27
Figure 6 Stability of AOCED in canned dog food at 40° C 28
Figure 7 Stability of DHA in Extruded Dog Food @ 25°C, Post Extrusion Application 30
Figure 8 Stability of EPA in Extruded Dog Food @ 25°C, Post Extrusion Application 31
Figure 9 Stability of EPA and DHA @25 C, Post Extrusion using simple averages 31
Figure 10 Stability of DHA in Extruded Dog Food @ 40°C, Post Extrusion Application 32
Figure 11 Stability of EPA in Extruded Dog Food @ 40°C, Post Extrusion Application 33
Figure 12 Stability of DHA in Extruded Dog Food @ 25°C, Pre-Extrusion Application 34
Figure 13 Stability of EPA in Extruded Dog Food @ 25°C, Pre-Extrusion Application 34
Figure 14 Stability of EPA & DHA Pre-Extrusion @ 25 C, simple averages 35
Figure 15 Stability of DHA in Extruded Dog Food @ 40°C, Pre-Extrusion Application 36
Figure 16 Stability of EPA in Extruded Dog Food @ 40°C, Pre-Extrusion Application 36
Figure 17 Stability of EPA & DHA in Extruded Dog Food @ 40° C, Simple Averages 37
Figure 18 Plasma DHA dams Figure 19 Plasma EPA dams 49
Figure 20 Plasma DHA puppies Figure 21 Plasma EPA puppies 49
Figure 22 Blood Plasma DHA Concentration over time, Dams 79
Figure 23 Blood Plasma EPA Concentration over time, Dams 80
Figure 24 Blood Plasma DHA concentration over time, puppies 81
Figure 25 Blood Plasma EPA concentration over time, puppies 82

List of Tables

Table 1 Composition of the commercial product 10
Table 2 Gross Composition (Crude Protein, Crude Fat, Total Fat, Crude Fiber, Ash, Moisture) 10
Table 3 Table Fatty Acid Profile (relative area % via AOCS Ce 1b-89) 10
Table 4 Raw materials used to manufacture Oil from *Schizochytrium sp.* Marine Microalgae 17
Table 5 Fermentation Sample Profile 19
Table 6 Product Specifications 21
Table 7 Comparison of algal oils for dog food and infant nutrition 22
Table 8 Stability of AOCED at 25° C and 40°C in Aluminum and HDPE Bottles 23
Table 9 Ingredients Used in Canned Dog Food 24
Table 10 Nutritional Analysis of Canned Dog Food 25
Table 11 Stability of AOCED in Canned Dog Food (25° C, 60% RH) 26
Table 12 Stability of AOCED in Canned Dog Food (40° C and 75% RH) 27
Table 13 Ingredient Composition of Kibble used in Shelf Life Study 28
Table 14 Stability of DHA and EPA in dry dog food @25 °C – Post-extrusion application 30
Table 15 Stability of DHA and EPA in dry dog food @ 40 °C – Post-extrusion application 32

Table 16 Stability of DHA and EPA in dry dog food @25°C – Pre-extrusion application....33
Table 17 Stability of DHA and EPA in dry dog food @40°C – Pre-extrusion application....35
Table 18 Homogeneity of DHA and EPA in dry dog food – Post-extrusion application....38
Table 19 Homogeneity of DHA and EPA in dry dog food – Pre-extrusion application....38
Table 20 Achieved AOCED intake. 39
Table 21 Heavy Metals 40
Table 22 Overview of *Schizochytrium* sp. applications in animal feed 46
Table 23 Summary of Evidence from Studies Reporting Bioavailability Outcomes in Dogs fed Various Sources of n-3 LCPUFA 52
Table 24 Summary of Published *Schizochytrium* sp. microalgae Confirmatory Safety Studies ...57
Table 25 Summary of Algal Oil (*Schizochytrium* sp.) toxicity study (Dahms, et al., 2011a) 58
Table 26 Summary of Algal Oil (*Schizochytrium* sp.) toxicity study (Dahms, et al., 2011b) 59
Table 27 Summary of Algal Oil (*Schizochytrium* sp.) toxicity study (Schmitt et al 2012)....59
Table 28 Safety and Tolerability Evidence for n-3 LCPUFA Supplementation of Canine Diets 65
Table 29 Dosing plan 69
Table 30 Treatment allocation 69
Table 31 Composition of Base Kibble (on As Is basis)....70
Table 32 Fat composition in the test diets (on As Is basis) 71
Table 33 Nutrient composition of the diets compared to the AAFCO recommendation 71
Table 34 Blood Plasma DHA concentration, Dams....78
Table 35 Blood Plasma EPA concentration, Dams....79
Table 36 Blood Plasma DHA concentration, puppies....80
Table 37 Blood Plasma EPA concentration, puppies....81

Abbreviations:

ALA	Alpha Linolenic Acid
AOCED	Algal Oil Containing EPA & DHA
ARA	Arachidonic Acid
DHA	Decosahexaenoic acid
DPA	Decosapentaenoic Acid
EPA	Eicosapentaenoic acid
LA	Linoleic Acid
LCPUFA	Long Chain PolyUnsatuated Fatty Acids
PBMC	peripheral blood mononuclear cell
PGE2	Prostaglandin E2
PL	phospholipids
PUFA	PolyUnsatuated Fatty Acids
PV	Peroxide Value
TG	Triglycerides

Part 1: Signed Statements and Certification

1.1 Submission of GRAS Notice

Veramaris is hereby confirming that this GRAS conclusion dossier has been produced in accordance with 21 CFR 570.225.

1.2 Name and Address of Notifier

Veramaris USA LLC
650 Industrial Road
Blair, NE 68008
USA

A joint venture of DSM Nutritional Products and Evonik Industries.

Person responsible for the dossier

James La-Marta
45 Waterview Boulevard
Parsippany, New Jersey 07054
Tel: 973-257-8325

1.3 Name and Address of Manufacturer

Veramaris USA LLC
650 Industrial Road
Blair, NE 68008
USA
(402) 533-1500

1.4 Name and Address of the Distributor

DSM Nutritional Products
45 Waterview Boulevard
Parsippany, NJ 07054
973-257-8500

1.5 Name of the Notified Substance

The common or usual name of the notified substance is Marine Micro-algae Oil, an oil from the marine micro algae, *Schizochytrium sp.* rich in the omega-3 fatty acids, docosahexaenoic acid (DHA) and ei identified in some reports as AOCED, algal oil containing EPA and DHA.

1.6 Intended Conditions of Use

AOCED from marine microalgae *Schizochytrium sp.* Is intended to be used as an ingredient in canned and dry/extruded dog foods for all life stages at a level not to exceed 1.5% wt/wt of the diet on a dry matter basis. The ration of DHA to EPA will be about 2.5:1. AOCED will be used to replace fish oil` commonly used in food for dogs.

1.7 Statutory Basis for the GRAS Conclusion

Pursuant to 21 C.F.R. § 570.30(a)(1), a panel of independent experts assembled by DSM Nutritional Products on behalf of Veramaris, the GRAS Panel, has been asked to review the accumulated data regarding the safety of AOCED, containing high levels of the omega-3 fatty acids, DHA and EPA, in order to evaluate through scientific procedures, if AOCED would be safe for consumption by dogs and therefore, to also conclude that AOCED would be Generally Recognized As Safe for use as an ingredient in food for dogs specified above in Section 1.5.

1.8 Exemption from Premarket Approval Requirements

The notified substance is not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on the conclusion by Veramaris USA LLC that the substance is GRAS under the conditions of its intended use.

1.9 Availability of Information

The data and information that are the basis for Veramaris' GRAS determination is available for the FDA's review and copying upon request during normal business hours at:

DSM Nutritional Products
45 Waterview Blvd
Parsippany, NJ 07054

We also agree to provide a complete digital copy of the data and information upon request.

1.10 Freedom of Information Act (FOIA) Exemptions

Parts 2 through 7 of this notification do not contain data or information that exempt from disclosure under the Freedom of Information Act.

1.11 Certification

To the best of our knowledge, this GRAS notice is a complete, representative, and balanced submission that includes unfavorable information, as well as favorable information, known to Veramaris USA LLC and pertinent to the evaluation of the safety and GRAS status of the use of this substance.



James La Marta, Ph.D., CFS
Sr. Manager Regulatory Affairs
Agent for Veramaris USA LLC

Date: 18 September 2019

2: Identity of the Notified Substance

2.1 Common or usual name of the notified substance

The common and usual name of the substance is: algal oil from marine microalgae *Schizochytrium* sp.

2.2 Characterization of the product

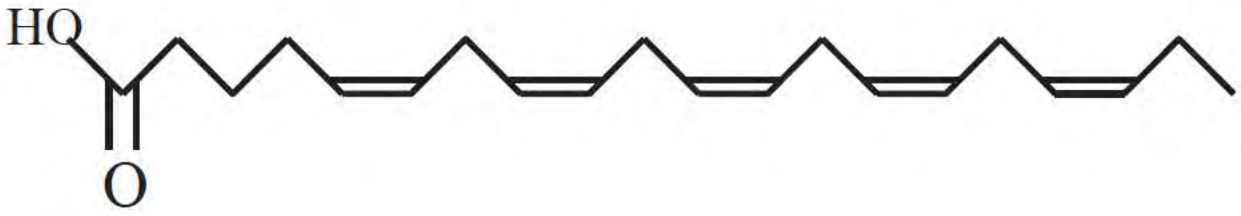
2.2.1 Chemical Identity

The commercial product is an oily material produced by the marine microalgae *Schizochytrium sp*. It is a source of the long chain polyunsaturated fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).

Figure 1 Structure of Docosahexaenoic Acid (DHA, C22:6*n*-3)



Figure 2 Structure of Eicosapentaenoic Acid (EPA, C20:5*n*-3)



2.2.2 Physical Properties

Appearance: Orange to golden brown oil

Solubility in water: Insoluble

Solubility in solvents: Partly miscible with acetone and methanol. Completely miscible with chloroform and hexane.

2.2.3 Composition of the commercial formulation

The commercial product is composed of the algal oil with added mixed tocopherols used as an antioxidant.

Table 1 Composition of the commercial product

Ingredient	Amount	Regulation
Algal Oil from Schizochytrium sp.	Min. 98.85%	Subject of this dossier
Tocopherols	Max. 0.15%/1500 ppm	21 CFR 582.3890

At the maximum recommended use level of 1.5% as noted in Section 1.5, the level of tocopherols contributed by algal oil will not exceed 22.5 ppm in the complete dog food.

2.2.4 Chemical Composition

Veramaris produced four non-consecutive pilot batches of the algal oil for analytical purposes. The results (b) (4) ese batches are summarized in Table 2. The analyses were conducted by (b) (4) using validated or verified test methods. Certificates of analysis are provided in Annex 1.

Table 2 Gross Composition (Crude Protein, Crude Fat, Total Fat, Crude Fiber, Ash, Moisture)

	Test Method	(b) (4)
Crude Fat (%)	AOAC 954.02	
Total Fat (%)	AOAC 996.06	
Free Fatty Acid as Oleic (%)	AOCS Ca 5a-40	
Insoluble Impurities (%)	AOCS Ca 3a-46	
Ash (g/100 g)	AOAC 923.03	
Moisture (%)	AOAC 930.15	
Moisture & Volatiles (%)	AOCS Ca 2c-25	
Protein (%)	AOAC 2001.11	
Total Dietary Fiber (%)	AOAC 991.43	

Table 3 Table Fatty Acid Profile (relative area % via AOCS Ce 1b-89)

	(b) (4)
6:0 Caproic	
8:0 Caprylic	
10:0 Capric	
12:0 Lauric	
13:0 Tridecanoic	

	(b) (4)
14:0 Myristic	
14:1 Myristoleic	
15:0 Pentadecanoic	
15:1 Pentadecenoic	
16:0 Palmitic	
16:1 Palmitoleic	
16:2 Hexadecadienoic	
16:3 Hexadecatrienoic	
16:4 Hexadecatetraenoic	
17:0 Margaric	
17.1 Margaroleic	
18.0 Stearic	
18:1n-9 Oleic	
18:1n-7 Vaccenic	
18:2n-6 Linoleic	
20:0 Arachidic	
18:3n-6 Gamma-Linolenic	
20:1 Eicosenoic	
20:1n-9 Eicosenoic	
18:3n-3 alpha-linolenic	
21:0 Heneicosanoic	
18:4n-3 Stearidonic	
20:2n-6 Eicosadienoic	
22:0 Behenic	
22:1n-9 Erucic	
22:1n-11 Cetoleic	
20:3n-6 homo-gamma-Linolenic acid	
20:3n-3 Eicosatrienoic	
20:4n-5 Eicosatetraenoic	
20:4n-6 Arachidonic	
23:0 Tricosanoic	
22:2n-6 Docosadienoic	
20:4n-3 Eicosatetraenoic	

(b) (4)

22:4n-3 Eicosatetraenoic	
24:0 Lignoceric	
20:5n-3 Eicosapentaenoic	
24:1 Nervonic	
21:5n-3 Heneicosapentaenoic	
22:4n-6 Docosatetraenoic	
22:5n-6 Docosapentaenoic	
22:5n-3 Docosapentaenoic	
22:6n-3 Docosahexaenoic	
Unknown	

2.3 Description of the production organism

2.3.1 Classification of the organism: *Schizochytrium sp.*

Below is an overview of the organism's taxonomy according to the Uniprot database (Uniprot, 2014).

Kingdom:	Chromalveolata (recent refinement of Chromatista)
Division:	Stramenophiles
Class:	Labyrinthulomycetes
Order:	*Saprolegniales
Family:	Thraustochytriaceae
Genus:	Schizochytrium
Species:	sp. ATCC PTA-10208

*DSM believes *Thraustrochytriales* is more accurate but otherwise agrees with UniProt.

Schizochytrium sp. are thraustochytrids that belong to the Chromista kingdom (Bennett et al., 2017). The genus Schizochytrium is characterized by multiple binary cell divisions leading to clusters of sporangia. Schizochytrium spores are biflagellate at discharge and the number of spores discharged can range from two to one hundred.

Thraustochytrids are microscopic, unicellular algae. The earliest research of thraustochytrids placed them in the fungi because of their heterotrophic nature and superficial resemblance to chytrids (Sparrow, 1936). Current analysis using molecular biology techniques have demonstrated that thraustochytrids are not fungi, but are related to the heterokont algae (Cavalier-Smith, 2018) and as a result are now considered microalgae. Current phylogenic analysis indicates that the members of the Chromista are all photosynthetic, but some groups such as the Thraustochytridae have lost their chloroplast and the capability of photosynthesis and as a result, are exclusively heterotrophic (Tsui et al. 2009).

It should be noted that taxonomic categorization of microorganisms is in flux due to advances in molecular biology that result in slight shifts in the allocation of organisms to new groups and occasionally assignment of new names.

2.3.3 Parental strain

The microalgae parent strain was isolated from the intertidal coastline in 2007. Preliminary examination of the organism indicated that it is a Thraustochytrid. Subsequent detailed examination of the organism was conducted by Dr. Gunther Bahnweg, Head of Plant Toxicology and Mycology, Institute of Biochemical Plant Pathology, GSF National Research Centre for Environment and Health, Munich Germany. Dr. Bahnweg has studied thraustochytrids for over 30 years and published extensively on the organism (1979a, 1979b). His examination concluded that this microalga possessed the definitive characteristics of the genus Schizochytrium, and further concluded it was a previously unpublished species of that genus. Both DNA sequences and morphology characteristics were utilized in the identification of the microalgae and it has also been deposited with the ATCC as PTA-10208.

2.3.4 Production strain

Veramaris has developed an improved strain from the patented wild-type parent strain using a classical mutagenesis screening program. This program utilized well-accepted techniques commonly used in industrial strain improvement programs. No recombinant DNA technology was employed. The parent, ATCC PTA-10208, underwent three successive mutagenesis steps using a standard UV exposure procedure. The production strain was selected as a single colony out of the surviving population after screening for oil production ability and DHA to EPA ratio. The selected strain has consistent DHA and EPA content, and high biomass density under large scale fermentation conditions. Further manipulation of the fermentation media composition, pH and temperature led to an optimal oil production level without adversely affecting the DHA to EPA ratio.

2.3.5 Absence of Toxins

Schizochytrium sp. Is a thraustrochytrid and a member of the Chromista kingdom (Stramenopilia), which includes the golden algae, diatoms, yellow-green algae, haptophyte and cryptophyte algae, and oomycetes.

Within the microalgae in the Chromista (Stramenopilia), there are two toxins known to be produced, domoic acid and pymnesin. Domoic acid is a potent neurotoxin which causes amnesic shellfish poisoning in humans. It is a naturally occurring amino acid whose production appears to be limited to a few species of microalgae (diatoms) in the genus Pseudonitzschia (and possibly by one species of Chrysochromulina, a flagellated species of golden algae) (Villac et al., 1993). Species of the genus Pseudonitzschia are common members of marine phytoplankton throughout the world. Four of these diatom species have been identified as being able to produce domoic acid, and these species can be generally found in the colder waters of the Northern Hemisphere (Fritz et al., 1992; Garrison, et al., 1992; Lundholm et al., 1994).

In the phylum Heterokonta, the thrautochytrids are in a separate subphylum and class from the diatoms, so one would not expect to find domoic acid in *Schizochytrium sp.* Prior confirmatory testing of *Schizochytrium sp.* dried microalgae for domoic acid was performed using standard HPLC methods – ultraviolet (modified version of AOAC Official Method 991.26) and ELISA (Biosense). Both methods quantitatively detect domoic acid and these analyses showed no evidence of domoic acid present in *Schizochytrium sp.* dried microalgae.

The other toxins found in a member of the Chromista (Stramenopilia) are limited to two species of Prymnesium (*P. parvum* and *P. patelliferum*). These toxins (called prymnesins by some) exhibit a broad spectrum of activity including lethal effects on gill breathing animals, cytotoxic effects on erythrocytes, nucleated mammalian cells, protozoa, and bacteria. Prymnesin toxins are acidic polar phosphor proteolipids, which because of their chemical nature, form micelles in water. These toxins are not heat stable. See Annex 2 for the analysis of a related strain in the DSM collection used for algal oil production for consumption by humans.

There are no literature reports of this organism producing toxins or being pathogenic nor does the sponsor have any data indicating the initially isolated strains nor the daughter after over 30 years of strain improvement have produced toxins under the conditions of large-scale fermentation. Analysis of related and parent strains in the DSM collection used for the manufacture of algal oil for human consumption did not reveal the presence of domoic acid (Annex 3). Analysis of a pilot batch of the production strain performed in 2019 also showed no production of domoic acid (Annex 13). Toxicology studies with the

production strain confirmed the absence of toxins. Another strain in the DSM collection was approved for use in food for adult dogs under a Food Additive Petition, 21 CFR 573.615. (Fed Reg 2018)

The strain used for AOCED production has not been genetically engineered, no transgenic DNA or RNA have been introduced into the organism. Since the parent strains have been evaluated and not found to produce toxic compounds and no new genetic elements have been introduced into the strain that could carry toxin production genes it is reasonable to assume that the production strain is also devoid of toxin production ability. The target animal safety study supports this contention as no adverse effects were seen in the adult nor juvenile animals that consumed the food with AOCED.

Algal oil is produced via a fermentation process using heterotropic *Schizochytrium sp*., a microscopic, primarily saprotrophic, unicellular microalgae which is usually found in estuarine and marine environments around the world. The scientific literature indicates that thraustochytrids, especially those of the genus Schizochytrium, are regularly consumed as food by a wide range of filter feeding invertebrates (clams and mussels). The available published and unpublished scientific data show no evidence that these organisms produce toxins. Blue-green algae and photosynthetic species of Dinophyta produce most of the toxic compounds produced by microalgae, and the *Schizochytrium sp*. Is in a separate kingdom from both of these types of microalgae.

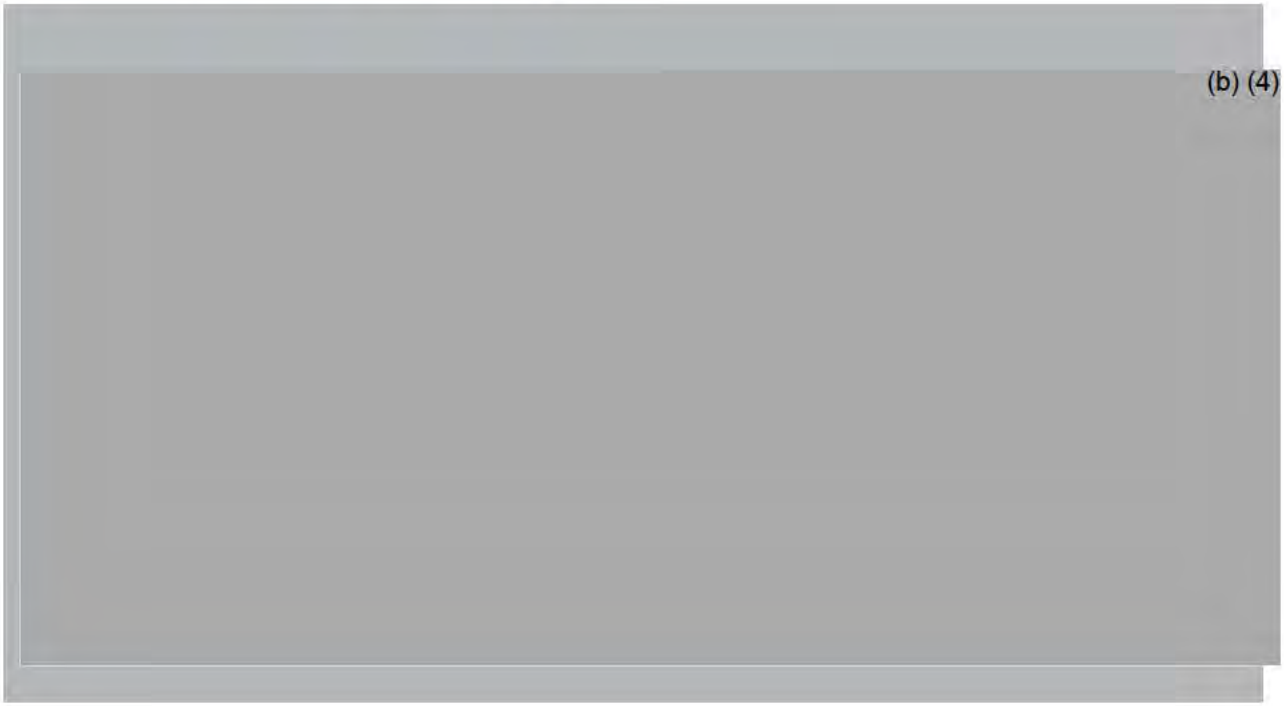
Due to the unavailability of authentic prymnesin standards, *Schizochytrium sp.* microalgae have not been directly analyzed for the presence of prymnesin toxins. However, a bioassay for prymnesin has been developed (Houdan et al., 2004; Graneli et al., 2003; Larsen et al., 1993; Vanhaecke et al., 1981) utilizing *Artemia nauplii* as the test organism. Results of this bioassay on *Schizochytrium sp*. fermentation broth from parent strains show no significant different in the mortality of Artemia culture from the control, indicating the absence of prymnesin toxin.

2.4 Manufacturing process for Oil from *Schizochytrium* sp. Marine Microalgae

2.4.1 Overview of Manufacturing Method

The manufacturing process for algal oil from *Schizochytrium* sp. marine microalgae consists of the following steps: fermentation, cell lysis, recovery of the oil phase, and quality control of the finished product. The entire process is performed in accordance with the Food Safety Modernization Act (FSMA) and its implementing regulations, including current Good Manufacturing Practices (cGMP). An overview of the process is provided in Figure 3.

Figure 3 Overview of the manufacturing process



2.4.2 Raw Materials

The raw materials used for the fermentation and recovery of the product are suitable for the intended use, leading to the required safety status of the product. The raw materials used for the media are of feed-grade quality or better and meet predefined quality standards that are strictly monitored and controlled by the Quality Assurance Department. Internal specifications for the raw materials are attached in Annex 4. The composition of the fermentation medium has been developed for optimum production of algal oil with the desired fatty acid profile.

Table 4 Raw materials used to manufacture Oil from *Schizochytrium sp.* Marine Microalgae

Ingredient	Approved Use	Ingredient	Approved Use
Ammonium Sulfate	21 CFR[1] 184.1143	Sodium Chloride	AAFCO OP[2] 57.31
Anhydrous Ammonia	AAFCO OP 87.11	Sodium hydroxide	21 CFR 582.1763
Calcium Chloride	AAFCO OP 57.51	Sodium Molybdate	AAFCO OP 57.145
Calcium Pantothenate	21 CFR 582.5212	Sodium Sulfate	AAFCO OP 57.109
Citric Acid	21 CFR 582.6033	Thiamine HCl	21 CFR 582.5875
D-Biotin	21 CFR 582.5159	Zinc Sulfate	AAFCO OP 57.118
Cupric Sulfate	AAFCO OP 57.69	Yeast Extract	AAFCO 96.11
Glucose syrup	AAFCO OP 87.35	Phosphoric Acid	21 CFR 582.1073
Water	Potable	Cyanocobalamin	AAFCO OP 90.11
Silicone Anti Foam	21 CFR 582.1711	Nickel Sulfate	21 CFR 184.1537
Ferrous Sulfate	AAFCO OP 57.83	Potassium Chloride	AAFCO OP 57.102
Magnesium Sulfate	AAFCO OP 57.88	Monosodium glutamate	21 CFR 582.1
Manganese Chloride	AAFCO OP 57.91	Mono-Potassium phosphate	21 CFR 582.5628
Protease from fermentation of a nonpathogenic and nontoxigenic strain of Bacillus licheniformis	AAFCO OP 30.1	Tocopherols	21 CFR 582.3890

[1] The Code of Federal Regulations (CFR)

[2] The Association of American Feed Control Officials (AAFCO) is an association of local, state, and federal agencies who regulate the sale and distribution of animal feeds. Every year AAFCO publishes the Official Publication (OP) which includes a list of feed ingredients approved for use in the United States.

2.4.3 Fermentation Process

Veramaris's algal oil ingredient is manufactured by fed-batch culture fermentation using the strain of *Schizochytrium* sp. described above. During each step of fermentation, physical and chemical control measures are incorporated.

Frozen seed of Schizochytrium sp. isolate is thawed and grown through a series of process steps, which include transfers from shake flasks to puntbus, and then to seed fermenters, and finally progressing to a large-scale production fermenter. Temperature, agitation, pressure, pH, and dissolved oxygen are controlled during the initial stages of fermentation.

Generally speaking, products formed by organisms are produced as a result of their response to environmental conditions such as nutrients and ions. Carbon compounds are major sources of cellular carbon and energy. Nitrogen is incorporated into cell mass in the form of proteins and nucleic acids. Oxygen is required as a terminal electron acceptor in aerobic metabolism. Phosphorus is present in nucleic acids and in the cell wall. Sulfur is present in proteins and some coenzymes. Sodium and potassium are required for energy metabolism and are important in the transport of charged species. Potassium and magnesium are cofactors for many enzymes. Trace metals are mainly cofactors and play a regulatory role in many enzyme reactions. Vitamins usually function as coenzymes to stimulate cell growth and synthesis of some metabolites.

Fermentation media is continuously sterilized via a heat exchanger and charged to pre-cleaned and pre-sterilized fermenters. While in the main fermenter, temperature, airflow, overpressure, agitation, dissolved oxygen and carbon dioxide, pH, ammonia feed, foaming, and glucose feed are all controlled to optimize growth of the organism, oil yield, and fatty acid profile of the oil. Various samples are taken during fermentation to control the process. These are summarized in Table 5. Samples are taken to determine fatty acid profile at the end of the seed and main fermentations. Glucose is sampled every 4 hours during the cell growth phase and every 6 hours during the oil production phase. Glucose feed rate is adjusted based on the measurement of glucose concentration. In the final seed fermenter and in the main fermenter, ammonia is sampled every 4 hours. Ammonium sulfate may be added to maintain the appropriate ammonia concentration. In the seed fermenter, the phosphate concentration is measured to confirm if the addition of monopotassium phosphate is needed to maintain cell growth. Wet fatty acid profile is used to measure DHA and EPA concentrations in the main fermentor every 12 hours. These samples are analyzed using the same test method as that for full fatty acid profile except the sample is undried and no internal standard is added. Indication of biomass concentration using infrared balance allows for determination of the amount of tocopherols to add before pasteurization. ABS is a measure of optical density at a wavelength of 465 nanometers; this number should be very low. If the starting media, also called mash, is contaminated this value will increase. Samples are taken throughout the fermentation process, from the inoculum to the main fermenter, to confirm absence of microbiological contamination. The fermentation broth is examined under a phase contrast microscope to look for any foreign cells. Also, fermentation broth is put into sterile Tryptone Soy Broth (TSB) tubes and the tubes are static incubated at 35°C ± 2°C for 48 hours, after which they are examined. In the event of contamination, the facility internal laboratory isolates the contaminant and utilizes a third-party laboratory for identification. The fermentation broth is discarded if the contaminant is identified as a pathogen.

Table 5 Fermentation Sample Profile

Analysis	Inoculum			Seed Fermenter and Main Fermenter				
	Starting Mash	Every 24 Hr (or more frequently)	Before Use	Starting Mash	Every 12 Hr (or more frequently)	Every 24 Hrs	Grow out	Feed
Fatty Acid Profile			X			X	X	
Glucose	X	X	X	X	X 4-6hrs		X	X
Ammonia			X	X	X 4 hrs			
Phosphate					X 4hrs until depletion			
Wet Fatty Acid Profile					X			
Biomass (infrared)			X			X	X	
ABS(465)	X			X				
Microbiological purity	X	X	X	X		X	X	

2.4.4 Recovery Process

Unpasteurized fermentation broth is heated to 60 °C and pasteurized for a minimum of 1 hour with agitation. This step kills the microorganism. Temperature is monitored throughout pasteurization. Mixed tocopherols are added to the pasteurized fermentation broth. The amount added depends on the total amount of biomass in the fermentation broth, but it is up to 1500 ppm. At 55-65 °C, the broth is pH adjusted with caustic and a protease accepted by AAFCO for use in animal food is added to lyse the cells. 0.3% enzyme is added based on the weight of the broth. The broth is then demulsified under the combined effects of pH and heat, which also deactivates the enzyme. Specifically, the pH of the broth is adjusted with 50% caustic and sodium chloride is added. The temperature of the broth is increased to 90-94 °C for 12-48 hours. The pH of the broth is monitored online during the demulsification process; offline pH is also checked to confirm the online reading. When demulsification is complete, the pH is adjusted to 7.5-9.0 with phosphoric acid or caustic.

A centrifuge is then used to separate the oil from the water and solids present in the demulsified broth.

After 15 minutes of feeding material to the centrifuge, samples are collected. Thereafter, sampling is done each hour and the back pressures on the centrifuge are changed if necessary. The oil from centrifugation is collected in a holding tank. It is then dried with nitrogen sparge, heat (40-60 °C), and vacuum to a moisture of < 0.5%. The dried oil is then transferred to totes for storage.

2.4.6 Method to ensure stability of the production organism

DSM maintains a master cell bank (MCB) of cryovials in a liquid nitrogen storage freezer. The MCB is evaluated periodically to confirm that the production characteristics have not degraded. A working cell bank (WCB) is maintained at each production facility and is replenished from the master cell bank, as needed. WCB samples are checked for identity, viability, microbial purity, and media, by enrichment and viewing morphology (colony shape and microscopy). If all these parameters are correct, the strain is tested for production capacity in laboratory scale level fermenters. Only if the productivity and the product quality meet the required standards, is the new WCB accepted for production runs.

Each production run originates with a new WCB cryovial minimizing the chances of a strain becoming unstable and leading to poor oil quality.

2.5 Specifications

Representative samples from each production batch are subjected to evaluation by the quality control department to ensure conformance to the established specification, following the method indicated for each material characteristic. The specifications for algal oil from marine microalgae *Schizochytrium sp.* . are shown below.

Table 6 Product Specifications

Specification		Method	(b) (4)
DHA + EPA content (mg/g)	Min. 500	AOCS Ce 1b-89	
DHA content (mg/g)	Min. 250	AOCS Ce 1b-89	
EPA content (mg/g)	Min. 100	AOCS Ce 1b-89	
Free fatty acids (%)	Max. 5	AOCS Ca 5a-40	
Moisture (%)	Max. 0.75	AOAC 930.15	
Crude Fat (%)	Min. 92	AOAC 954.02	
Peroxide Value meq/Kg	Max. 0.5	AOCS Ce 1b-89	

The range of DHA concentration is from 250 to 400 mg/g and the range of EPA concentration is from 100 to 250 mg/g when the minimum EPA + DHA concentration is 500 mg/g. A range of ratios is possible as are higher levels of total omega-3 fatty acids as evident in Table 6 above.

2.6 Comparison to Algal Oil used in Human Nutrition

The oil produced by the process described above yields a product similar to the algal oil notified in human GRAS, GRN 553 in which the use of the oil rich in Omega-3 fatty acids is infant formula. The oil described for infant formula complies with the USP-NF specification for 'Schizochytrium Oil'.

Table 7 Comparison of algal oils for dog food and infant nutrition

Specification	Dogs	Infants
DHA + EPA content (mg/g)	Min. 500	Min. 500
DHA content (mg/g)	Min. 250	Min. 350
EPA content (mg/g)	Min. 100	Max. 100
Free fatty acids (%)	Max. 5	Max. 4
Moisture (%)	Max. 0.75	Max. 0.2
Crude Fat (%)	Min. 92	NA
Peroxide Value meq/Kg	Max. 0.5	Max. 0.5

2.7 Analytic Methods

As noted in the table above, all the analytical methods employed to ensure that the product meets the specifications are readily available compendial methods.

2.8 Stability

A series of stability studies were performed with the anticipated commercial product, AOCED and with prototypes of dog food produced under manufacture conditions typical of the industry and stored at 25°C and 40°C.

2.8.1 Stability of AOCED

The stability of AOCED was evaluated at four temperatures; -20°C, 5°C, 25°C and 40°C and in two packages, coated aluminum bottles and opaque, high density polyethylene (HDPE) screw cap bottles to simulate commercial packaging materials. At all conditions the AOCED was stable for 6 months, the anticipated typical commercial storage time for the oil, DHA and EPA levels remained above the minimum specification and the formation of free fatty acids was inhibited by the antioxidants. Annex 5 contains the analytical reports and the sampling protocol. Annex 6 contains the summary report for both packages at 25° C and 40°C. The table below presents the average values for the four lots used in the study.

Table 8 Stability of AOCED at 25° C and 40°C in Aluminum and HDPE Bottles

	Aluminum 25°C			HDPE 25°C			Aluminum 40°C			HDPE 40°C		
Months	EPA mg/ g oil	DHA mg/g oil	Peroxide Value meg/Kg	EPA mg/ g oil	DHA mg/g oil	Peroxide Value meq/Kg	EPA mg/ g oil	DHA mg/g oil	Peroxide Value meq/Kg	EPA mg/ g oil	DHA mg/g oil	Peroxide Value meq/Kg
0	122	430	0.3	123.25	430.5	0.4	123.25	430.5	0.4	123.25	430.5	0.4
1	122.25	430.75	0.525	120.75	420.75	0.975	123.25	431.75	0.4	119.25	416.5	1.65
2	120.75	425.75	0.675	121.25	425	1.6	122.5	426.75	0.2	122.25	425.25	2.55
3			1.067			2.1			< 0.1			2.825
4	121	430	2.55	122	430.25	2.975	122.5	431.5	< 0.1	121.25	425.75	2.7
5			2.35			3.6			< 0.1			2.5
6	121.25	428.75	2.75	122	427	5.025	122.5	429	< 0.1	121.25	424	2.475
9	121	431	6	121.5	422.5	5.725						
12	123.5	430.5	6.7	124	427.75	6.05						

A peroxide value >5 is considered to be an indication the oil is starting to turn rancid. (Ismail et al., 2016), and a value ≥10 is considered to indicate full rancidity (NSF/ANSI Standard 173 – 2013)

2.8.2 Stability of Algal Oil in Canned Dog Food

To measure the storage stability of AOCED in canned dog food, the food was formulated to be representative of typical commercial formulae (see Table 7) and to meet the requirements for adult maintenance. The ingredients and metal cans used in this study are in current commercial use by pet food companies.

The wet dog food was produced at (b) (4) After grinding the chicken liver (b) (4) the ingredients were mixed with the algal oil and heated in a Groen steam jacketed kettle to reach 170° F. The mixture was filled in 13 oz metal cans and sealed before being retorted (SSA Surdry Stock America Sterilization Systems) at 250° F for about 75 minutes to reach sterilization ($F_o \geq 8$). Samples were taken after retort and stored at either 25° C and 60% relative humidity (RH) or 40° C and 75% RH for 12 months. After the initial timepoint, one can from each lot was analyzed every three months for DHA and EPA (AOAC 996.06), moisture (AOAC 925.09), and peroxide value (AOCS Cd 8-53). DHA and EPA concentrations in the samples were corrected for moisture and reported on a dry matter basis. Sample analysis was conducted at (b) (4)

Table 9 Ingredients Used in Canned Dog Food

Ingredients	%
Chicken, M. Deboned	63.471
Water	22.381
Meat By-Product (pork)	10.000
Chicken Liver	2.000
Brewer's Rice	1.000
AOCED	0.410
Vitamin and Mineral Premix	0.150
Guar Gum	0.148
Carrageenan	0.148
Potassium Chloride	0.125
Natural Flavors	0.100
Salt	0.037
Choline Chloride	0.029
Total	**100.00**

[1] Three lots of AOCED were used in the stability study. The lot numbers are (b) (4), and (b) (4).

Table 10 Nutritional Analysis of Canned Dog Food

Nutrients (calculated)	AS Fed	DM	AAFCO Dog Food Nutrient Profile for Adult Maintenance[1]
Moisture, %	75.97	24.03	N/A
Crude protein, %	11.4	47.44	18.0
Arginine, %	0.5884	2.45	0.51
Histidine, %	0.278	1.16	0.19
Isoleucine, %	0.471	1.96	0.38
Leucine, %	0.6849	2.85	0.68
Lysine, %	0.7648	3.18	0.63
Methionine, %	0.2513	1.05	0.33
Methionine-cystine, %	0.3745	1.56	0.65
Phenylalanine, %	0.3637	1.51	0.45
Phenylalanine-tyrosine, %	0.6684	2.78	0.74
Threonine, %	0.3903	1.62	0.48
Tryptophan, %	0.1073	0.45	0.16
Valine, %	0.4545	1.89	0.49
Crude fat, %	8.97	37.33	5.5
Linoleic acid, %	0.9174	3.82	1.1
Alpha-Linolenic acid, %	0.374	1.56	ND
Arachidonic acid, %	0.0938	0.39	N/A
EPA+DHA, %	0.2152	0.90	ND
LA+AA:ALA+EPA+DHA	1:0.6	1:0.6	Max 30:1
Calcium, %	0.221	0.92	0.5-2.5
Phosphorus, %	0.1712	0.71	0.4-1.6
Ca:P ratio	1.3	1.3	1:1 – 2:1
Potassium, %	0.19	0.79	0.6
Sodium, %	0.09	0.37	0.08
Chloride, %	0.084	0.35	0.12
Magnesium, %	0.0222	0.09	0.06
Iron, mg/kg	39.24	163.30	40
Copper, mg/kg	4.68	19.48	7.3
Manganese, mg/kg	2.37	9.86	5.0
Zinc, mg/kg	40.34	167.87	80
Iodine, mg/kg	0.9938	4.14	1.0-11
Selenium, mg/kg	0.0945	0.39	0.35-2
Vitamin A, IU/kg	8067.44	33572.37	5000-250000
Vitamin D, IU/kg	259.54	1080.07	500-3000
Vitamin E, IU/kg	35.95	149.60	50
Thiamine, mg/kg	3.5	14.57	2.25

Nutrients (calculated)	AS Fed	DM	AAFCO Dog Food Nutrient Profile for Adult Maintenance[1]
Riboflavin, mg.kg	2.86	11.90	5.2
Pantothenic acid, mg/kg	5.48	22.80	12
Niacin, mg/kg	29.13	121.22	13.6
Pyridoxine, mg/kg	2.49	10.36	1.5
Folic acid, mg/kg	0.2627	1.09	0.216
Vitamin B12, mg/kg	0.0119	0.05	0.028
Choline, mg/kg	450	1872.66	1360

[1] Based on Dry matter and Minimum unless otherwise stated

DHA and EPA concentration and their retentions as well as peroxide value of three lots of AOCED in the wet dog food are shown in Table 8 (25° C, 60% RH) and Table 9 (40° C and 75% RH). Overall, DHA and EPA were stable in the wet food at both conditions for 12 months. This study will continue for a total of 36 months.

Table 11 Stability of AOCED in Canned Dog Food (25° C, 60% RH)

			Time points, month				
Lots	Measures		Initial*	3	6	9	12
(b) (4)	EPA	Concentration, %	0.21	0.21	0.21	0.22	0.20
		Retention#, %		100	100	101	93
	DHA	Concentration, %	0.71	0.73	0.69	0.69	0.67
		Retention#, %		103	97	97	95
	PV	meq/kg fat	<2.0	<2.0	<2.0	<2.0	<2.0
(b) (4)	EPA	Concentration, %	0.21	0.21	0.21	0.21	0.21
		Retention#, %		99	99	100	101
	DHA	Concentration, %	0.67	0.70	0.70	0.66	0.67
		Retention#, %		104	104	99	100
	PV	meq/kg fat	<2.0	<2.0	<2.0	<2.0	<2.0
(b) (4)	EPA	Concentration, %	0.21	0.21	0.21	0.20	0.20
		Retention#, %		100	100	99	99
	DHA	Concentration, %	0.63	0.66	0.66	0.57	0.7
		Retention#, %		104	104	90	110
	PV	meq/kg fat	<2.0	<2.0	<2.0	<2.0	<2.0

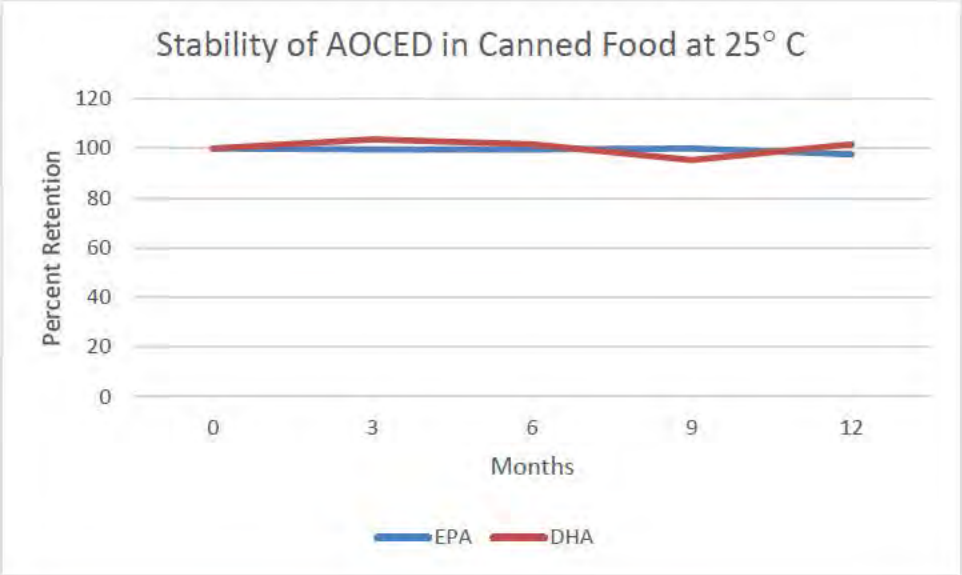


Figure 4 **Stability of ACED in canned dog food at 25° C**

Table 12 **Stability of AOCED in Canned Dog Food (40° C and 75% RH)**

			Time points, month				
Lots	Measures		Initial*	3	6	9	12
(b) (4)	EPA	Concentration, %	0.21	0.21	0.17	0.21	0.22
		Retention#, %		100	80	98	101
	DHA	Concentration, %	0.71	0.73	0.64	0.72	0.73
		Retention#, %		103	90	101	103
	PV	meq/kg fat	<2.0	<2.0	<2.0	<2.0	<2.0
(b) (4)	EPA	Concentration, %	0.21	0.21	0.21	0.21	0.21
		Retention#, %		101	100	99	99
	DHA	Concentration, %	0.67	0.63	0.67	0.62	0.70
		Retention#, %		94	100	92	105
	PV	meq/kg fat	<2.0	<2.0	<2.0	<2.0	<2.0
(b) (4)	EPA	Concentration, %	0.21	0.20	0.16	0.21	0.21
		Retention#, %		98	79	100	99
	DHA	Concentration, %	0.63	0.65	0.57	0.62	0.66
		Retention#, %		103	90	98	104
	PV	meq/kg fat	<2.0	<2.0	<2.0	<2.0	<2.0

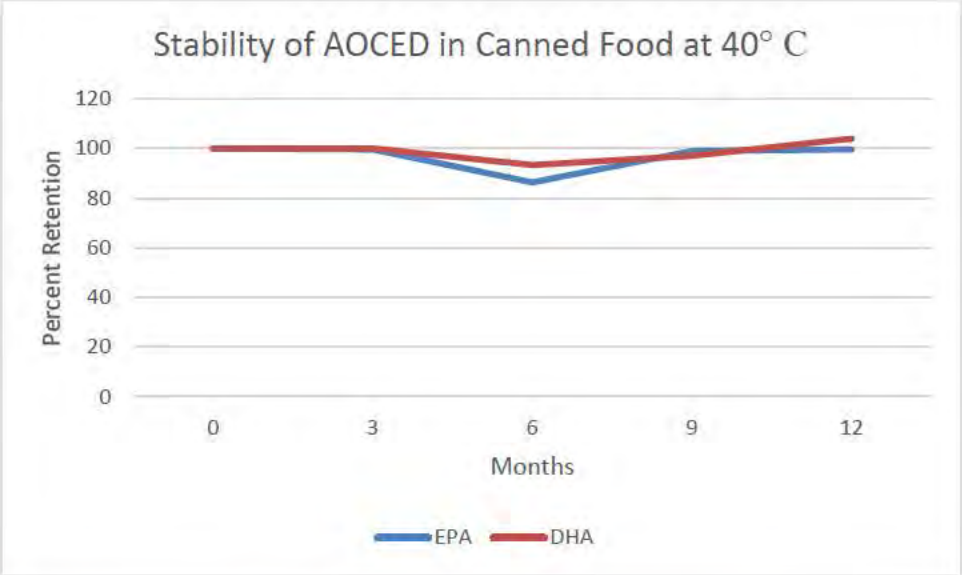


Figure 5 **Stability of AOCED in canned dog food at 40° C**

The results indicate that in a model matrix of canned dog food AOCED is stable for at least 12 months. Actual stability in commercial formulations will need to be confirmed by the pet food manufacturers using their food formulations and processing conditions. The dip in the DHA concentration at 40°C and 6 months was probably due to an error in sampling or analysis as the 12 month samples showed a more probable value.

2.8.3 Storage Stability of AOCED in Dry Dog Food

In order to measure the stability of AOCED in dry dog food, extruded kibble, over time, two different applications were studied: addition of AOCED pre-extrusion and addition of AOCED post-extrusion. Three lots of AOCED were used. The lot numbers were: (b) (4), and (b) (4) Each lot was applied at 1.45%. The dry dog food was formulated to be representative of commercial dry dog food (see Table 12 for composition) and produced at the (b) (4)

Table 13 **Ingredient Composition of Kibble used in Shelf Life Study**

Ingredient Name	%
Chicken By Product Meal	23.21
Whole Corn	22.71
Dried Eggs	13.28
Brewers Rice	10.91
Chicken Fat	9.23
Whole Milo	4.73
AFB Bioflavor B20002	2.84
Corn Gluten Meal 60%	1.75

Ingredient Name	%
Beet Pulp	1.65
Algal Oil	1.45
Dicalcium Phosphate	1.42
Potassium chloride	0.71
Vitamin Premix	0.29
Calcium carbonate	0.19
Verdilox GT Dry	0.10
Trace Mineral	0.10
Choline Chloride	0.08

In the pre-extrusion application, AOCED was injected into the preconditioner of a Wenger X20 extruder during the dry kibble production. The major extrusion parameters were: feed rate, 172 kg/hour; preconditioner discharge temperature, 98° C; die temperature, 176° C; and cone head pressure, 185 psig. The extruded kibbles which already contained algal oil were dried in a Wenger dryer at 127° C for 23 minutes and cooled for 7 minutes before coating with chicken fat and flavors. In the post-extrusion application, AOCED was mixed with the chicken fat before coating the dry kibbles previously extruded without AOCED.

Samples for the storage stability tests were obtained from the finished dry dog food after both applications, put into metalized 5 mil KPET/VMPET/PE zip bags (Uline S-20713GLD, Uline) that were heat sealed, and stored at either 25 °C and 60% RH or 40 °C and 75% RH for 24 months. After the initial analysis, a bag from each batch was analyzed every three months for DHA and EPA (AOAC 996.06), moisture (AOAC 925.09), and peroxide value (AOCS Cd 8-53). DHA and EPA concentrations were corrected for moisture and reported on a dry matter basis. The sample analysis was conducted at (b) (4)

The statistical analysis report and analytical data for the stability of AOCED in extruded dog food post extrusion application can be found in Annex 7.

Table 14 **Stability of DHA and EPA in dry dog food @25 °C – Post-extrusion application**

			Time points, month						
Lots	Measures		Initial	3	6	9	12	18	24
(b) (4)	EPA	Concentration, %	0.18	0.16	0.16	0.17	0.16	0.16	0.17
		Retention, %		91	91	98	91	91	97
	DHA	Concentration, %	0.68	0.61	0.62	0.63	0.63	0.61	0.63
		Retention, %		90	91	93	92	89	93
(b) (4)	EPA	Concentration, %	0.19	0.18	0.18	0.17	0.17	0.17	0.17
		Retention, %		100	99	94	93	93	94
	DHA	Concentration, %	0.65	0.64	0.64	0.61	0.62	0.59	0.59
		Retention, %		99	98	94	95	92	90
(b) (4)	EPA	Concentration, %	0.18	0.17	0.17	0.17	0.17	0.17	0.17
		Retention, %		95	95	96	95	95	95
	DHA	Concentration, %	0.62	0.57	0.57	0.58	0.59	0.58	0.58
		Retention, %		92	92	94	96	94	94

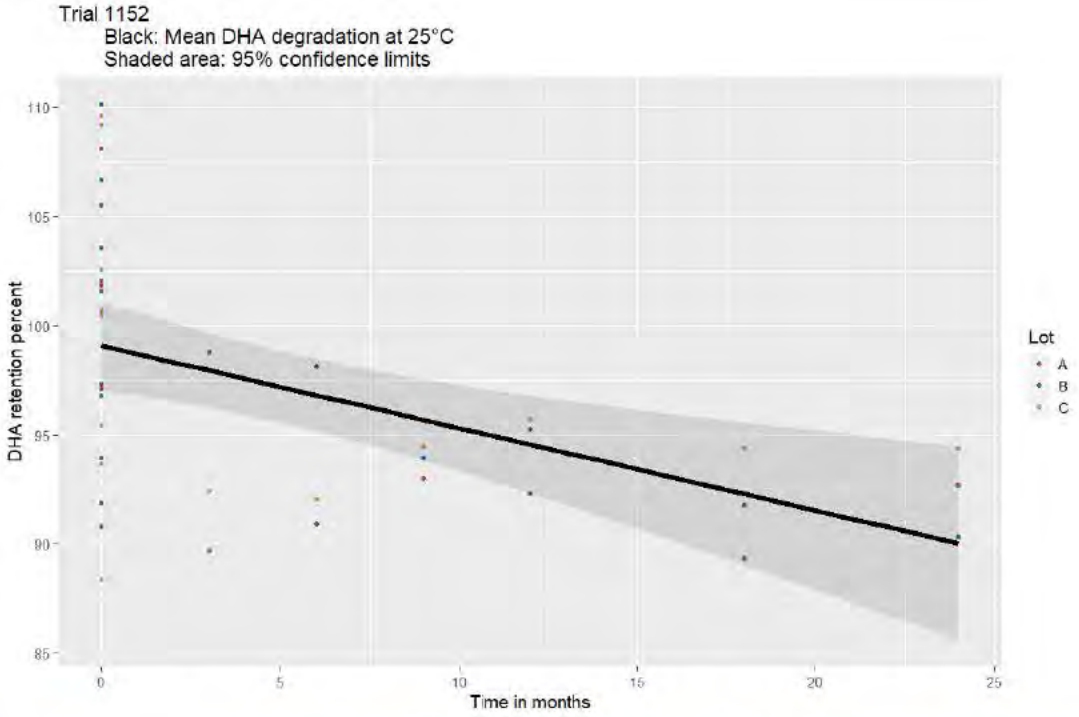


Figure 6 **Stability of DHA in Extruded Dog Food @ 25°C, Post Extrusion Application**

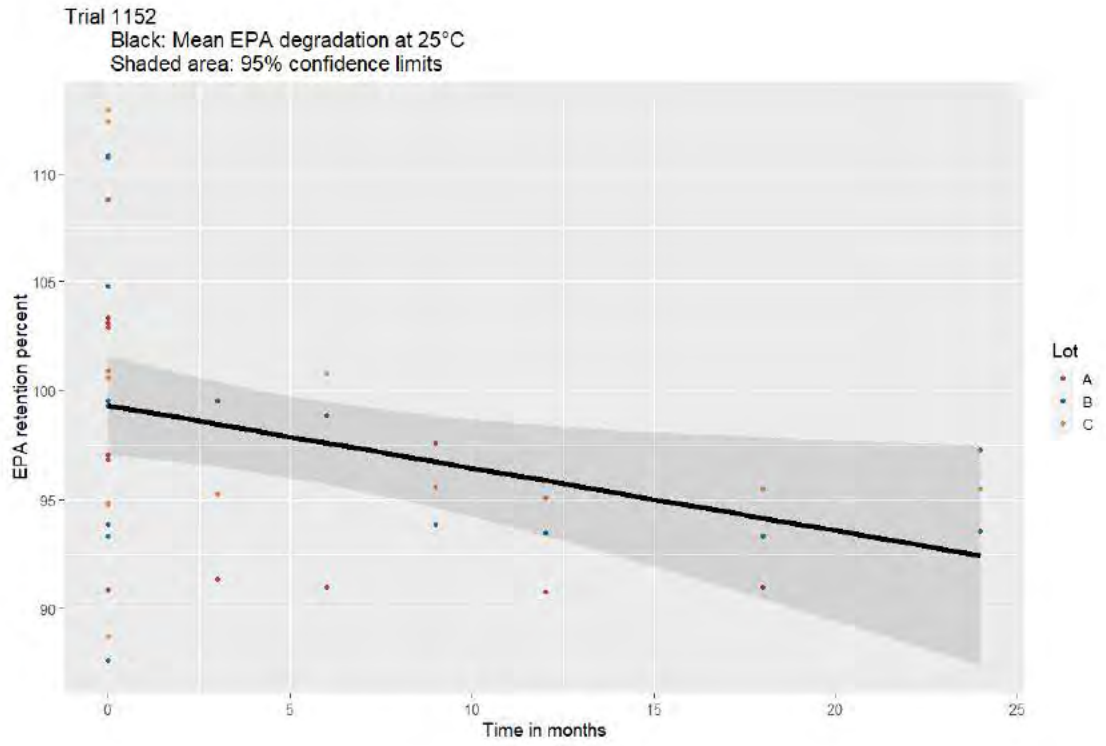


Figure 7 **Stability of EPA in Extruded Dog Food @ 25°C, Post Extrusion Application**

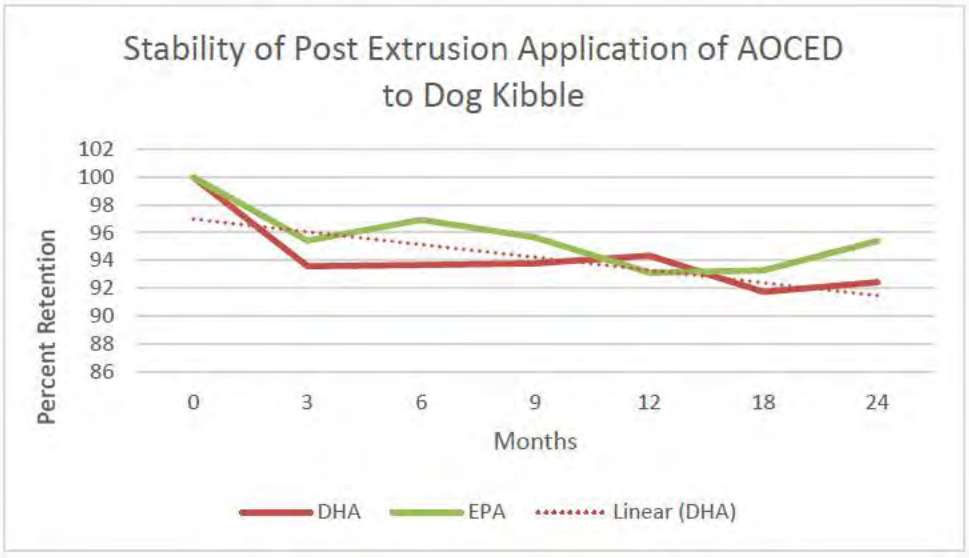


Figure 8 **Stability of EPA and DHA @25 C, Post Extrusion using simple averages**

Table 15 **Stability of DHA and EPA in dry dog food @ 40 °C – Post-extrusion application**

			Time points, month						
Lots	Measures		Initial	3	6	9	12	18	24
(b) (4)	EPA	Concentration, %	0.18	0.16	0.16	0.17	0.17	0.15	0.12
		Retention, %		92	91	93	92	87	68
	DHA	Concentration, %	0.68	0.62	0.62	0.63	0.62	0.58	0.46
		Retention, %		92	91	93	91	86	68
(b) (4)	EPA	Concentration, %	0.19	0.17	0.17	0.18	0.15	0.16	0.14
		Retention, %		94	94	95	83	84	78
	DHA	Concentration, %	0.95	0.62	0.61	0.62	0.53	0.54	0.46
		Retention, %		96	94	95	81	84	72
(b) (4)	EPA	Concentration, %	0.18	0.17	0.17	0.18	0.17	0.15	0.16
		Retention, %		96	96	97	97	85	86
	DHA	Concentration, %	0.62	0.59	0.61	0.58	0.59	0.54	0.50
		Retention, %		95	98	94	96	87	81

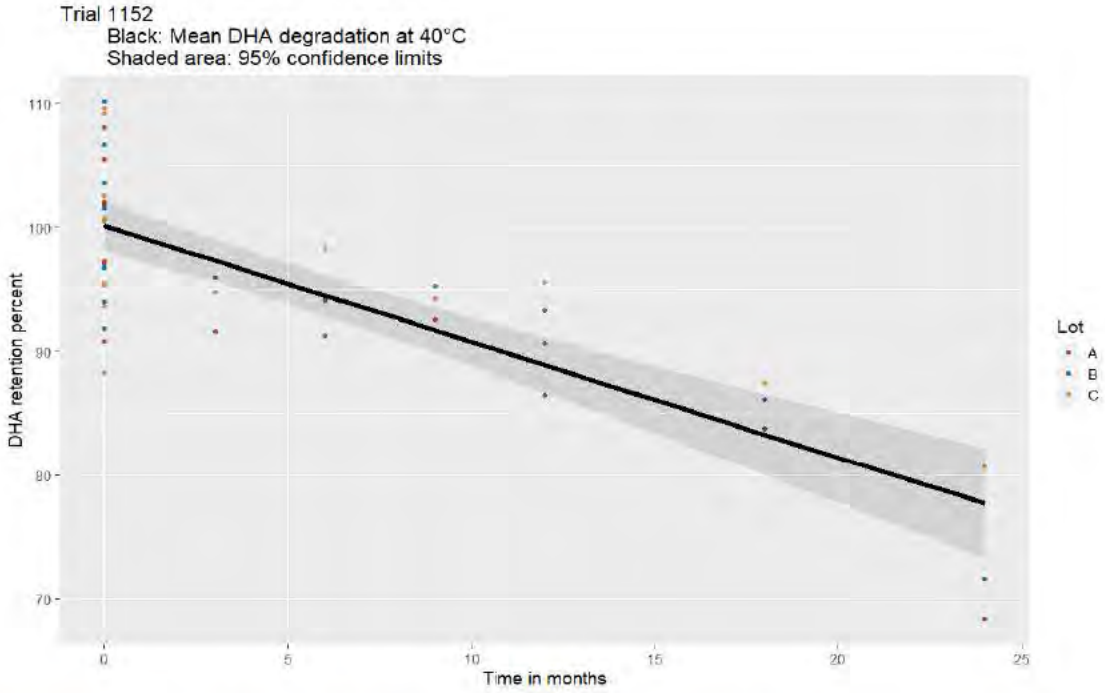


Figure 9 **Stability of DHA in Extruded Dog Food @ 40°C, Post Extrusion Application**

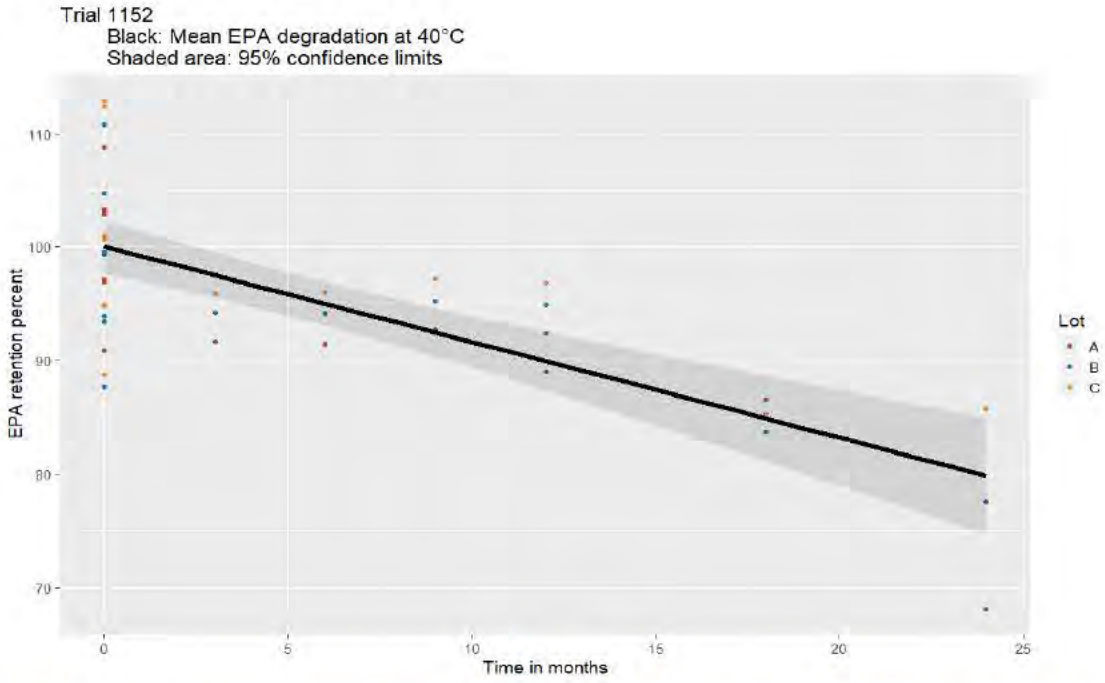


Figure 10 **Stability of EPA in Extruded Dog Food @ 40°C, Post Extrusion Application**

Pre-extrusion application

The statistical analysis report and analytical data for the stability of AOCED in extruded dog food pre-extrusion application can be found in Annex 8.

Table 16 **Stability of DHA and EPA in dry dog food @25°C – Pre-extrusion application**

			Time points, month						
Lots	Measures		Initial	3	6	9	12	18	24
(b) (4)	EPA	Concentration, %	0.179	0.163	0.162	0.174	0.162	0.162	0.173
		Retention, %		91.1	90.5	97.2	90.5	90.5	96.6
	DHA	Concentration, %	0.679	0.609	0.617	0.631	0.627	0.606	0.629
		Retention, %		89.7	90.9	92.9	92.3	89.2	92.6
(b) (4)	EPA	Concentration, %	0.185	0.184	0.183	0.174	0.173	0.173	0.173
		Retention, %		99.5	98.9	94.1	93.5	93.5	93.5
	DHA	Concentration, %	0.648	0.64	0.635	0.609	0.617	0.595	0.585
		Retention, %		98.8	98.0	94.0	95.2	91.8	90.3
(b) (4)	EPA	Concentration, %	0.181	0.172	0.182	0.173	0.172	0.173	0.173
		Retention, %		95.0	100.6	95.6	95.0	95.6	95.6
	DHA	Concentration, %	0.617	0.57	0.568	0.583	0.59	0.582	0.582
		Retention, %		84.9	84.6	86.9	87.9	86.7	86.7

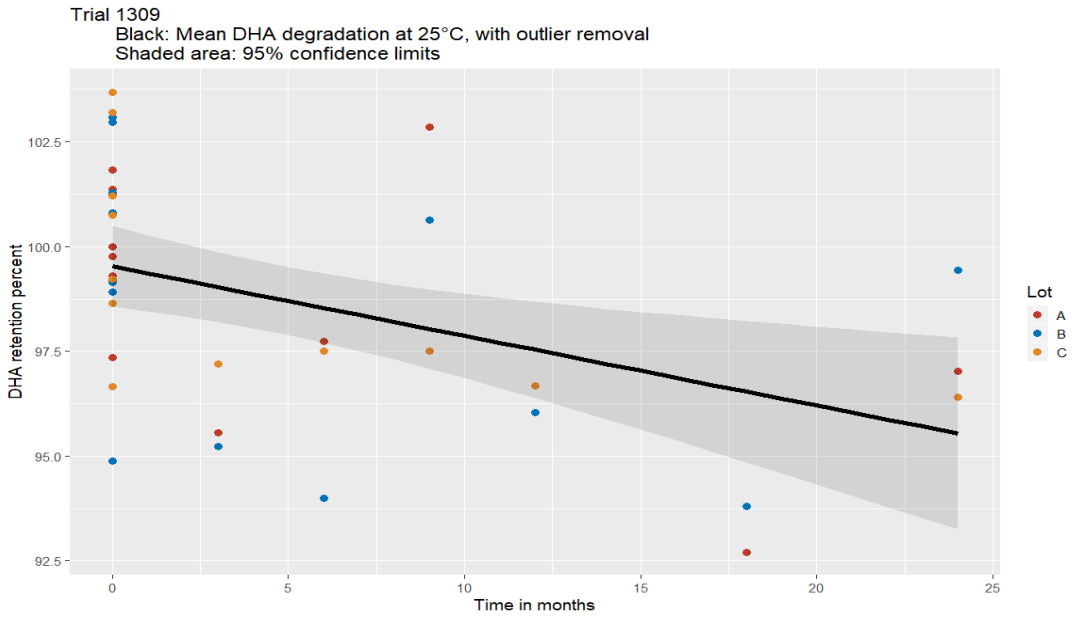


Figure 11 Stability of DHA in Extruded Dog Food @ 25°C, Pre-Extrusion Application

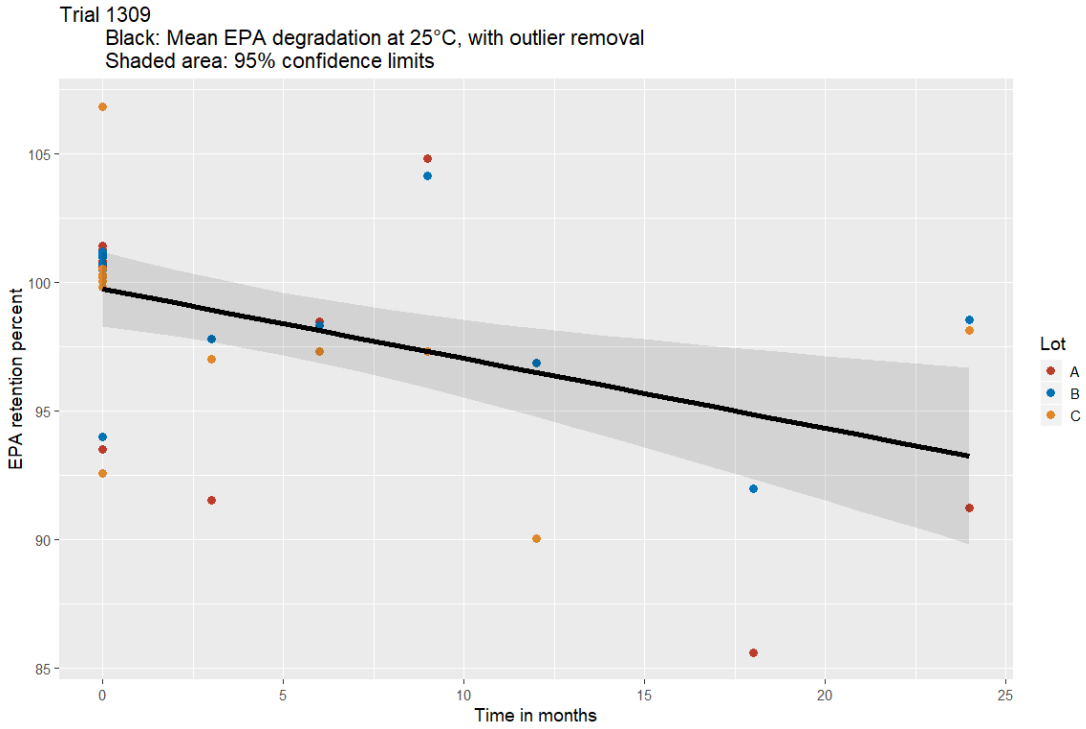


Figure 12 Stability of EPA in Extruded Dog Food @ 25°C, Pre-Extrusion Application

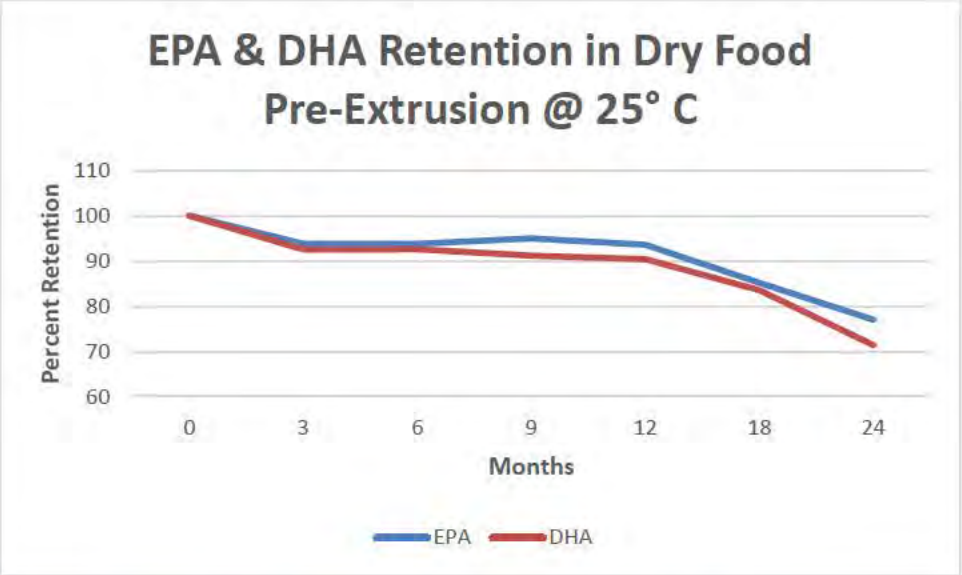


Figure 13 Stability of EPA & DHA Pre-Extrusion @ 25 C, simple averages

Table 17 Stability of DHA and EPA in dry dog food @40°C – Pre-extrusion application

			Time points, month						
Lots	Measures		Initial	3	6	9	12	18	24
(b) (4)	EPA	Concentration, %	0.179	0.164	0.163	0.166	0.165	0.155	0.121
		Retention, %		91.6	91.1	92.7	92.2	86.6	67.6
	DHA	Concentration, %	0.679	0.622	0.62	0.629	0.616	0.585	0.464
		Retention, %		91.6	91.3	92.6	90.7	86.2	68.3
(b) (4)	EPA	Concentration, %	0.185	0.174	0.174	0.176	0.17	0.155	0.144
		Retention, %		94.1	94.1	95.1	91.9	83.8	77.8
	DHA	Concentration, %	0.648	0.64	0.622	0.61	0.6	0.543	0.464
		Retention, %		98.8	96.0	94.1	92.6	83.8	71.6
(b) (4)	EPA	Concentration, %	0.181	0.173	0.174	0.176	0.175	0.154	0.155
		Retention, %		95.6	96.1	97.2	96.7	85.1	85.6
	DHA	Concentration, %	0.617	0.585	0.607	0.582	0.59	0.54	0.498
		Retention, %		87.2	90.5	86.7	87.9	80.5	74.2

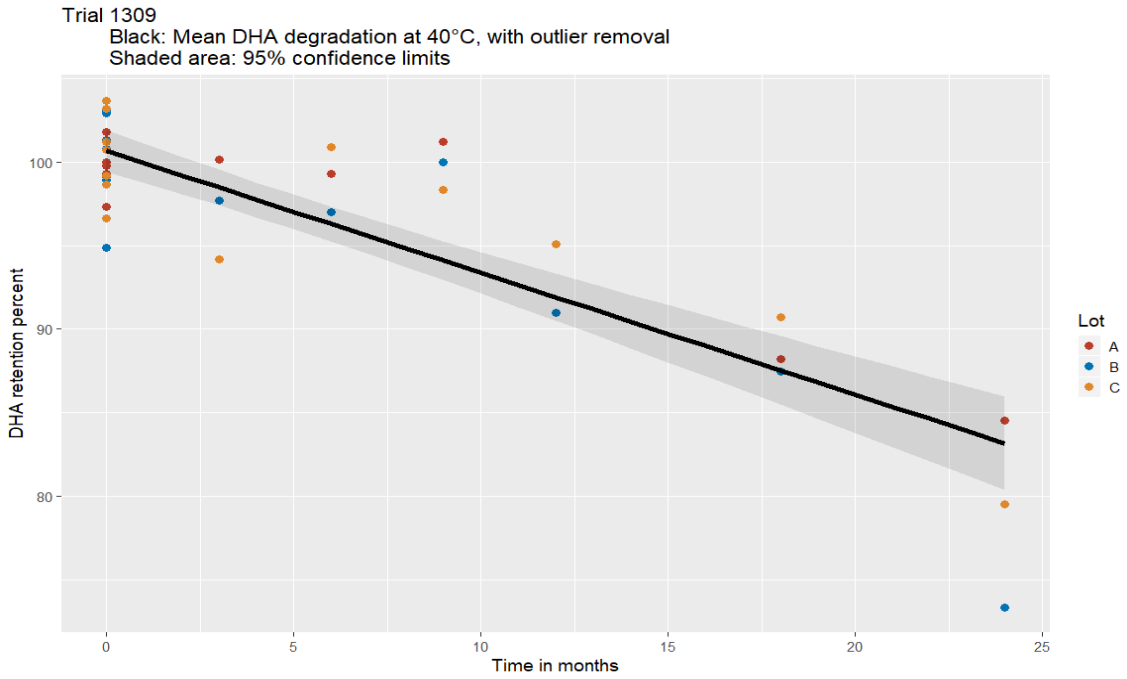


Figure 14 **Stability of DHA in Extruded Dog Food @ 40°C, Pre-Extrusion Application**

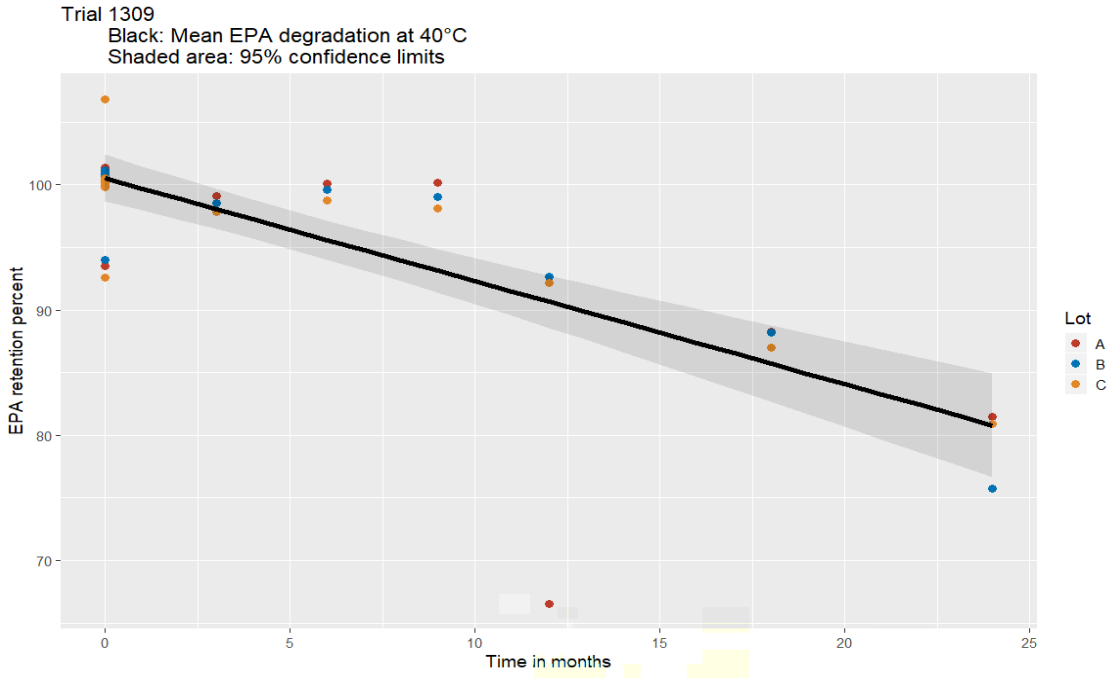


Figure 15 **Stability of EPA in Extruded Dog Food @ 40°C, Pre-Extrusion Application**

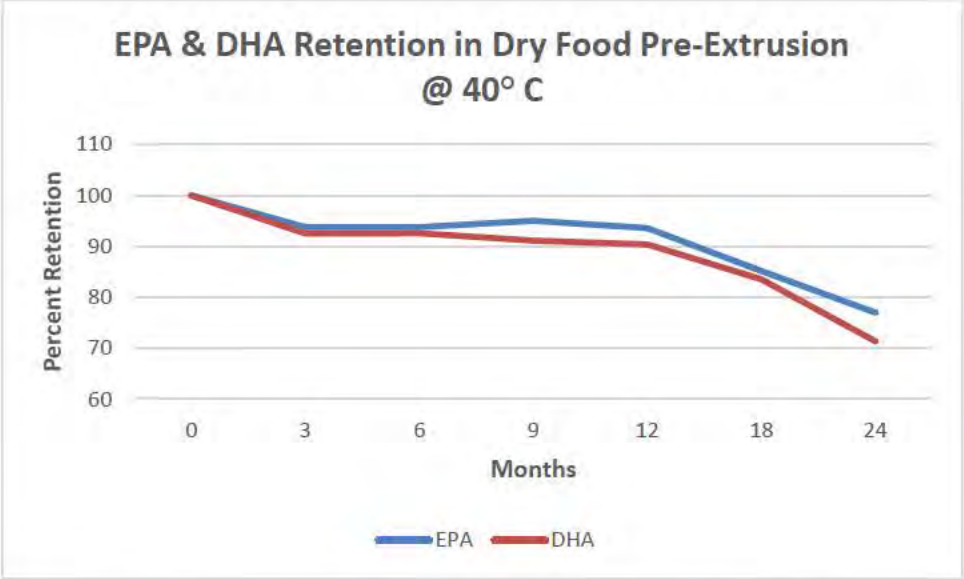


Figure 16 Stability of EPA & DHA in Extruded Dog Food @ 40° C, Simple Averages

2.8.4 Homogeneity

In order to measure the ability of AOCED to be homogenously added to dry dog food, two different applications were studied: addition of AOCED pre-extrusion and addition of AOCED post-extrusion. Three lots of AOCED were used. The lot numbers are: (b) (4), and (b) (4). Each lot was present in the dry dog food formula at 1.45%. The dry dog food was produced at the (b) (4)

In the post-extrusion application, AOCED was mixed with the chicken fat before coating the dry kibbles previously extruded without AOCED. In both applications, finished dry dog food of each coating batch (200 lbs.) was packaged in 8 bags with equal amount and a sample was taken from each bag. Samples were analyzed for DHA and EPA (AOAC 996.06), as well as moisture (AOAC 925.09). DHA and EPA concentrations in the samples were corrected for moisture and reported on a dry matter basis. The coefficient of variation (CV) was calculated for DHA and EPA of 8 samples. Sample analysis was conducted at (b) (4)

DHA and EPA concentrations and the CV for three lots of AOCED in the dry dog food are shown in Table 15 (post-extrusion) and Table 16 (pre-extrusion). Overall, DHA and EPA were distributed well in the dry dog food and indicated by the low CV of 8 samples.

Table 18 Homogeneity of DHA and EPA in dry dog food – Post-extrusion application

Lots	(b) (4)					
Fatty acids	EPA, %	DHA, %	EPA, %	DHA, %	EPA, %	DHA, %
Sample 1	(b) (4)					
Sample 2						
Sample 3						
Sample 4						
Sample 5						
Sample 6						
Sample 7						
Sample 8						
Mean	0.18	0.68	0.19	0.65	0.18	0.62
SD	0.010	0.037	0.016	0.042	0.016	0.046
CV, %	5.6	5.5	8.4	6.5	8.7	7.4

Table 19 Homogeneity of DHA and EPA in dry dog food – Pre-extrusion application

Lots	(b) (4)					
Fatty acids	EPA, %	DHA, %	EPA, %	DHA, %	EPA, %	DHA, %
Sample 1	(b) (4)					
Sample 2						
Sample 3						
Sample 4						
Sample 5						
Sample 6						
Sample 7						
Sample 8						
Mean	0.16	0.60	0.17	0.62	0.16	0.55
SD	0.004	0.009	0.004	0.016	0.006	0.015
CV, %	2.6	1.5	2.4	2.7	3.8	2.7

Part 3: Dietary Exposure

3.1 Dietary Exposure to the notified substance

Algal oil from marine microalgae *Schizochytrium sp.* (AOCED) is intended to be a replacement for or alternative to fish oil. It is not intended to be added to diets of dogs in excess of current levels of fish oil. Therefore, an increase in the current exposure to omega-3 fatty acids is not expected.

3.1.1 Target Animal

AOCED is meant for consumption by dogs via the intentional addition to dog food to replace fish oil. Using the target animal study as an example of exposure, the mid-dose, the highest anticipated commercial use level resulted in an exposure of between 638.6 and 248.6 mg/Kg BW/day as illustrated in the table below.

Table 20 Achieved AOCED intake.

Dietary group	Dams Gestation (GD 0-62)	Dams Lactation (PPD 0-55)	Puppies Combined Post-weaning Weeks 1-2	Puppies Males Post-weaning Weeks 3-26	Puppies Females Post-weaning Weeks 3-26
Low dose AOCED	138.3	319.4	314.0	231.7	236.6
Mid dose AOCED	248.6	638.6	568.5	435.5	440.2
High dose AOCED	474.9	1243.9	1310.0	959.5	975.8

Values represent average daily AOCED intake over a period (mg/kg body weight/day).

3.2 Dietary Exposure to any other substance that is expected to be formed in or on food

AOCED is a mixture of fatty acids high in omega-3 fatty acids and like any material with unsaturated fat it is prone to oxidation through thermal abuse and/or exposure to light or oxygen. The typical degradation products from the oxidation of fatty acids are short chain ketones and aldehydes. The stability study performed with the AOCED product in dry and canned dog food indicate that the formation of the degradation products is minimal as represented by the peroxide values.

3.3 Dietary Exposure to any other substance that is present with the notified substance either naturally or due to its manufacture (e.g., contaminants or by-products)

Four lots of AOCED were tested for the presence of heavy metals as noted in the table below. The report from the Third-party lab is in Annex 9.

Table 21 Heavy Metals

	Test Method	[redacted] (b) (4)			
Arsenic (ppm)	AOAC 2013.06	< 0.02	< 0.02	0.03	< 0.02
Cadmium (ppm)	AOAC 2013.06	< 0.01	< 0.01	< 0.01	< 0.01
Lead (ppm)	AOCS Ca 17-01	< 0.05	< 0.05	< 0.05	< 0.05
Mercury (ppm)	AOAC 2013.06	< 0.010	< 0.05	< 0.010	< 0.010

The measured concentrations were below the maximum permissible level of heavy metals allowed in feed in Canada. (CFIA)

The same four lots of oil were tested for the presence of and extensive group of pesticides, including organochlorine, pyrethroid, and organophosphorus. No concentrations of concern were in the four lots of AOCED. See Annex 10.

Part 4: Self-limiting levels of use

It is expected that, as with other sources of omega-3 fatty acids, such as fish oil, that the use levels of AOCED from marine microalgae *Schizochytrium sp.* are self-limiting due to palatability and possible difficulties in kibble production.

Part 5 Common use in food prior to 1958

Veramaris is unaware of any documented use of the AOCED or other algal oils being used in any animal food application before 1958. Production of AOCED for use as a source of DHA and EPA did not commence on an industrial scale until the 1990's with the introduction of an AOCED for use in aquaculture by the Omega Tech company. A parent of the production strain was derived from the Omega Tech culture bank.

Part 6 Narrative of the basis for the GRAS conclusion

6.1 Long chain Polyunsaturated Fatty Acid Metabolism in Dogs

The ability of dogs to metabolize α-linolenic acid (ALA, 18:3n-3) to its longer chain derivatives including EPA, docosapentaenoic acid (DPA, 22:5n-3), and DHA appears to be limited and similar to that found in most mammalian species (Dunbar et al, 2010). Conversion of ALA involves a sequence of steps involving a system of desaturase and elongase enzymes in common with the metabolism of the arachidonic acid (ARA, 20:4 n-6) precursor, linoleic acid (LA, 18:2n-6). Thus, the tissue presence of LA can inhibit the desaturation of ALA to 18:4n-3 while that of ALA can inhibit LA desaturation (Brenner and Peluffo, 1966). As a result, dramatic differences in the accumulation of n-6 and n-3 Longchain poluyunsaturated fatty acids (LCPUFA) in brain and other tissues has been observed in several species including dogs when varying amounts of these fatty acids are fed (Dunbar et al, 2010; reviewed in Brenna et al, 2009) and are detailed below.

Regarding the conversion of ALA to longer chain n-3 derivatives in dogs, Km and Vmax, kinetic constants of Δ-6 desaturase in canine liver using both ALA and LA as substrates in the presence of one another have been estimated and provide additional insight into this competition (Dunbar and Bauer, 2002). Both Km and Vmax for ALA is higher than for LA 12.4 umol/L vs 5.4 umol/L and 62.4 pmol/mg-min vs 41.8 pmol/mg-min, respectively. These findings suggest that high tissue amounts of ALA are necessary to exceed the Δ6-desaturase Km for this substrate compared to LA.

Furthermore, saturable equations originally developed using rodent and human diet trials by Lands et al (1992) have been modified for dogs based on feeding studies. Specific for dog plasma, total phospholipids, fatty acid fractions and neutrophils, these equations provide estimates of the relationship between increasing dietary ALA at constant dietary LA (in energy %) and resultant enrichment of n-3 LCPUFA in these canine tissues (Bauer et al, 2002). Brenna et al (2009) used the human equation to calculate an equivalency factor of 15-1 with respect to differences between dietary DHA compared to ALA on resultant n-3 LCPUFA of plasma PL. Using the canine equation, a factor of approximately 12-1 was obtained indicating similar limited conversion of dietary ALA in this species compared to providing preformed long chain derivatives (Bauer, personal communication). It should be noted that the above equations consider only EPA and DPA n-3, and that DHA accumulation is not typically accounted for. Taken together, however, these findings help demonstrate, in part, the limited conversion of ALA to n-3 LCPUFA in dogs (and humans), especially in the presence of LA.

The extent to which DHA accumulates using ALA supplements in dogs has been studied in feeding experiments to some degree. In adult dogs, a diet containing approximately 25% of total energy as fat with 2.5% energy ALA in the absence of n-3 LCPUFA and at tissue saturating concentrations of LA (7.3% energy LA) was conducted. This diet resulted in early and significant increases in serum PL and

triglyceride (TG) ALA, EPA, and DPA n-3 but not DHA. Also, it was noteworthy that only EPA enrichment but not DHA was seen in the serum cholesterol ester (CE) fractions (Dunbar et al, 2010). Another study investigated a 40.8% total fat energy diet containing 4.1% energy as ALA from flaxseed oil for 28 days and found similar results in both plasma PL and neutrophils as compared with a beef tallow diet (0.017% energy ALA) (Waldron et al. 2012). Similar enrichments of only EPA and DPA n-3 have been observed in human plasma using a 4 week feeding period (Marangoni et al, 2007). These alterations have been repeatedly observed in humans and various other animal species (reviewed in Brenna et al, 2009; Dunbar et al, 2010) and are consistent with other evidence that plasma enrichment of DHA after ALA supplementation is less effective compared to providing smaller dietary amounts of preformed DHA per se (Brenna et al 2009, Heinemann et al, 2005). By contrast, studies in rats have shown more efficient conversion of ALA to DHA in liver and enrichment in plasma (Rapoport et al, 2007). Given that there is resistance for serum DHA levels to increase in dogs fed high dietary ALA, the canine is thus more similar to humans in this respect compared to rats (Brenna et al 2009).

The accumulation of DPA n-3 seen in both fasting PL and TG fractions when ALA enriched diets are fed is consistent with secretion after tissue synthesis from dietary ALA (Dunbar et al, 2010). Conversion of DPA n-3 to DHA has been reported in canine neural tissues (Alvarez et al, 1994) and thus it is likely that DHA synthesis occurs after uptake of fatty acid precursors by neural, but possibly not other tissues, from the circulation. These findings along with those of Pawlosky et al.(1994) with felines suggest that production of DPA n-3 from ALA may serve as an important circulating reservoir for tissue DHA synthesis with transport of DPA n-3 via plasma lipids to neural tissues. Although dietary ALA results in EPA and DPA n-3 enrichment of plasma PL and TG fractions, it is of interest that neither DPA n-3 nor DHA was observed in the serum CE fraction in the study of Dunbar et al (2010). It should also be noted that, when fish oil was fed to dogs, DPA n-3 was again absent in the CE fraction even though some small amounts of DHA were seen, especially compared with PL and TG fractions (Bauer et al, 1997). Previous studies investigating lecithin:cholesterol acyl transferase (LCAT) in various species have also reported CE-DPA n-3 to be absent in canines (Subbaiah et al, 1996; Liu et al, 1995). Taken together, these findings indicate that DPA n-3, and perhaps 22 carbon fatty acids in general, may not be preferred substrates for cholesterol esterification via reverse cholesterol transport as mediated by the LCAT enzyme. Also because no appreciable accumulation of DHA occurred in the CE fraction with flaxseed feeding, DHA is apparently seen only in the presence of a sufficient preformed dietary source. Given that DHA in human plasma CE is present in low concentrations as well, the importance of this finding for both dogs and humans is that CE-DHA may serve as a potential biomarker of dietary DHA sufficiency and should be investigated further. In view of these findings, provision of preformed DHA is preferred in order to assure a suitable supply of this fatty acid for those tissues requiring it.

6.2 History of the Use of Algal Products in Animal Food

Dried marine microalgae *Schizochytrium* sp. is used as an animal feed ingredient for several species around the world. That material is approximately 50% oil. The material that is the subject of this GRAS is the oil produced by the same genus and species of algae.

Since 1995, a spray-dried form of *Schizochytrium* sp. has been used world-wide as a feed ingredient in aquaculture (Barclay and Zeller, 1996). The corresponding product HUFA2000 originally developed by OmegaTech has been successfully utilized as a DHA source for shrimp larva culture and finfish (red seabream, Japanese flounder) with no reports of adverse effects (OmegaTech, 1998).

In addition, dried *Schizochytrium* sp. microalgae has been used as a poultry feed ingredient since 1996. This feed ingredient is used in Europe at an average rate of 1.5% (by weight) of feed providing approximately 165 mg DHA/hen/day. The DHA concentrations in the resulting eggs range from 120-150 mg/egg. These eggs have been commercialized in Europe since 1996 and in the U.S. since 1998 under the Gold Circle Farms® brand. Dried golden algae is now commercially marketed in Mexico, China, Spain, Portugal, Benelux countries, Italy, Norway, Israel and Australia (Fabricant, 2000).

The dried marine microalgae was determined to be GRAS (Generally Recognized As Safe) as a source of DHA when incorporated into the feed rations of laying hens and broiler chickens at up to 4.3% or 2.8%, respectively. The corresponding product DHA GOLD™ was commercialized by Omega Tech, Inc. in 1998 (Abril et al., 2000).

In 2014, DSM Nutritional Products filed a food additive petition (FAP 2288, Fed. Reg. 2014) for the use of *Schizochytrium* sp. dried algae (DHAgold) as a source of docosahexaenoic acid (DHA) for use in standard pelleted foods for adult dogs. Recently, FDA published the final rule to DSM's FAP with the conclusion that the dried whole cells of nonviable, nontoxigenic, nonpathogenic marine microalgae *Schizochytrium* sp. may be safely used as a source of DHA and other omega-3 fatty acids as complete, dry adult maintenance food for dogs in accordance with specifically defined conditions (Fed. Reg. 2018).

In 2017 DSM Nutritional Products, with the aid of external experts concluded that the use of the DHAgold was generally recognized As Safe (GRAS) for use in food for ornamental birds and small mammals.

Today, different microalgae forms (algae, dried algae, algae meal, algal oil and algae extracts) are accepted as feedstuffs within the EU and thus there is no need for extensive approvals. The EU catalogue has listed algae meal as a product of algae oil manufacture, obtained by extraction of algae which has been inactivated (EU Regulations 2017;). More specifically, Germany has even listed a species of *Schizochytrium* (*S. limacinum*) in the positive list for straight feedstuffs since 2015 (Positive List for Straight Feeding Stuffs, 12th Edition, August 2017). Accordingly, algae meal such as dried microalgae *Schizochytrium* sp. is considered safe and is recognized for use in different applications in animal feed rations in accordance with the EU catalogue and German positive list for feed materials. Table 21 shows an overview of globally utilized dried-whole cell *Schizochytrium* sp. microalgae products used in animal feed.

Table 22 Overview of *Schizochytrium* sp. applications in animal feed

Year	Company	Country	Application
1995	OmegaTech	worldwide	HUFA2000, a spray-dried form for aquaculture (shrimp, larva culture, and finfish)
1996	OmegaTech	EU	Drum-dried form for poultry
1998	OmegaTech	USA, Australia, Mexico, Germany, Spain, Portugal, Benelux countries, Italy, Norway, Israel	DHA GOLD™ for broiler chickens and laying hen feed
2002	Martek Biosciences	USA	DHA GOLD™ for swine
2013	Martek Biosciences/DSM	China	DHA GOLD™ for swine
2013	Martek Biosciences/DSM	China	DHA GOLD™ for aquaculture
2017	DSM	USA	DHA GOLD™ for ornamental birds and small mammals
2018	DSM	USA	DHA GOLD™ for dogs
2018	DSM	China	DHA GOLD™ for layers, broilers finisher swine, dogs, cats, aquaculture

Additionally, Mordenti et al. evaluated the efficacy of DHAgold in rabbit feed fed to breeding does and their progeny at 2g/Kg of feed. No adverse effects were noted except in the early growth phase were there appeared to be a reduction in feed intake by does consuming the algal treatment. There was a significant difference in fatty acid profile in the loin and thigh muscles of both the does and their progeny in the algal treatment compared to control. (Mordenti et al. 2009)

In 2015 DSM Nutritional Products and EVONIK Industries entered into a partnership to develop a new strain of *Schizochytrium sp*. that would produce an oil with a DHA to EPA ratio similar to fish oil. The new production strain was developed from the culture collection of DSM Nutritional Products using a strain lineage that has been proven to be safe for producing an oil rich in polyunsaturated fatty acids for consumption by both animals and humans, including infants. The table above supports the internationally recognized safety of the algae.

As noted in Section 2 of this dossier, an oil high in DHA and EPA can be produced consistently from the new strain of *Schizochytrium sp*. algae. Stabilities studies with AOCED alone and in typical dog food products, dry kibble and canned indicate that the material itself is stable for at least one year when stored according to the instructions on the label and that commercial dog food products containing AOCED will be stable for at least one year.

Exposure calculations based upon typical use levels of fish oil, the material that AOCED will replace do not indicate that the consuming animals could be easily exposed to an excessive amount of the material.

Safety studies with AOCED detailed in Section 3.1 support the safety of the material at the maximum expected use level.

Veramaris also concluded in 2018 that Condensed Algal Residue Solubles, the fermentation solids left from the extraction of the oil from the algae, is generally recognized as safe (GRAS) for use as an ingredient in food for beef cattle based on scientific procedures and the review of an external panel.

6.2 Literature

Veramaris performed a search of the literature on 9 May 2019 to determine if any there were any reported adverse effects in animals related to the consumption of *Schizochytrium* algae, product produced by Schizochytrium or any other algae products produced by other closely related species of algae. The Embase, Web of science, VetMed, CAB Abstracts and PubMed databases were searched and then parsed for peer-reviewed, controlled studies conducted in healthy canines of any age, orally administered a source of EPA/DHA ≥ 7 days, and reported a safety or bioavailability outcome of interest (see **Annex 12** for inclusion/exclusion criteria). Studies were excluded for any of the following reasons: studies conducted in wild or diseased animals; administration of n-3 fatty acids other than EPA/DHA or the combination of these with other active ingredients; intravenous or topical fatty acid administration; no control group; acute feeding study (e.g. less than 7 days or one-time bolus administration); narrative review, case report, case study, abstract, letter, or other non-peer reviewed publications. Studies that could not be excluded or met all inclusion criteria were retrieved for full-text review. Reasons for exclusion at full-text screening included insufficient information to calculate the dose of n-3 LCPUFA administered, outcomes of interest weren't reported, or DHA/EPA was provided with other active ingredients. Data from studies included at full-text review were extracted into an Excel spreadsheet to facilitate qualitative synthesis. Studies from the screened literature review are summarized in evidence tables and discussed collectively in section 7.1 of this dossier.

6.3 Safety of the proposed use of AOCED

Veramaris performed a complex *in vivo* study with dogs, the intended species that will consume the AOCED, to determine if the material was safe for the intended use. The FDA Center for Veterinary Medicine reviewed the protocol for a gestation, lactation and growth study wherein female Beagle dogs were fed AOCED from conception through the weaning of the puppies and then those puppies were tracked through the growth phase of development, 34 weeks.

The results of that study confirmed that the intended use was safe within the concentrations anticipated to be employed in food for dogs; more details are provided in section 7.6 of this dossier and in Annex 11.

6.4 Efficacy of the proposed use of AOCED

During the GLG study (Annex 11) and Dahms et al. 2019, the plasma DHA and EPA levels were measured in both the dams and the puppies to confirm that the addition of increasing levels of AOCED resulted in increased levels of DHA and EPA in the plasma of the animals as shown in the figures below. A more detailed discussion is in section 7.4.8.3 of this dossier.

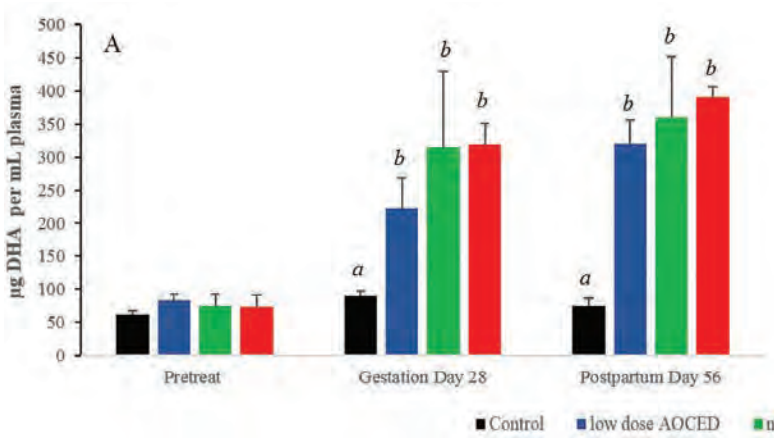


Figure 17 Plasma DHA dams

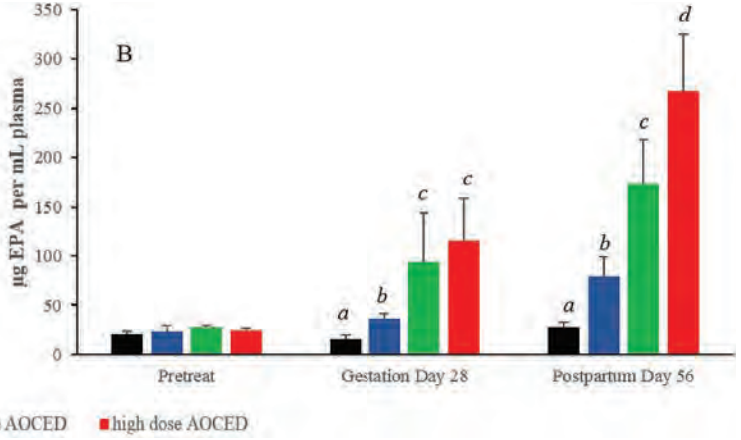


Figure 18 Plasma EPA dams

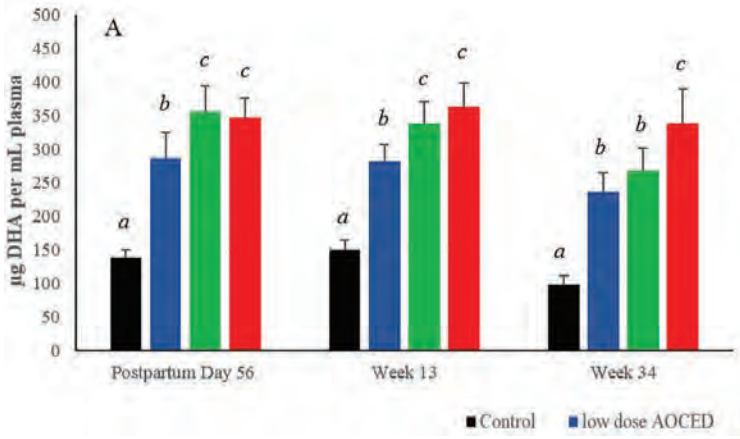


Figure 19 Plasma DHA puppies

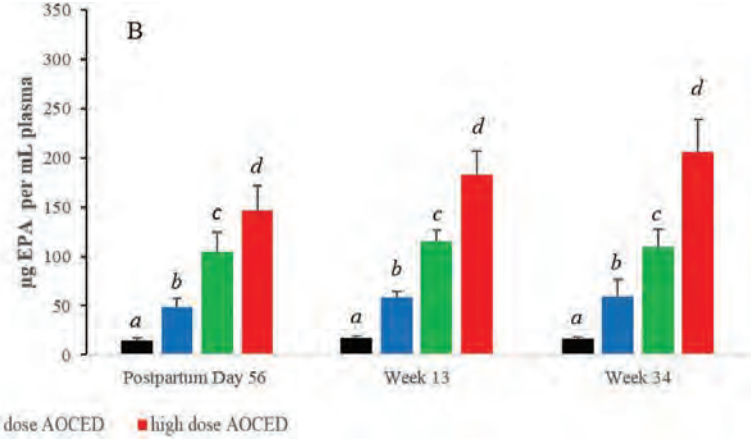


Figure 20 Plasma EPA puppies

7 Supporting data and information

7.1 Canine Metabolism of n-3 Polyunsaturated Fatty Acids (PUFA) and Bioavailability from Dietary Sources

7.1.1 Studies during gestation, lactation, and puppy development: n-3 LCPUFA Synthesis from Dietary ALA

One study evaluated puppies fed n-3 LCPUFA enriched commercially prepared diets containing both dry extruded and canned foods. The total fat contents of the diets were not disclosed but their fatty acid composition (in relative %) were as follows: adult dry food, 1.3% ALA, 0.6% DPA, 0.5% DHA; puppy dry food, 0.8% ALA, 0.1% DPA, 0.1% DHA; canned food, 0.6% ALA, 0.2% DPA, 0.3% DHA). The mothers of dogs were fed the adult dry food ad libitum until one week prior to whelping at which time the dry food was supplemented with the canned food (75/25, w/w) continuing until pups were weaned. The puppies were fed a mixture of the puppy dry and canned foods after weaning Results showed a much higher amount of DHA in puppy retinas at 47-66 days of age compared to controls (Delton-Vandenbroucke et al, 1998). Another canine reproduction study fed diets containing more than 10-fold ALA (with minimal n-3 LC PUFA) compared with n-3 LCPUFA (from fish oil) and demonstrated no enrichment of DHA in either the dams' plasma phospholipids or milk fractions on the high ALA diet (Heinemann et al, 2005). The high ALA diet contained 68.2 g ALA/kg dry matter (DM) and only 0.2 g ALA/kg DM while the high fish oil diet contained 2.0 g ALA/kg DM and 5.5 g DHA/kg DM. Also, milk from dams fed the high ALA diet was markedly enriched in ALA but not DHA. When fed to their puppies during suckling, significant DHA accumulation in the phospholipid fractions occurred (Heinemann et al, 2005; Bauer et al, 2004). However, the puppies appeared to lose their ability to convert ALA to DHA after weaning (42 days) even though they were weaned to the same diet as their dams had been fed previously (Heinemann et al, 2005). This latter finding is similar to that reported for adult dogs (Dunbar et al, 2010). Thus, neonatal dogs appear to preferentially synthesize DHA from ALA at a time of life when demand for this fatty acid is especially high (i.e. during suckling) but only for a short time. A dose response for this effect remains to be established. Of interest, however, is that this observation is similar to that found in humans (infants, young adults, and adults) where a downward trend in ALA conversion ability is seen with increasing age (reviewed in Brenna et al, 2009).

7.1.2 Studies in adult dogs: DHA Bioavailability from n-3 LCPUFA Sources

Recent studies (published 2010 to the present) examining the bioavailability of dietary DHA from various sources of n-3 LCPUFA are summarized in Table 22 (Evidence Table). Most studies reporting bioavailability outcomes were conducted in adult dogs in a parallel randomized controlled trial (RCT) design. Plasma (whole or phospholipid fraction) was the most commonly studied tissue for LCPUFA content. Studies were equally divided between those providing DHA-rich ingredients or fish oil. Most studies provided ≤ 100 mg DHA/kg body weight (bw; Table Y), although the mean DHA dose of the included studies is higher, reflecting the inclusion of two toxicological dose-response studies with DHA ethyl esters (Dahms et al., 2016a and 2016 b).

In adult dogs, significant increases in serum phospholipids were reported in response to 16-17.5 mg DHA/kg bw after 14 days of supplementation with two different salmon oils (~1.3% DHA vs 3.4% DHA; Hesta et al., 2012). Statistically significant increases in DHA plasma phospholipids were reported by Ramadeen et al. in 21 days of supplementation with between 33-52 mg DHA/kg bw from DHA-rich algal oil (DHASCO). Fish oil supplementation providing ~24 mg DHA/kg bw resulted in significantly increased serum DHA in the 90 day study conducted by Hall and co-workers (2011b). Further, when examining dose responsiveness, Hall et al., 2011b found a non-proportional dose response between 24-73 mg DHA/kg bw. Previously, Hall et al. (2006) reported that 175 mg DHA/kg bw was necessary to saturate DHA plasma levels. The highest dose provided by Hall and co-workers (2011b) was 73 mg DHA/kg bw. Based on the earlier results by Hall et al. (2006), an 18 kg dog would thus need to consume 3.15 g of DHA per day to reach maximal plasma levels. By contrast, the NRC safe upper limit for the combination of DHA and EPA is 370 mg/Kg BW, yielding an upper limit for this same dog of 6.66 g per day.

Table 23 Summary of Evidence from Studies Reporting Bioavailability Outcomes in Dogs fed Various Sources of n-3 LCPUFA

Citation	Study Type	Population (Age; sex; breed; subjects/trt; total subjects)	Intervention (Duration; Source; Administration Route; n-3 LCPUFA Dose)	Results and Author's Conclusions
Dahms et al., 2016	RCT	7 mo; Mixed; Beagle; n=3/trt; n=30 total	56 days; DHA-EE; Oral gavage; 100, 500, 1000, 2000 mg DHA/kg bw; EPA free	*Bioavailability* – plasma LCPUFA – non significant increased DHA but no clear DHA dose response; significantly decreased ARA ≥ 500; significantly increased EPA dose response. Diets designed to be ARA free.
Dahms et al., 2016	RCT	7 mo; Mixed; Beagle; n=3/trt; n=24 total	270 days; DHA-EE; Oral gavage; 150, 1000, 2000 mg DHA/kg bw; EPA free	*Bioavailability* – plasma LCPUFA – dependent on dose, 3.5-8.0 wt% DHA vs 3.0% for CONT at end of study; DHA dose response but not dose proportional; significantly reduced ARA and increased EPA but no significant difference between 1000-2000 mg DHA/kg bw at study end. Diets designed to be ARA free.
Hadley et al., 2017	RCT	9.8 yrs; Mixed; Beagle; n= 12/trt; n=24 total	174 days; dehydrated single-cell algal (DHA) biomass; Formulated kibble; 18 mg DHA/kg bw; EPA NR	*Bioavailability* – plasma PL LCPUFA - significantly increased DHA; ARA was not different between the groups, EPA not reported. Diets designed to contain 0.02% ARA
Hall et al., 2011b	RCT	5.3 yrs; Mixed; Beagle; n=10/trt; n=50 total	90 days; Fish oil; Formulated dry food; 24.3; 43.0; 73 mg DHA/kg bw; 33.7; 58.0; 108 mg EPA/kg bw	*Bioavailability* – serum LCPUFA - DHA increased significantly but not dose proportional, EPA significantly increased dose responsive; ARA significantly decreased in two highest doses. Diets contained similar ARA (0.04-0.07%). Dietary designed to contain 0.04-0.07% ARA
Hesta et al., 2012	RCT	5.5-9.0 yrs; Mixed; Beagle; NR; n=17 total	14 days; Salmon oil; Formulated kibble; 16-17.5 mg DHA/kg bw; 12 mg EPA/kg bw	*Bioavailability* – serum PHOSPHOLIPIDS LCPUFA – EPA and DHA increased significantly. ARA not reported
Ramadeen et al., 2012	RCT	1-3 yrs; Mixed; mixed-breed; n= 20 control; 8 DHA; 6 EPA; n=total 34	21 days; DHASCO or Purified EPA; oral gavage; 33-52 mg DHA/kg bw; 32-52 mg EPA/kg bw	*Bioavailability* – plasma PL LCPUFA – significantly higher levels of DHA or EPA dependent upon treatment. Dietary DHA significantly increased DHA and numerically increased EPA. Dietary EPA significantly increased EPA and numerically increased DHA. ARA not reported.
Risso et al., 2016	Cross-over RCT; free-living	2-5 yrs; Male; mixed-breed; n=5/trt; n=5 total	120 days with one 120 day wash out; Fish oil; capsule added to diet; diet not specified 8.0 mg DHA/kg bw; 4.0 mg EPA/kg bw	*Bioavailability* – semen EPA significantly increased; ARA significantly decreased; non-significant increase in DHA. Diets designed to contain 1.4% ARA.

Citation	Study Type	Population (Age; sex; breed; subjects/trt; total subjects)	Intervention (Duration; Source; Administration Route; n-3 LCPUFA Dose)	Results and Author's Conclusions
Stoeckel et al., 2013	RCT	NR; Mixed; Beagle; n=10/trt; n=30 total	112 days; Refortin DHA-rich supplement or Fish Oil; Refortin capsule added to diet; diet not specified Fish oil formulated diet; 40.8 mg DHA/kg bw; 12 mg EPA/kg bw (Refortin); 22.9 mg DHA/kg bw; 34.5 mg EPA/kg bw (FO)	*Bioavailability* – plasma LCPUFA - both diets increased n-3 FA after 1 week and reached a plateau after 4 weeks. There were no significant differences in AA between FO and CONT during the whole experimental period. In FO, AA slightly increased at week 1 and offered significant differences to its values at weeks 2, 4 and 8. After week 1, the median AA proportion in FO tended to decrease below the median AA value of week 0 (statistically not significant). In Refortin, the decrease in AA did not offer statistically significant differences before week 12 and did return to the baseline level within the first 2 weeks of the washout period. Diet designed to contain 0.25-1.13% ARA.
Stoeckel et al., 2011	RCT	2.2 yrs; Mixed; Beagle; n=10/trt; n=30 total	168 days; Refortin DHA-rich supplement or Fish Oil; Refortin capsule added to diet to dry food; Fish oil formulated diet; 40.8 mg DHA/kg bw; 12 mg EPA/kg bw (Refortin); 22.9 mg DHA/kg bw; 34.5 mg EPA/kg bw (FO)	*Bioavailability* – RBC membrane LCPUFA - DHA and not EPA was preferably incorporated into the EM. Significant changes of membrane total n-3 FA, EPA and DHA were observable from the first week of the study. The content of these FA in EM reached a plateau no later than eight weeks. In contrast, total n-6 FA and AA were not equilibrated after 12 weeks, suggesting that the decrease of n-6 FA membrane content in reaction to dietary changes might be delayed. " Diets designed to contain 0.25-1.13% ARA.
Walters et al., 2010	RCT; free-living	6 yrs; NR; NR; n=18/trt; n=54 total	21 days; Omega Pet EPA DHA; Capsule added to "usual" diet; 100 mg DHA/kg bw; 100 mg EPA/kg bw	*Bioavailability* – plasma LCPUFA – significantly increased DHA and EPA. ARA not reported.

APPT - activated partial thromboplastin time; ARA – arachidonic acid (20:4 n-6); AA – arachidonic acid (20:4 n-6); bw – body weight; d= days; CBC – complete blood count; CONT – control; CRP – c-reactive protein ; DHA – docosahexaenoic acid (22:6 n-3); EE – ethyl ester; EM – erythrocyte membrane; EPA – eicosapentaenoic acid (20:5 n-3); FA – fatty acid; FO – fish oil; IAUC – insulin area under the curve; GSH - glutathione; IgA – immunoglobulin A; IgG – immunoglobulin G; mo – months; n-3 – omega-3; n-6 – omega-6; LCPUFA – long-chain polyunsaturated fatty acids; NR – not reported; OSPT - one-stage prothrombin time ;PL- phospholipid; PR interval – P-wave to QRS complex interval; PT – prothrombin time; QRS duration – duration of main spike on an ECG line; QT interval – beginning of QRS complex to end of T wave; QTc – corrected QT interval; RBC – red blood cell; RCT – randomized controlled trial; RR interval – inter-beat interval; TT – thrombin time; TXA2 – thromboxane A2; TXB2 – thromboxane B2; wk – weeks; wt% - weight percent; yrs-years

7.1.4 Adult dogs: Tissue EPA levels following n-3 LCPUFA supplementation

EPA is typically found in fish oil in amounts at least equal or higher than DHA (Yi et al., 2014). DHA can also be retroconverted in vivo resulting in increased EPA tissue levels in response to supplementation with DHA-rich sources (Arterburn et al., 2006). Accordingly, most recent studies report significantly increased canine blood/tissue EPA levels regardless of source provided as supplementation (Table 22). One study compared a DHA-rich and an EPA-rich supplement via oral gavage in a study of adult mixed breed dogs (Ramadeen et al., 2012). These authors report statistically significant increases in plasma PL levels of DHA or EPA dependent upon the primary fatty acid in the supplement. Non-significant increases in DHA were observed in response to the EPA supplement, and vice versa with the DHA supplement.

7.1.5 Adult dogs: Tissue ARA levels following n-3 LCPUFA Supplementation

Five studies supplementing n-3 LCPUFA to adult dogs reported blood/tissue arachidonic acid (ARA; 20:4 n-6) levels (Hadley et al., 2017; Hall et al. 2011b; Risso et al., 2016; Stoeckel et al. 2011; Stoeckel et al., 2013). The ARA content of the diet was reported in most studies, ranging from 0.04% to 1.4% of feed. Despite ARA availability from the diet, three of the five studies reported significant reductions in tissue ARA in response to DHA/EPA supplementation. Risso et al. (2016) provided a low dose (8 mg DHA/kg bw) of DHA from fish oil in a 120 day crossover trial and reported significantly decreased ARA levels in semen. In a 90-day trial, Hall et al. (2011b) found no reduction in serum LCPUFA following lower dose supplementation of 24.3 mg DHA/kg bw from fish oil but did find significant reductions with higher DHA doses (43-73 mg DHA/kg bw). Similarly, Stoeckel et al reported no decline in plasma ARA following 112 days of fish oil supplementation providing ~23-40 mg DHA/kg bw (2013) but reported declines in red blood cell ARA with these levels after 168 days (2011). In contrast, Hadley et al. supplemented with a low level of DHA (18 mg DHA/kg bw) from DHA algal biomass but reported no change in ARA in plasma PL DHA after 90 days. These results suggest that fish oil supplementation is more likely to result in ARA tissue reductions, particularly with longer duration feeding, when compared to sources free of EPA. EPA is a direct antagonist of ARA in tissue membranes (Arterburn et al., 2006), thus EPA-free sources of DHA (e.g. DHA algal biomass; DHASCO) may, at similar doses, be less likely to result in tissue ARA level reduction than fish oil, which supplies between equal or higher EPA as DHA.

There is no recommended dietary intake level of ARA for adult dogs. The NRC recommended allowance for growth is 0.08 g/1000 kcal. It is unclear from the available evidence what level of dietary ARA would prevent tissue ARA reductions following fish oil supplementation, but current evidence suggests a minimum greater than 1.4% of feed is likely needed. This level is the highest fed among the studies included in the current review, but still resulted in reduced ARA in semen following 120 days of feeding fish oil (Risso et al., 2016).

7.1.6 Studies during Gestation, Lactation, and Puppy Development: DHA, EPA and ARA levels following DHA ethyl esters supplementation

Dahms et al. (2016b) reports n-3 LCPUFA bioavailability from a dose-response design in two RCTs with 7 month-old puppies. The first study provided 100, 500, 1000, and 2000 mg DHA/kg bw via oral gavage from purified DHA ethyl ester for 8 weeks (56 days), the second study provided 150, 1000, and 2000 mg DHA/kg bw for 9 months (270 days). DHA levels in plasma LCPUFA were increased following 56 days of supplementation, but there was no clear dose response. The 270 day trial resulted in significantly increased plasma DHA levels ranging from 3.5-8.0% of total fatty acids for the DHA diet vs 3.0% for the control diet.

Plasma DHA increased between 150 and 1000mg/kg bw/day but not between 1000 and 2000mg/kg bw/day and there were increases from Day 1 to 92 but not between days 92 and 273.Doses 4500mg/kg bw/day in the 8-week and all doses in the 9-month study resulted in DHA increases in the brain. The dose of 150mg/kg bw/day is sufficient to achieve maximal brain concentrations if DHA is administered chronically. For shorter than 6 months of supplementation, higher doses are required.

Despite lack of preformed EPA, supplementation with purified DHA-EE for either 56 or 270 days resulted in a statistically significant, EPA dose response, in puppy plasma (Dahms et al., 2016b). These results are not surprising as DHA can be retroconverted *in vivo* to produce small amounts of EPA (Arterburn et al., 2006).

7.1.7 Summary and Conclusions from the literature

Adult dogs do not accumulate DHA in plasma when fed ALA, although DPA n-3 is seen which may be a circulating reservoir for uptake and neural cell DHA synthesis. Puppies appear to synthesize DHA from ALA enriched milk but lose this ability after weaning. Providing preformed DHA is therefore preferred for growth and development of puppies and may be necessary for adult health maintenance. DHA is readily bioavailable in a variety of tissues from a variety of preformed DHA sources in both adult dogs and puppies. Tissue ARA levels decrease with fish oil supplementation, and with higher-doses of DHA, particularly when diets are ARA-free. EPA accumulates directly or via retroconversion from DHA depending on the source of DHA fed. The minimum dose to reach plasma DHA saturation is unknown but may be less than the 175 mg DHA/EPA per kg bw suggested by older literature.

7.2 Review of the Safety of *Schizochytrium sp.* in other species

7.2.1 Dried Whole Cell Biomass

As noted in Section 6.2, dried whole cell *Schizochytrium* sp. microalgae has been sold for use in animal feed under tradename DHAgold™ since 1995. The organism used to produce DHA GOLD™, while still a member of the genus *Schizochytrium*, is a different species from that used to produce the algal oil which is the subject of this notification.

Both organisms have been thoroughly examined by Dr. Gunter Bahnweg (Bahnweg, unpublished, 2010; Bahnweg, unpublished, 2009). He concluded that both organisms possess the definitive characteristics of the genus *Schizochytrium*. Morphological examinations, biochemical compositions, and DNA sequence characteristics indicate that these organisms are closely related, and thus, safety studies conducted with either species should be considered relevant.

Published safety studies have shown that algae from *Schizochytrium* sp. is safe in classical toxicology models, including a subchronic rat feeding study (Hammond et al., 2001a), a single generation rat reproduction study (Hammond et al., 2001c), and gene toxicology studies (Hammond et al., 2002).

Table 24 Summary of Published *Schizochytrium* sp. microalgae Confirmatory Safety Studies

Study Type	System	Doses	Results
In vitro **Genetic Toxicity**			
• Ames bacterial mutagenicity	*S. typhimurium* (TA98, TA100, TA102, TA1535, TA1537)	500 µg/plate	Not mutagenic[1]
• AS52/XPRT mammalian mutagenicity	Chinese hamster ovary cells	500-5000 (-S9); 200-1000 µg/ml (+S9)	Not mutagenic[1]
• Chromosomal aberration	Human peripheral lymphocytes	125 - 750 µg/ml	Not clastogenic[1]
In vivo **Genetic Toxicity**			
• Micronucleus assay	Mouse bone marrow	500, 1000 and 2000 mg/kg bw orally	Not clastogenic[1]
Subchronic Toxicity			
• 13-week	Rat (20/sex/group)	400, 1500, 4000 mg/kg bw/day in the diet	No relevant adverse effects were observed at any dose level[2]
Reproductive Toxicity			
• One-generation study	Rat (30/sex/group)	0.6%, 6% and 30% of diet (up to 17,800/ 20,700 mg/kg bw/d for males/females)	No changes in fertility or developmental indices[3]
Developmental Toxicity			
	Rat (25 mated females/group)	0.6%, 6% and 30% of diet on GD 6 - 15.	NOAEL = 22,000 mg/kg bw/d for both maternal and developmental toxicity[4]
	Rabbit (22 mated females/group)	180, 600 and 1800 mg/kg bw/day orally by gavage on GD 6 - 19.	Maternal toxicity NOAEL = 600 mg/kg bw/d; developmental NOAEL = 1800 mg/kg bw/day[4]

1 Hammond et al., 2002
2 Hammond et al., 2001(a)
3 Hammond et al., 2001(c)
4 Hammond et al., 2001(b)

7.2.2 Oil

Studies conducted with algal oil from *Schizochytrium* sp., the same parent organism with which this algal oil is produced, are summarized in the following two tables.

The algal oil was initially developed in 2010 for use in human dietary supplements. Chronic and sub-chronic feeding studies have been conducted in rats using multiple intake levels. The administration of algal oil did not affect health or growth. No adverse effects were noted in the 90 day study, therefore, the no-observed-adverse-effect level (NOAEL) of algal oil in this study was placed at highest level administered viz. at 5% in the diet (equivalent to at least 3250 mg/kg bw/day). Finally, genotoxicity studies demonstrate that the algal oil is not mutagenic when studied in vivo and in vitro.

Table 25 Summary of Algal Oil (*Schizochytrium* sp.) toxicity study (Dahms, et al., 2011a)

Study Type	System	Algal Oil Dose	Results
***In vitro* Genetic Toxicity**			
Ames bacterial mutagenicity	5 strains of *Salmonella typhimurium* and *Escherichia coli*	15.8-5000 µg/plate w/ and w/o metabolic activation	Not mutagenic
Mammalian Chromosome Aberration	Human lymphocytes	1, 2.5, 3, 4, and 5 µL/mL w/ and w/o metabolic activation	Not genotoxic
***In vivo* Genetic Toxicity**			
Micronucleus assay	Mouse peripheral blood	2000 mg/kg bw	Not genotoxic
Subchronic Toxicity			
14 day	Rat (10/sex/group)	1%, 3% and 6% of total diet	Expected tolerance of 6% in a study of longer duration
90 day	Rat (10/sex/group)	0.5%, 1.5%, and 5% of the diet	NOAEL at 5% (equivalent to 3250 mg/kg bw/day)

NOAEL = no-observed-adverse-effect level.

In 2011, a related production strain with lower EPA content (a specification of maximum 10% EPA) from the same *Schizochytrium* species was developed for use in human infant formula. Algal Oil from *Schizochytrium* sp. was evaluated by testing for gene mutations, clastogenicity and aneugenicity, and in a 90-day *in utero* Sprague-Dawley rat dietary study (Fedorova-Dahms et al, 2011).

All studies were performed in accordance with Good Laboratory Practice.

Table 26 Summary of Algal Oil (*Schizochytrium* sp.) toxicity study (Dahms, et al., 2011b)

Study Type	System	Algal Oil Dose	Results
***In vitro* Genetic Toxicity**			
Ames bacterial mutagenicity	5 strains of *Salmonella typhimurium* and *Escherichia coli*	Up to 5000 μg/plate w/ and w/o metabolic activation	Not mutagenic
Mammalian Chromosome Aberration	Human lymphocytes	1, 2.5, 3, 4, and 5 μL/mL w/ and w/o metabolic activation	Not genotoxic
***In vivo* Genetic Toxicity**			
Micronucleus assay	Mouse peripheral blood	2000 mg/kg bw	Not genotoxic
Subchronic Toxicity			
90 day (with in utero phase)	Rat (20 F_1/sex/group)	0.5%, 1,5%, and 5% of the diet	NOAEL greater than 5% (equivalent to 4260 mg/kg bw/day)

NOAEL = no-observed-adverse-effect level.

Another set of toxicological studies, geneotoxicity, acute and subchronic with rats, was performed with the oil from *Schizochytrium* strain ONC-T18, (Schmitt et al. 2012).

Table 27 Summary of Algal Oil (*Schizochytrium* sp.) toxicity study (Schmitt et al 2012)

Study Type	System	Algal Oil Dose	Results
***In vitro* Genetic Toxicity**			
Ames bacterial mutagenicity	5 strains of *Salmonella typhimurium* and *Escherichia coli*	Up to 5000 μg/plate w/ and w/o metabolic activation	Not mutagenic
Mammalian Chromosome Aberration	Human lymphocytes	12.5, 25.0, 50.0, 100, 175, 250, 350, 500, 750, and 1000 lg/mL w/o metabolic activation and 100, 250, 500, 750, 1000, 1250, and 1500 lg/mL with activation	Not genotoxic
***Acute* Toxicity**			
Single dose	Female rats	5000 mg/kg bw	Not toxic

Subchronic Toxicity			
90 day	Rat (10/sex/group)	1.0%, 2,5%, and 5% of the diet	NOAEL greater than 5% (equivalent to 3305 male and 3679 female,mg/kg bw/day)

7.3 Review of the Safety of DHA and EPA in Dogs

Hall first reviewed possible adverse events related to n-3 LCPUFA supplementation of canine diets in 1996. Little direct canine evidence was available at that time leading Hall to primarily rely on human data in an effort to identify areas of concern for n-3 LCPUFA safety and tolerance in dogs. Hall identified four primary areas of potential concern in canines including risk of bleeding after prolonged use (Hall concluded risk seemed very low); disruption of normal linoleic acid (LA) metabolism with high doses; increased vulnerability to lipid peroxidation of tissues due to increased tissue accumulation of n-3 LCPUFA; and possible decreases in immune and inflammatory responses sufficient to compromise normal defenses. In 2013, Lenox and Bauer reviewed the current canine literature focusing on these, and a few additional, areas of potential concern. The following literature review considers areas of concern identified by both Hall (1996), and Lenox and Bauer (2013), and adds (based on evidence availability in the literature) growth/body weight; cardiac function; clinical chemistry; hematology; inflammation; immune function; integumentary health; lipid oxidation; platelet function and coagulation; and circulating vitamin E levels (Canine Safety and Tolerance, Table 25).

Canine Growth and Body Weight Maintenance Following n-3 LCPUFA Supplementation

Four studies (Dahms et al., 2016b; DeGodoy et al., 2015; Hall et al., 2011b; Pellegrino et al., 2018) reported growth and/or body weight outcomes following supplementation with a variety of n-3 LCPUFA sources (TABLE 25). Dahms et al. (2016b) are the only to report growth outcomes following extended supplementation of young dogs (7 months), reporting no statistically significant differences in mean body weights at end of study, or toxicologically relevant differences in weight gain or feed consumption with DHA doses up to 2000 mg DHA/kg bw. Studies in adult dogs reported no treatment-related changes in body weight or fat/lean body mass (Table 25).

Canine Cardiac Function Following n-3 LCPUFA Supplementation

Two studies (Dahms et al., 2016b; Pellegrino et al., 2018) reported cardiac function outcomes in response to n-3 LCPUFA supplementation (TABLE 25). In young dogs, Dahms et al (2016b) reported no differences in measures of cardiac function following supplementation with up to 2000 mg DHA/kg bw for 9 months.

Pellegrino et al. (2018) investigated the use of low dose DHA supplementation (8 mg/kg bw) for 12 weeks in a cross-over design on exercise tolerance of adult dogs. The authors observed decreased pre- and post-exercise heart rates in response to fish oil supplementation, concluding that fish oil supplementation "slightly" improved the physiological response of dogs to exercise training. Decreased heart rate in response to n-3 LCPUFA supplementation is common in humans (Hidayat et al., 2018), even at low doses of DHA for the same duration studied by Pellegrino et al. (Theobald et al., 2007). Although the daily intake provided by Pellegrino is lower (~150 mg/day DHA) than expected to be effective for heart rate reduction in humans, the combination with exercise (which also can lower resting heart rate) likely explains the improved efficacy of a lower n-3 LCPUFA dose.

Canine Clinical Chemistry Following n-3 LCPUFA Supplementation

Four studies, in adult dogs, reported various clinical chemistry outcomes (DeGodoy et al., 2015, 2018; Hall et al., 2011b; Jamikorn et al., 2014) (TABLE 25). DeGodoy and co-workers focused on the role of DHA supplementation on various markers of glucose metabolism in normal weight (2015) and obese (2018) dogs. The researchers reported no differences in glucose metabolism in normal weight dogs but observed a decrease in glucose half-life after supplementation of 27 mg DHA/kg bw from fish oil in a 69 day cross-over trial, suggesting an improvement in glucose clearance. The remaining studies reported no treatment related differences in complete blood counts or serum biochemistries.

Dahms et al. (2016b) reported dose response reductions in serum cholesterol and triglycerides at the end of a 9 month supplementation period with DHA-EE in young dogs (TABLE 25). Reduced blood lipids is one of the most common findings of DHA/EPA supplementation in humans, at a range of intakes, from a variety of sources and is considered to contribute to reduced heart disease risk (Musa-Veloso et al., 2010; Innes and Calder, 2018). Reductions observed in young dogs were consistent with historical control normalized ranges (Dahms et al, 2016b). Otherwise, with the exception of elevated end of study AST in female dogs at the mid and high dose (within historical norms), no treatment-related changes were noted. No toxicologically or statistically relevant changes in urinalysis were reported.

Canine Hematology Following n-3 LCPUFA Supplementation

Two studies in adult dogs (Hall et al., 2011b; Jamikorn et al., 2014) reported no treatment-related changes in complete blood counts after supplementation with various sources of n-3 LCPUFA for 56-90 days at doses ranging between 11-110 mg DHA/kg body weight (TABLE 25). In young dogs, Dahms et al. (2016b) reported significantly reduced reticulocyte values in male dogs supplemented with 2000 mg DHA/kg bw at all time points studied in a 9-month supplementation trial. The authors observed no corresponding histological changes in bone marrow, liver or kidney. The authors hypothesize that the reductions in circulating ARA levels, resulting from the feeding of an ARA free diet enriched with n-3 LCPUFA, likely contributed to the observed reticulocyte reduction as ARA is suggested to play a role in erythropoiesis (Dahms et al., 2016b).

Canine Inflammatory Responses Following n-3 LCPUFA Supplementation

In the current review, only two studies (Hall et al. 2011; Walters et al., 2010) reported biochemical measures of inflammation. Consistent with previous work, Hall et al. (2011) reported decreased urine levels of 11-dehydro TXB_2 , a metabolite of the eicosanoid-derived inflammatory mediator TXA_2, in response to fish oil supplementation providing up to 73 mg DHA/kg bw. Walters et al. (2010) reported no treatment-related differences in C-reactive protein, a systemic marker of inflammation, but did report decrease urine levels of prostaglandin metabolites in response to fish oil or a DHA-rich dietary supplement. Previous reports have suggested that dietary n-3 LCPUFA may affect the inflammatory stage of wound healing (Mooney et al., 1998; Scardino et al., 1999), however, while both studies reported biochemical changes in response to n-3 LCPUFA, neither reported histological differences in wound healing. No studies in the current review followed up on these early observations regarding wound healing.

Modulation of Canine Immunity Following n-3 LCPUFA Supplementation

In the current review, two studies of adult dogs (Hesta et al., 2012: Stoeckel et al., 2013) reported immune outcomes (TABLE 25). Hesta et al. (2012) examined plasma IgA and IgG levels after 14 days of supplementation with two different salmon oils and found no differences between groups or from baseline. Stoeckel et al (2013) reported significantly lower leucocyte counts versus control after 12 weeks of feeding a DHA-rich dietary supplement to adult dogs. The authors attribute their observations to the combination of n-3 LCPUFA in a diet formulated to be low in vitamin E. The authors did not report dietary vitamin E content.

In young dogs supplemented with high-dose DHAEE for 9 months, a non-dose responsive decrease in thymus gland weights was noted at end of study necropsy. These observations were not considered treatment-related and consistent with normal thymus reduction in response to maturation (Dahms et al., 2016b).

Early studies have observed decreases in various markers of canine immune function (Wander et al., 1997; Hall et al., 1999) in response to n-3 LCPUFA supplementation despite seemingly adequate dietary vitamin E (e.g. α-tocopherol added to the diet exceeded NRC recommendations). Previously, to better determine the optimal amount of vitamin E in n-3 LCPUFA diets Hall et al. (2002) investigated three amounts of α-tocopherol acetate (17, 95 and 448 mg/kg diet) in diets with high-dose (4.5-4.8 g combined EPA+DPA n-3+DHA/kg diet) from menhaden fish oil for 17 weeks (Hall et al., 2002). Dogs consuming low concentrations of α-tocopherol acetate had lower percentages of CD8+ T cells, compared with dogs consuming medium or high α-tocopherol acetate concentrations. Also, dogs consuming low α-tocopherol acetate concentrations had higher CD4+ lymphocyte to CD8+ T cell ratios. On day 4 of week 15, the percentage of CD8+ T cells was highest in dogs fed intermediate concentrations of α-tocopherol acetate, compared with other dogs; however, the CD4+ lymphocytes to CD8+ T cell ratio was higher only in dogs fed low concentrations of α-tocopherol acetate with high concentrations of n-3 fatty acids. Le Blanc et al. (2007) also investigated varying vitamin E levels with high dose n-3 LCPUFA supplementation. Canine lymphocyte proliferation and peripheral blood mononuclear cell (PBMC) PGE2 production was investigated in 15 Walker-cross hounds fed an enriched fish oil diet containing two varying vitamin E concentrations of 58 IU/kg and 459 IU/kg respectively compared to a safflower oil supplemented control with 80 IU/vitamin

E/kg (Le Blanc et al., 2007). The fish oil diets contained 4.35 g/kg of combined EPA+DPA n-3 + DHA. After 12 weeks the high fish oil diets resulted in significant decreases in lymphocyte proliferation. PBMC production of PGE2 was significantly reduced in groups receiving fish oil supplementation. The level of fish oil supplementation used in this study appeared to suppress the lympho-proliferative response in healthy, young dogs but the response was attenuated by high levels of dietary vitamin E supplementation.

In summary, neutrophil membrane structure is enriched, phagocytic function is improved, and PGE2 production is decreased with supplemental n-3 LCPUFA (Vaughn et al., 1994; Waldron et al. 2012; Byrne et al., 2000). Lymphocyte proliferation and peripheral blood mononuclear cell PGE2 is decreased (LeBlanc et al, 2007). The combination of results from early studies, and those in the current review, confirm that adequate Vitamin E is important in n-3 LCPUFA enriched canine diets for maintaining normal immune function.

Canine Integumentary Health Following n-3 LCPUFA Supplementation

In the current review, only Dahms et al. (2016a; 2016b) reported observations related to skin health. In both short (8 weeks) and longer term (9 months) supplementation of young dogs (7 months) with high dose DHA (≥ 500 mg DHA/kg bw) provided by DHA EE, the authors observed dry flakey skin. At 1000 mg DHA/kg bw or higher, both short and longer term supplementation resulted in yellow/yellow-orange hair coat discoloration.

Markers of Lipid Peroxidation Following n-3 LCPUFA Supplementation of Canine Diets

In the current review, two longer term studies (>100 days) in adult dogs reported measures of lipid peroxidation (Hadley et al., 2017; Walters et al., 2010) at up to 100 mg DHA/kg bw. Neither study reported significant differences from baseline or between groups in plasma of 8-iso-$PGF_2\alpha$ (Hadley et al., 2017) or red blood cell glutathione, oxidized glutathione or the ratio of the two (Walters et al., 2010). Neither study reported dietary vitamin E levels.

Canine Platelet Function and Coagulation Following n-3 LCPUFA Supplementation

In 1996 Hall speculated, based largely on human data, about the potential for risk of bleeding after prolonged use of n-3 LCPUFA in canine diets, ultimately concluding that the risk “seems to be very low”. Lenox and Bauer (2013) concluded similarly, but cautioned against the combination of a high risk patient (thrombocytopenia) and prolonged n-3 LCPUFA supplementation or interactions with anti-coagulant drugs. In the current review, Westgrath and co-workers (2018) studied low-dose fish oil (5 mg DHA/kg bw) alone or in combination with aspirin for 28 days in a cross-over RCT. Combining aspirin with fish oil significantly increased the platelet inhibitory effect of aspirin, but fish oil alone had no effect on platelet function. The authors reported no bleeding events. Two additional studies in adult dogs measured coagulation outcomes (Hesta et al., 2012; Jamikorn et al., 2014) and found no treatment-related changes with up to 110 mg DHA/kg bw. Similarly, in young dogs Dahms et al. (2016b) found no treatment related effects on standard coagulation parameters following up to 2000 mg DHA/kg bw for 9 months. These data suggest that, as

previously concluded, dietary n-3 LCPUFA alone pose little risk for bleeding in healthy canines fed n-3 LCPUFA enriched diets, but that drug interactions should be monitored in canine patients.

Circulating Vitamin E Levels Following n-3 LCPUFA Supplementation of Canine Diets

Given the potential for n-3 LCPUFA to increase tissue peroxidation (Hall, 1996), studies of canine LCPUFA supplementation have considered adequate dietary vitamin E to prevent lipid peroxidation and maintain normal immunity (see sections above). Two studies in the current review also measured circulating vitamin E levels in adult dogs following supplementation of up 73 mg DHA/kg bw for up to 100 days (Hall et al., 2011b; Stoeckel et al., 2013). Hall et al. (2011b) supplemented fish oil enriched diets with a minimum of 575 mg vitamin E/kg diet and reported a significant increase in serum E levels overtime regardless of DHA dose. In contrast, Stoeckel et al. (2013) reported that a "low" (dose not reported) level of dietary E, likely resulted in decreased leucocyte counts after 16 weeks of ~41 mg DHA/kg bw from DHA-rich dietary supplements. Data from earlier studies, and those in the current review, confirm that adequate dietary vitamin E supplementation is an important consideration in the formulation of n-3 LCPUFA enriched canine diets. Vitamin E content at a minimum of > 100mg/kg diet but less than 450 mg/kg diet provides the likely range of desired vitamin E in n-3 LCPUFA enriched diets to prevent oxidation, preserve circulating vitamin E, and maintain normal immunity.

Table 28 Safety and Tolerability Evidence for n-3 LCPUFA Supplementation of Canine Diets

Citation	Study Type	Population (Age; sex; breed; subjects/trt; total subjects)	Intervention (Duration; Source; Administration Route; n-3 LCPUFA Dose)	Results and Author's Conclusions
Dahms et al., 2016	RCT	7 mo; Mixed; Beagle; n=3/trt; n=30 total	8 wk; DHA-EE; Oral gavage; 100, 500, 1000, 2000 mg DHA/kg bw; EPA free	*Integumentary* - ≥500 mg/kg bw = dry flakey skin; ≥1000 mg/kg bw = yellow fur. Authors attribute decreased ARA and skin and coat changes attributed to ARA-free base diet. Vitamin E content of diet NR "There was no toxicity related to administration of DHA-EE in male or female beagle dogs for 8 weeks (56days) at dose levels of 100, 500, 1000 and 2000mg/kg/day."
Dahms et al., 2016	RCT	7 mo; Mixed; Beagle; n=3/trt; n=24 total	9 mo; DHA-EE; Oral gavage; 150, 1000, 2000 mg DHA/kg bw; EPA free	*Integumentary* - ≥1000 mg/kg bw dry flakey skin; yellow-orange fur *Hematology* - decreased reticulocyte value 2000, males only, throughout study. No corresponding histological changes in bone marrow, liver, or kidney (Dahms et al., 2016b). ARA-free diet may be responsible for skin abnormalities and reticulocyte depression due to ARA role in erythropoiesis
Dahms et al., 2016b	RCT	7 mo; Mixed; Beagle; n=3/trt; n=24 total	9 mo; DHA-EE; Oral gavage; 150, 1000, 2000 mg DHA/kg bw; EPA free	*Body weight* - no statistically significant differences in mean body weights or toxicologically relevant differences in mean body weight gains or mean food consumption *Hematology* - decreased reticulocyte value at 2000 mg DHA/kg bw, males only, throughout study. No corresponding histological changes in bone marrow, liver, or kidney (Dahms et al., 2016). Other changes not considered toxicologically relevant/within historical norms. *Coagulation* – No effects of trt on standard coagulation parameters. *Clinical Chemistry* – Dose response reduction in serum cholesterol and triglycerides at end of study Elevated AST in female dogs at mid and high dose, but within historical norms. No toxicologically relevant changes in urinalysis. *Cardiac* – no statistical differences between any treated groups and the control group for heart rate, RR interval, PR interval, QRS duration, QT interval, nor QTc *Necropsy* – Hair coat discoloration and skin flaking at mid dose; thymus weights reduced but not dose-responsive. Vitamin E content of diet NR "Therefore, based on the results of this study, the no-observed adverse-effect level (NOAEL) of DHA-EE was considered to be 2000 mg/kg bw/day."
De Godoy et al., 2015	Cross-over RCT	2.5 yrs; Female; Beagles; n=4/trt; n= 8 total	69 d with one 30 d washout; Fish oil; Formulated kibble; 70 mg DHA/kg bw; 46 mg EPA/kg bw	*Clinical Chemistry* - no effect of FO treatment on glucose IAUC or peak area *Body weight* – no effect of FO treatment 162 mg vitamin E/kg food

Citation	Study Type	Population (Age; sex; breed; subjects/trt; total subjects)	Intervention (Duration; Source; Administration Route; n-3 LCPUFA Dose)	Results and Author's Conclusions
De Godoy et al., 2018	Cross-over RCT	9 yrs; Obese female; mixed breed; NR; n=7 total	69 d with one 30 d washout; Fish oil; Formulated kibble; 27 mg DHA/kg bw; 40-43 mg EPA/kg bw	*Clinical Chemistry* - a decrease of 11.5% of glucose half-life on day 30 in the FO treatment suggesting improved ability to clear glucose following a glucose tolerance test 180 mg vitamin E/kg food
Hadley et al., 2017	RCT	9.8 yrs; Mixed; Beagle; n= 12/trt; n=24 total	174 d; dehydrated single-cell algal (DHA) biomass; Formulated kibble; 18 mg DHA/kg bw; EPA NR	*Oxidation* - Isoprostanes - no difference from baseline or between diets Vitamin E content of diet NR
Hall et al., 2011	RCT	5.3 yrs; Mixed; Beagle; n=10/trt; n=50 total	90 d; Fish oil; Formulated dry food; 24.3; 43.0; 73 mg DHA/kg bw; 33.7; 58.0; 108 mg EPA/kg bw	*Inflammation* - Urine levels of 11-dehydro TXB2, the major metabolite of the inflammatory mediator TXA2, are decreased after feeding diets enriched with fish oil. ≥ 640 IU vitamin E/ kg food "These results suggest a role for feeding (n-3) enriched diets along with an increase in lean-body mass to reduce the production of inflammatory eicosanoid mediators in the treatment of canine inflammatory diseases."
Hall et al., 2011b	RCT	5.3 yrs; Mixed; Beagle; n=10/trt; n=50 total	90 d; Fish oil; Formulated dry food; 24.3; 43.0; 73 mg DHA/kg bw; 33.7; 58.0; 108 mg EPA/kg bw	*Serum Vitamin E* – increased overtime; not significant between groups. ≥ 640 IU vitamin E/ kg food. *Clinical Chemistry* – no differences in serum biochemistry indices from baseline or between trts *Hematology* - no significant differences in CBC *Body Weight* – No effect of trt on bw; fat mass or lean body mass
Hesta et al., 2012	RCT	5.5-9.0 yrs; Mixed; Beagle; NR; n=17 total	14 days; Salmon oil; Formulated kibble; 16-17.5 mg DHA/kg bw; 12 mg EPA/kg bw	*Coagulation* – no difference in platelet counts; APTT; or OSPT *Immune* - plasma IgA and IgG concentrations also remained similar between groups and among periods. Vitamin E content of diet NR "Short-term effects of salmon oil on blood coagulation, acute phase response and humoral immune response were absent, perhaps because of the low administration dose."
Jamikorn et al., 2014	RCT	1-3 yrs; Mixed; Beagle; N=10/trt; N=40 total	8 wks; PCSO-524 New Zealand green-lipped mussel; Capsules/dietary supplement; diet not specified; 11; 33; 110 mg DHA/day (amt per kg/bw NR); 15; 44; 146 mg EPA/day (amt per kg bw NR)	*Hematology* – no CBC differences between groups *Clinical Chemistry* – no differences between groups *Coagulation* - TT, PT and APTT were not significantly different between groups 188 mg E/100 g dietary supplement "In conclusion, the dietary polyunsaturated fatty acid supplement PCSO-524® in healthy Beagle dogs demonstrated no change in feed intake, behavior, CBC and blood chemistry values, which suggested that this supplement did not have a harmful effect."

Citation	Study Type	Population (Age; sex; breed; subjects/trt; total subjects)	Intervention (Duration; Source; Administration Route; n-3 LCPUFA Dose)	Results and Author's Conclusions
Pellegrino et al., 2018	Cross-over RCT; free-living	2-6 yrs; Male; Weimaraner (n = 1), Labrador retriever (n = 2), Belgian shepherd (n = 1), Boxer (n = 1) and Mixed breed (n = 3); n=7 or 8/trt; n=8 total	12 weeks with 8 week washout; Fish oil; Capsule added to kibble; 8.0 mg DHA/kg bw; 4.0 mg DHA/kg bw	*Body weight* – no difference between groups *Cardiac* – decreased pre- and post-exercise heart rate in response to FO *Body Temperature* – decreased post-exercise rectal temperature in response to FO Vitamin mineral premix formulated at 0.048% of diet, contains 60 mg Vitamin E "FO supplementation slightly improved the physiological response of dogs to exercise during training."
Stoeckel et al., 2013	RCT	NR; Mixed; Beagle; n=10/trt; n=30 total	16 weeks; Refortin DHA-rich supplement or Fish Oil; Refortin capsule added to diet; diet not specified Fish oil formulated diet; 40.8 mg DHA/kg bw; 12 mg EPA/kg bw (Refortin); 22.9 mg DHA/kg bw; 34.5 mg EPA/kg bw (FO)	*Plasma Vitamin E* – No significant difference between groups. Vitamin E content of diet NR, described by authors as "low". *Immune* – leucocyte counts in both Refortin and CONT were well within the clinical range, but Refortin resulted in significantly lower leucocyte count than CONT at week 12. Authors attribute this observation to diet formulated to be low in Vitamin E.
Walters et al., 2010	RCT; free-living	6 yrs; NR; NR; n=18/trt; n=54 total	21 days; Omega Pet EPA DHA; Capsule added to "usual" diet; 100 mg DHA/kg bw; 100 mg EPA/kg bw	*Oxidation* – no difference between treatments for RBC GSH and oxidized GSH. *Inflammation* – no differences between trts for CRP; significantly lower urinary 8-epiprostaglandin F2α (iPF2α-III) Vitamin E content of diet NR.
Westgarth et al., 2018	Cross-over RCT; free-living	1.5-8.9 yrs; Mixed breed; dogue de Bordeaux; Golden Retriever; Doberman; standard poodle; Bernese; Weimaraner; Lab n=6 FO; n=9 FO+aspirin; n=15 total	28 days; Ascenta Canine Omega-3; Capsule added to dry food; 5 mg DHA/kg bw; 20 mg EPA/kg bw	*Coagulation* - Fish oil alone did not significantly affect hemostatic tests, but combining aspirin with fish oil had a greater platelet inhibitory effect than that produced by aspirin alone on some measures of platelet function. There were no bleeding events noted by either the investigators or dog owners in our study. "Our results suggest that therapy with fish oil for up to 4 weeks does not significantly affect haemostasis compared to baseline, perhaps because the anti-platelet effects of fish oil alone might be too mild to detect with the platelet function tests we used. "

APPT - activated partial thromboplastin time; ARA – arachidonic acid (20:4 n-6); AA – arachidonic acid (20:4 n-6); bw – body weight; d= days; CBC – complete blood count; CONT – control; CRP – c-reactive protein ; DHA – docosahexaenoic acid (22:6 n-3); EE – ethyl ester; EM – erythrocyte membrane; EPA – eicosapentaenoic acid (20:5 n-3); FA – fatty acid; FO – fish oil; IAUC – insulin area under the curve; GSH -glutathione; IgA – immunoglobulin A; IgG – immunoglobulin G; mo – months; n-3 – omega-3; n-6 – omega-6; LCPUFA – long-chain polyunsaturated fatty acids; NR – not reported; OSPT - one-stage prothrombin time ;PL- phospholipid; PR interval – P-wave to QRS complex interval; PT – prothrombin time; QRS duration – duration of main spike on an ECG line; QT interval – beginning of QRS complex to end of T wave; QTc – corrected QT interval; RBC – red blood cell; RCT – randomized controlled trial; RR interval – inter-beat interval; TT – thrombin time; TXA2 – thromboxane A2; TXB2 – thromboxane B2; wk – weeks; wt% - weight percent; yrs-years

7.4 Target Animal Safety Studies

7.4.1 Objective of the study

The objective of the study was to evaluate the safety and bioavailability of algal oil containing EPA and DHA as a source of EPA and DHA when administered via diet to beagle dogs throughout gestation, lactation, and growth up to 34 weeks old. This study design was utilized based upon the recommendation of the FDA Center for Veterinary Medicine. The study report is in Annex 11 and the summary of the toxicology studies was published in June of 2019, see Dahms et al. 2019.

The bioavailability of AOCED is discussed further in Section 7.4.8.3 as a means of demonstrating efficacy.

7.4.2 Study design

AOCED was incorporated into extruded dry foods for dogs at 0, 0.75%, 1.5% and 3.0% levels on a dry matter basis at the expense of chicken fat. A larger high dose was considered during discussions with CVM but a 3X dose resulted in an imbalance in fatty acid levels in the food that could not be overcome and would exceed the current maximum safe dose of EPA plus DHA per the NRC. Therefore, a 2x dose was used as the high dose.

The diets were fed to healthy female Beagle dogs starting at mating and throughout gestation and lactation. Puppies were fed their maternal corresponding diets for 26 weeks after weaning.

24 female Beagle dogs were assigned to the study. At the time of randomization, they were between 1.5 and 2.9 years of age with body weights ranging from 9.3 to 11.6 kg. The animals were mated 2 or 3 times with one day intervals between matings. Breeding occurred over 12 days. A different male was used for each female for a total of 24 different males. Successful mating was defined as observation of a tie. Six females per group were mated in order to have a minimum of five pregnancies per group. When all six dams in a group were confirmed pregnant, one dam was randomly selected to be released from the study so that five females per group continued on the study. After transport from the breeding facility to the main research facility, dams were assigned to pens in order of ascending mating number for blinding purposes.

Parturition occurred over 11 days. On post-partum day 1 (PPD 1), the size of the litters with more than six puppies was standardized by random selection to yield six puppies. The removed puppies were cross fostered. On PPD 4, the size of each litter was further adjusted to 4 puppies per litter, with at least one male and one female per litter. Starting on PPD 49, a daily period of separation was introduced. This was gradually increased until complete separation on PPD 56. At weaning on PPD 56, one puppy per sex per litter was randomly retained for the 26-week growth phase of the study. Dams and puppies not selected were transferred to the colony.

Table 29 Dosing plan

Treatment Group	Dosage Level (X of targeted dose)	Target Dosage Level (% of Algal Oil in the Diet on DM basis)	Actual DHA+EPA content (% in the diet on as is basis)	DHA+EPA Content (% in the diet on DM basis)	Number of Animals		
					F_0 Generation (Dams)	F_1 Generation (Puppies)	
					Females	Males (Spare)	Females (Spare)
Group 1 (Control)	0	0	0.11%	0.12%	5	4(1)	4(1)
Group 2	½ X	0.75%	0.41%	0.44%	5	4(1)	4(1)
Group 3	1 X	1.5%	0.77%	0.83%	5	4(1)	4(1)
Group 4	2 X	3.0%	1.55%	1.69%	5	4(1)	4(1)

The animals in Group 1 received the control diet, which was formulated to meet or exceed (without exceeding any maximums) the AAFCO dog food nutrient profile for growth and reproduction (2016), including the minimum requirement for EPA and DHA (0.05%). Instead of being achieved through the addition of algal oil, the EPA and DHA level in the control diet was achieved through the addition of fish oil. Fish oil was not used in the diets fed to Groups 2-4.

Table 30 Treatment allocation

Test diets	Chicken Fat, %	Fish Oil, %	Algal Oil, %
Group 1 (Control)	5.73	0.27	0
Group 2 (1/2 X)	5.28	0	0.72
Group 3 (1 X)	4.55	0	1.45
Group 4 (2 X)	3.11	0	2.89

7.4.3 Diets Offered Prior to the Initiation of the Treatment Period

Dams were fed a commercial standard diet (approximately 400 g of food/day of ProPet Puppy Performance 30/22) containing minimum 30% crude protein and minimum 22% crude fat for at least one week prior to receiving the control diet from Study Days -7 through -1. Daily oral dietary administration to dams (approximately 600 g of food/day) started on the day of the first successful mating and continued until shipment to (b) (4) the main research facility.

7.4.4 Diet Offered During the Study

The dry extruded test diets were manufactured a (b) (4) from May 15-23, 2017. The diets were produced once for the entire study duration. The basal diet, which was formulated to meet the AAFCO Dog Food Nutrient Profile for Growth and Reproduction (2016), was coated with chicken fat, fish oil, or algal oil to produce the test diets. The lot number of the algal oil used to make the diets for Groups 2-4 was (b) (4) The diets were analyzed to confirm that they met the AAFCO Dog Food Nutrient Profile

for Growth and Reproduction (2016) as well as the targeted DHA+EPA concentrations. The diets were made isocaloric with the control diet.

The diets were coded to blind the study center personnel to the test article concentration.

Ingredient composition of the base kibble is presented in Table XXXX while the test diets' composition is shown in Table 29 and 30.

Table 31 Composition of Base Kibble (on As Is basis)

Ingredient Name	%
Chicken by-product meal	26.0
Corn	25.4
Dried eggs	14.9
Brewers rice	12.2
Milo	5.3
Wheat	5.3
Dog Palatability Enhancer (AFB International, MO, USA)	3.2
Corn gluten meal	2.0
Beet pulp	1.9
Dicalcium Phosphate	1.6
Potassium chloride	0.8
Salt	0.7
Vitamin premix[1]	0.3
Calcium carbonate	0.2
Verdilox™ GT Dry[2]	0.1
Mineral premix[3]	0.1
Choline chloride	0.1
Total	100

[1]Contains vitamin E supplement, niacin supplement, thiamine mononitrate, D-calcium pantothenate, vitamin A supplement, pyridoxine hydrochloride, riboflavin supplement, vitamin D3 supplement, vitamin B12 supplement, folic acid, biotin, mineral oil, pea fiber, and calcium carbonate.
[2]Verdilox™ GT Dry is commercial antioxidant and flavoring product from Kemin Industries, Inc (Des Moines, Iowa).
[3]Contains ferrous sulfate, zinc oxide, manganous oxide, copper sulfate, sodium selenite, cobalt carbonate, calcium carbonate, mineral oil, and ethylenediamine dihydriodide.

Table 32 **Fat composition in the test diets (on As Is basis)**

Diet	Control	Low dose AOCED	Mid dose AOCED	High dose AOCED
Ingredients	% of Diet			
Base kibble	94	94	94	94
Chicken fat	5.70	5.25	4.52	3.08
Fish oil (14% EPA, 12% DHA)	0.27	0	0	0
AOCED	0	0.72	1.45	2.89
Verdilox™ GT Liquid	0.03	0.03	0.03	0.03
Total	100	100	100	100

Table 33 **Nutrient composition of the diets compared to the AAFCO recommendation**

	AAFCO Dog Food Nutrient Profile Based on Dry Matter Growth and Reproduction Minimum	CDS002 (DM basis)	CDS003 (DM basis)	CDS004 (DM basis)	CDS005 (DM basis)
Moisture*	N/A	7.4%	6.9%	7.1%	8.3%
Crude Protein	22.5%	30.89%	32.00%	32.29%	32.85%
Arginine	1.0%	1.84%	1.93%	1.98%	2.02%
Histidine	0.44%	0.67%	0.69%	0.70%	0.70%
Isoleucine	0.71%	1.30%	1.33%	1.35%	1.32%
Leucine	1.29%	2.45%	2.52%	2.55%	2.57%
Lysine	0.90%	1.88%	1.90%	1.86%	1.89%
Methionine	0.35%	0.73%	0.75%	0.76%	0.73%
Methionine-cystine	0.70%				
Cystine		0.45%	0.45%	0.47%	0.45%
Phenylalanine	0.83%	1.36%	1.41%	1.43%	1.42%
Phenylalanine-tyrosine	1.30%				
Tyrosine		0.86%	0.91%	0.99%	1.01%
Threonine	1.04%	1.22%	1.26%	1.27%	1.30%
Tryptophan	0.20%	0.36%	0.35%	0.38%	0.38%
Valine	0.68%	1.62%	1.68%	1.69%	1.67%
Crude fat	8.5%	17.53%	17.59%	17.66%	18.75%
Linoleic acid	1.3%	3.60%	3.52%	3.36%	3.02%
Alpha-linolenic acid	0.08%	0.17%	0.16%	0.16%	0.14%
Arachidonic acid		0.17%	0.19%	0.22%	0.26%

	AAFCO Dog Food Nutrient Profile Based on Dry Matter Growth and Reproduction Minimum	CDS002 (DM basis)	CDS003 (DM basis)	CDS004 (DM basis)	CDS005 (DM basis)
Eicosapentaenoic + Docosahexaenoic Acid	0.05%	0.12%	0.44%	0.83%	1.69%
(Linoleic + Arachidonic):(alpha-linolenic + Eicosapentaenoic + Docosahexaenoic) acid ratio	Maximum 30:1				
Calcium	1.2-2.5%	1.72%	1.64%	1.52%	1.36%
Phosphorus	1.0-1.6%	1.24%	1.21%	1.15%	1.09%
Potassium	0.6%	0.98%	0.96%	0.90%	0.82%
Sodium	0.3%	0.600%	0.590%	0.557%	0.513%
Chloride	0.45%	1.32%	1.27%	1.14%	1.04%
Magnesium	0.06%	0.109%	0.108%	0.107%	0.105%
Iron	88 ppm	540 ppm	519 ppm	465 ppm	408 ppm
Copper	12.4 ppm	26 ppm	26 ppm	23 ppm	22 ppm
Manganese	7.2 ppm	87 ppm	90 ppm	79 ppm	77 ppm
Zinc	100 ppm	282 ppm	275 ppm	262 ppm	243 ppm
Iodine	1.0-11 ppm	3.50 ppm	3.19 ppm	3.19 ppm	2.90 ppm
Selenium	0.35-2 ppm	0.84 ppm	0.93 ppm	0.82 ppm	0.77 ppm
Vitamin A	5000-250,000 IU/kg	34,665 IU/kg	31,364 IU/kg	22,978 IU/kg	23,555 IU/kg
Vitamin D	500-3000 IU/kg	2,959 IU/kg	2,256 IU/kg	2,659 IU/kg	2,246 IU/kg
Vitamin E	50 IU/kg	367 IU/kg	359 IU/kg	319 IU/kg	272 IU/kg
Thiamine	2.25 ppm	42.3 ppm	41.7 ppm	40.8 ppm	41.5 ppm
Riboflavin	5.2 ppm	27.6 ppm	19.1 ppm	19.8 ppm	8.6 ppm
Pantothenic acid	12 ppm	43.4 ppm	42.7 ppm	40.3 ppm	41.9 ppm
Niacin	13.6 ppm	232 ppm	230 ppm	249 ppm	201 ppm
Pyridoxine	1.5 ppm	20.2 ppm	20.1 ppm	18.7 ppm	18.8 ppm
Folic acid	0.216 ppm	4.20 ppm	4.10 ppm	3.78 ppm	4.35 ppm
Vitamin B_{12}	0.028 ppm	0.120 ppm	0.116 ppm	0.125 ppm	0.123 ppm
Choline	1360 ppm	3595 ppm	3420 ppm	3600 ppm	3315 ppm

* Moisture content was used to calculate values on a dry matter basis.

Upon receipt at the breeding and main research facilities, diets were stored at room temperature in temperature-controlled rooms. Fatty acid analysis of dietary samples collected throughout the study confirmed acceptable levels of EPA and DHA which ensured proper algal oil dosing of animals.

Dams received approximately 900 g of food per day from parturition until weaning. Starting at 5 weeks of age and until weaning, puppies were provided with a feeding pan (approximately 300 g of feed). During that period, the daily food intake was calculated for the dam plus its litter (i.e.: dam's bowl, plus feeding

pan) since the dam also had access to the feeding pan. After weaning, puppies selected for the study continued on their mothers' respective diets (approximately 400 g per day/dog for a 6-8 hours daily feeding period) for the additional 26 weeks until they reached 34 weeks of age. Puppies remained pair-housed for feeding during the first two weeks post-weaning to confirm ability to thrive, and then were individually housed for feeding for the remainder of the study.

7.4.5 Animal Care

The care and use of animals were conducted in accordance with the principles outlined in the current guidelines published by the Canadian Council on Animal Care and the guide for care and use of laboratory animals, an NRC publication, and USDA regulations. The test facility is accredited by the Canadian Council on Animal Care and AAALAC.

7.4.6 Housing

Dams (F_0) were individually housed in approximately 3' x 6' pens at the breeding facility and in approximately 5' x 6' European cages at the main research facility, equipped with an automatic watering system.

Approximately two weeks prior to parturition, a nesting box was provided to each dam. A litter pan was given to the puppies from weaning until approximately 3-4 months of age.

After weaning, puppies selected for the F_1 generation were pair housed in approximately 3' x 3' stainless steel dog cages equipped with an automatic watering system (water was provided ad libitum), but were separated during the 6-8 hour daily feeding period starting the third week post-weaning in order to acquire individual food consumption data. One male and one female were housed together in each group to harmonize the food consumption values between cages during the first two weeks post-weaning (of the youngest litter). Thereafter, puppies were pair housed by sex and by group. Throughout the weaning process and after weaning, dams were individually housed in approximately 3' x 3' stainless steel dog cages equipped with an automatic watering system. Puppies not selected to continue on study remained in European cages until their release from the study approximately two weeks after weaning. All cages were clearly labeled with cage cards, indicating a study number, animal tattoo number, blinded animal assignment number, sex, and replicate. All animals were transferred to the colony upon completion of the study.

7.4.7 Clinical Observations

During the gestation and lactation phases, assessments on dams included mortality checks, clinical observations, body temperature, heart rate, respiratory rate, body weights, food, consumption, parturition observations, and determination of litter size with external sex determination of puppies.

During the lactation and growth phases, assessments on puppies included mortality checks, clinical observations, height, head circumference, body temperature, heart rate, respiratory rate, body weights, and food consumption.

Personnel involved in the in-life data collection were blinded to the experimental groups. However, the Study Director, the Principal Investigator (at (b) (4), the Clinical Pathologist, the pharmacy staff and the departmental team leaders were not blinded.

These unblinded personnel did not participate in direct evaluation of the animals or data collection. Observations were performed cage-side and during scheduled detailed clinical examinations. Any clinical findings were referred to the Clinical Veterinarian. Clinical signs (ill health, behavioral changes, etc.) were recorded on all animals twice daily throughout the study. The nature of these observations included evaluation of general appearance, activity, and other indicators of changes in animal health and behavior, including fur conditions, gait, and mobility. Litter checks were performed once daily until PPD 56.

A detailed clinical examination was performed on each animal on the day of estrous and on the day of treatment initiation, and once within the week prior to transfer to (b) (4) and monthly thereafter. A detailed clinical examination was also performed on the day prior to or on the day of release from the study. During the detailed examination, animals were first observed in the cage for behavior, general appearance, and coordination. Then they were removed from the cage for close evaluation of general condition of the whole-body including head, thoracic, and abdominal areas through examination and palpation. Body temperature, heart rate, and respiratory rate were also evaluated.

For all puppies, height and head circumference were also measured weekly starting on PPD 7. In addition, a detailed examination, including body temperature, heart rate, and respiratory rate, was performed on all puppies assigned to the F_1 generation growth phase by blinded technical staff starting on PPD63 (1week post-weaning) and once monthly thereafter, including within 3 days prior to release from the study. This also included assessment of the general body condition, autonomic and central nervous system, somatomotor activity, gait, skin/fur condition, lymph nodes, eyes, mucus membranes, respiration, behavior, circulatory system, state of hydration, and lungs, bladder, reproductive system and gastrointestinal auscultation and/or palpation.

7.4.7.1. Mortality

Mortality checks were recorded concomitantly with the cage-side clinical signs observations during all phases of the study.

7.4.7.2 Body Weights

Body weights were recorded for all dams on the day of estrous and on the day of treatment initiation, and weekly thereafter.

Puppies were weighed every 3 or 4 days, i.e., PPD 0, 4, 10, 14, etc., until weaning, and weekly thereafter.

A body weight measurement was also performed on dams and puppies on the day prior to release from the study.

7.4.7.3 Food Consumption

Individual food intake was measured on all animals daily starting at imitation of feeding the reference/control diet (3-14 days prior to treatment start). In addition to the daily food consumption, achieved intakes were calculated on a weekly basis. Any spilled food was also weighed daily for each cage,

unless clearly contaminated with liquid or solid material (e.g. water, urine, feces, etc.). The amount of contaminated food (excluded from the spillage measured value) was visually estimated and documented.

The average of daily individual achieved intake of the test item in mg/kg/bw per week was calculated for both generations based on daily food consumption taking into account any spilled food.

The average exposure to AOCED in mg/Kg BW for the dams from week 1 to week 8 was 0 for the control group, 209.8 – 277.9 for the low dose, 378.3 – 494.4 for the mid-dose and 799.8- 1021.2 for the high dose.

For the puppies, the average exposure to AOCED in mg/Kg BW from week 3 to 26 was zero for the controls, for the male puppies the exposure decreased over time from 288.9 – 150.5 for the low dose group, 581.0 – 281.1 for the mid-dose group and 1215.3- 612.7 for the high dose group. For female puppies the exposure was 288.2 – 162.5 for the low dose group, 488.82 – 313.1 for the mid-dose group and1189.0 – 606.8 for the high dose group.

7.4.7.4 Parturition and litter observations

The time of onset and completion of delivery was recorded for each animal when possible. The day when parturition was completed was termed as PPD 0. Any signs of difficulty in parturition were recorded. Number of live, dead and malformed puppies was recorded at birth. Gross abnormalities were recorded, if present. Number of male and female puppies in each litter was determined by visually judging the anogenital distance and/or presence of a vulva or penis. Recordings of live and dead puppies continued daily from PPD 0 until weaning on PPD 56.

7.4.7.5 Clinical Pathology

Clinical pathology evaluations (hematology and clinical chemistry) were performed on all dams once during pretreatment and at weaning.

Coagulation and urinalysis were performed on all puppies during Weeks 13 and 34. Hematology and clinical chemistry evaluation was performed at weaning and every two months thereafter for a total of 4 occasions during the growth phase.

7.4.7.6 Statistical Analysis

The statistical analyses for this study were designed with reference to the Guidance for Industry #226: "Target Animal Safety Data Presentation and Statistical Analysis" of the Center of Veterinary Medicine (CVM), a division of the US Food and Drug Administration (FDA). As recommended by the guidance, no statistical adjustments for multiplicity were applied to avoid false negative findings and the significance level for comparisons against the control group was α=0.1 for safety endpoints. The interpretation of the results was based both on statistical significance and clinical relevance, as recommended by the guidance.

The statistical analyses were independently performed for the following three periods: gestation, pre and post weaning. The treatment group was used as a fixed effect in all models.

Analysis of variance (ANOVA), analysis of covariance (ANCOVA) as well as repeated measures ANOVA/ANCOVA and linear mixed models were employed, depending on the available number of timepoints within a period and whether a baseline measurement was available.

For parameters with only one timepoint within a period, with only one sex and without baseline value, a one-way ANOVA was applied, e.g. for pre-treatment body-weights of dams. If a baseline, i.e. pre-treatment value was also available then ANCOVA was applied, including the baseline as covariate, e.g. for clinical

pathology measurements of dams at weaning. Analysis on pre-weaning puppies included only those selected to continue on study after litters were equalized.
For parameters with more than one timepoint within a period, repeated measures equivalents of the above methods were employed to take into account potential effects over time. The fixed effects in the models were the treatment group, the time and their interaction, with the animal as subject and, when applicable, the pre-treatment value as covariate. For the efficacy parameters (EPA and DHA plasma levels), mixed effects models with random intercept by animal were used.
Three-way repeated measures ANOVA were used for longitudinal analyses on puppies, where males and females had to be differentiated, and when more than one follow-up timepoint within a period was available, e.g. for body weight of puppies post-weaning. The fixed effects in the model were the treatment group, sex, time and their two-way and three-way interactions with the animal as subject. For the pre-weaning period, the statistical unit was the puppy nested within litter.
Inter-group differences of the time to event curve estimates were tested using the log-rank test.

7.4.8 Results and Discussion

7.4.8.1 F_0 Generation

No clinical signs were considered related to the administration of algal oil during the gestation or the lactation periods of the dams during this study. Variations in stool consistency were observed in all groups, including the control group. Similarly, reduced/absent fecal output was observed across all groups throughout the gestation and lactation periods. Fecal changes are common in laboratory-housed beagles, especially during pregnancy and/or parturition, so they were not considered related to the consumption of the experimental diets.

There were no algal oil-related effects on body temperatures, heart rate, respiratory rate during the gestation or the lactation periods of the dams at any dose level.

There were no treatment related effects on food consumption in females during the gestation and lactation phases of the study. There were no statistically-significant differences between groups in body weights during gestation but there was a trend to higher body weights and body weight gains in all algal oil groups when compared to control. During the lactation period, average body weights of the dams were comparable across all groups and average body weight changes were not affected by the test diets.

There were no clinically significant changes observed in hematology and clinical chemistry parameters in the dams of the algal oil groups when compared to the control group at the completion of the lactation phase.

No dams were found dead or had to be euthanized during the study. However, three dams were released from the study shortly after completion of the parturition process since they were left with no live puppies. The three cases were not considered related to the administration of the test diets given their dissimilar etiology and were likely incidental in nature. All other dams displayed normal maternal behavior.

7.4.8.2 F_1 Generation

There were no algal oil related effects on litter size or viability index at birth. The percentage of live puppies at birth varied from 89% in the control group to 100% in the high dose group. Mean body weights of puppies at birth were similar across groups with a trend to higher values in the low and mid-dose algal oil groups in both males and females. The viability and survival indices were generally higher in the algal oil groups, especially in the high dose group were only a single death was observed out of 38 born puppies.

There were no clinical observations in puppies from birth to weaning that were considered attributable to the dietary treatments. Clinical signs included skin changes (bruises, dryness, redness, lump, scabbed, wounded), tail kinked, firm/soft swelling of flank or cervical dorsal areas, and fur thin/dull/stained. Most of the adverse clinical observations (decreased activity, weakness, recumbency, body thinness, cold to touch, signs of dehydration) were noted prior to PPD 5 in puppies that did not survive. These effects were considered incidental since they occurred across all groups including the control, are common in puppies of this age and species, and showed no relationship to dose levels.

On PPD 56, one puppy from the high dose group exhibited red buccal discharge, retching, labored and increased respiration, as well as being cold to the touch. This was observed shortly after blood sampling and was thus considered related to the procedure. The puppy was released from the study on PPD 56 and replaced by a spare from the same litter to continue to the growth phase of the study.

Mean body weights of puppies from birth to weaning were increased in the low and mid dose groups compared to the control in both sexes, reaching statistical significance on most occasions. There was no dose response, so these increases were considered incidental and not related to the administration of algal oil.

There were no algal oil related effects on height or height changes of the puppies from the first measurement on PPD 7 until weaning. During the lactation period, the mean litter head circumference of puppies in the low and mid dose groups was increased compared to that in the control in both sexes, reaching statistical significance on most measurement occasions, especially during the first half of the lactation phase. The differences mainly disappeared by weaning, and the mean values were similar among all groups. Given the lack of dose-response and transient nature, these increases were considered incidental and not related to the diets.

There were no mortalities in any group during the growth phase of the study which lasted for 26 weeks after weaning. Further, there were no algal oil-related clinical observations during this phase. Some sporadic changes in stool consistency occurred across all groups including the control and were, therefore, considered incidental. There were no differences among groups in body temperature, heart rate, and respiratory rate during the growth period. From weaning onward, mean body weights of the low and high dose puppies were increased compared to the control in both sexes, reaching statistical significance on most occasions from PPD 182 onward. Consequently, the overall mean body weight gains for the whole

growth phase (PPD 238 compared to 56) in the low and high dose groups were generally above the mean of the control group. In the males of the mid dose group, mean body weights in the second half of the growth phase were lower than those in the control. Given the lack of dose response, the body weight changes were considered incidental and not related to algal oil.

The group mean food consumption after weaning was comparable across all groups, including control, in both sexes. No changes in hematology, clinical chemistry and coagulation parameters were noted in puppies fed the test diets compared to those fed the control diet at the study completion. Differences were observed in some hematology parameters over the different time points during the study, but they were transient and consistent with normal biological variability in growing dogs and thus considered incidental. No changes were noted in coagulation parameters during the study at both measurements. Creatinine values increased over time in all animals with primary increases by PPD 168 and peaking at PPD 224. This was expected due to increased muscle mass during the growth period and was noted in all groups, including the control.

7.4.8.3 Effect of AOCED on blood levels of EPA and DHA

The concentration of DHA and EPA in the blood plasma of the test article treatments groups increased over time and with dose level versus the control as shown in the tables and charts below, indicating that AOCED is an effective source of those omega-3 fatty acids when incorporated into food for dogs, which is the proposed purpose of the material. The more detailed information regarding the analysis in Appendix 62 of the (b) (4) report, Annex 11.

Table 34 Blood Plasma DHA concentration, Dams

DHA	Description	Pretreat F0	GD28 F0	PPD56 F0
Group 1	Control	61.14 (8.63)	90.34 (6.85)	75.29 (11.43)
Group 2	Low dose	83.78 (9.25)	223.5 (45.4)	319.7 (36.6)
Group 3	Mid dose	75.14 (17.74)	313.9 (116.2)	359.6 (92.4)
Group 4	High dose	73.96 (17.87)	318.7 (32.3)	391.03 (14.40)

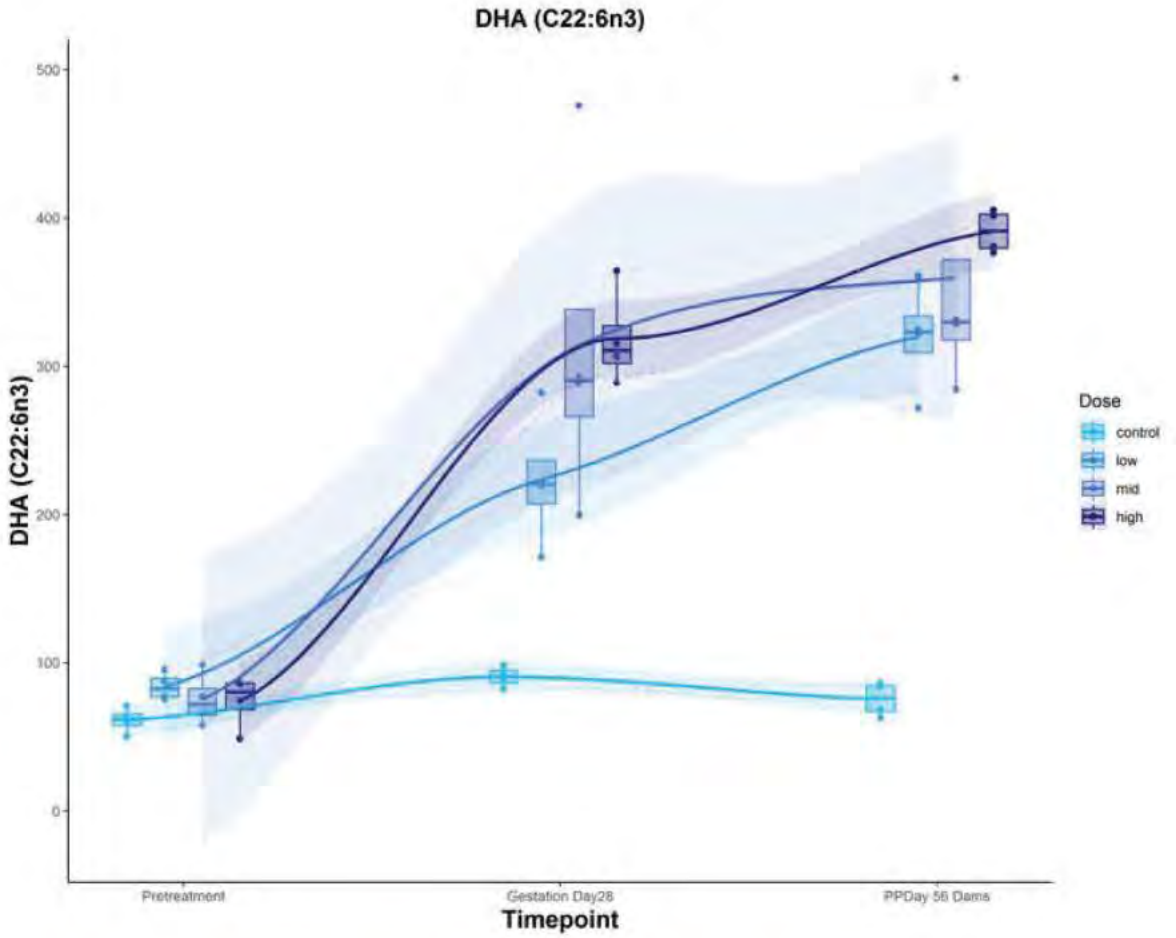


Figure 21 Blood Plasma DHA Concentration over time, Dams

Table 35 Blood Plasma EPA concentration, Dams

EPA	Description	Pretreat F0	GD28 F0	PPD56 F0
Group 1	Control	20.62 (3.37)	15.47 (4.11)	27.66 (4.41)
Group 2	Low dose	23.79 (5.67)	36.15 (5.16)	79.53 (19.80)
Group 3	Mid dose	27.91 (1.76)	94.20 (49.8)	173.6 (44.4)
Group 4	High dose	24.39 (2.69)	116.1 (42.5)	267.2 (57.9)

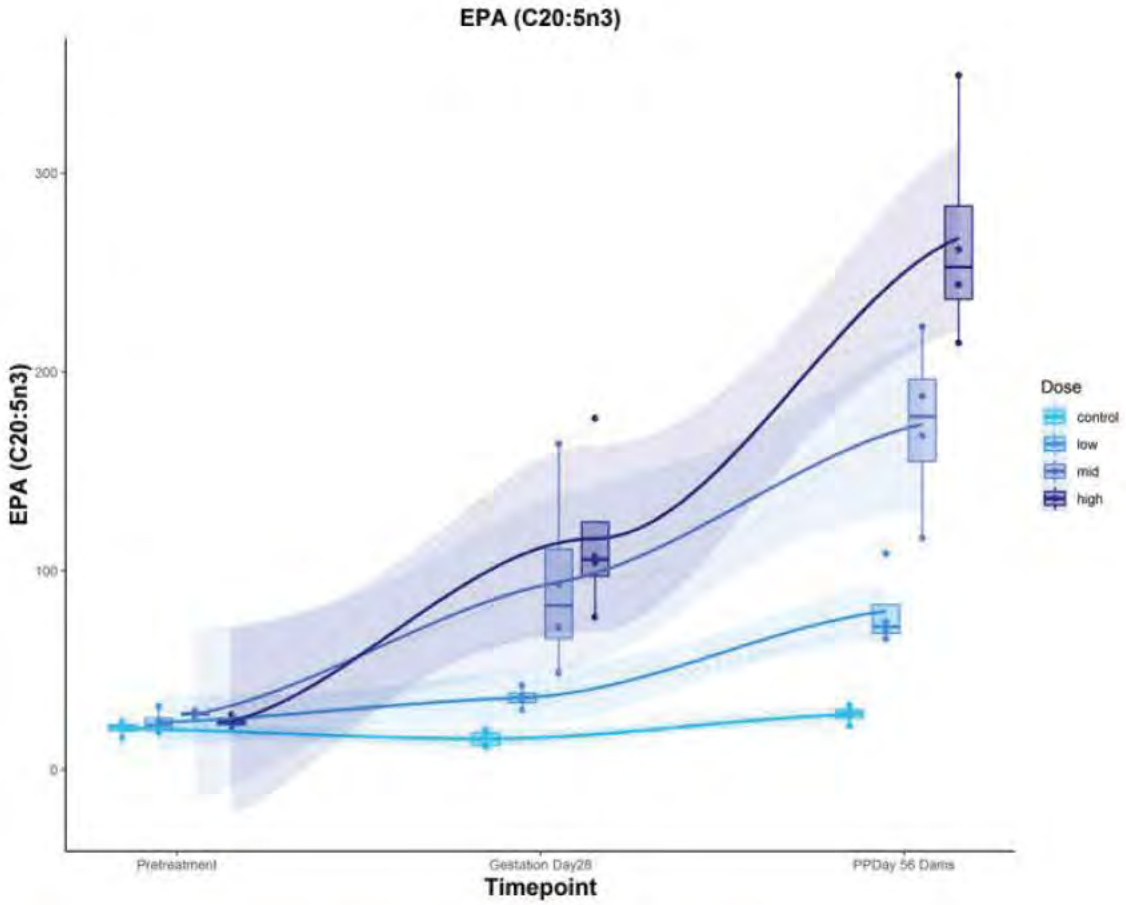


Figure 22 Blood Plasma EPA Concentration over time, Dams

Puppy Data

Table 36 Blood Plasma DHA concentration, puppies

DHA	Description	PPD 56 F1	Week 13 F1	Week 34 F1
Group 1	Control	138.61 (12.02)	150.31 (14.22)	99.28 (13.34)
Group 2	Low dose	295.52 (23.68)	282.6 (25.58)	237.35 (27.52)
Group 3	Mid dose	353.40 (42.9)	337.9 (32.3)	268.6 (33.70)
Group 4	High dose	339.65 (24.37)	363.8 (34.9)	338.5 (51.0)

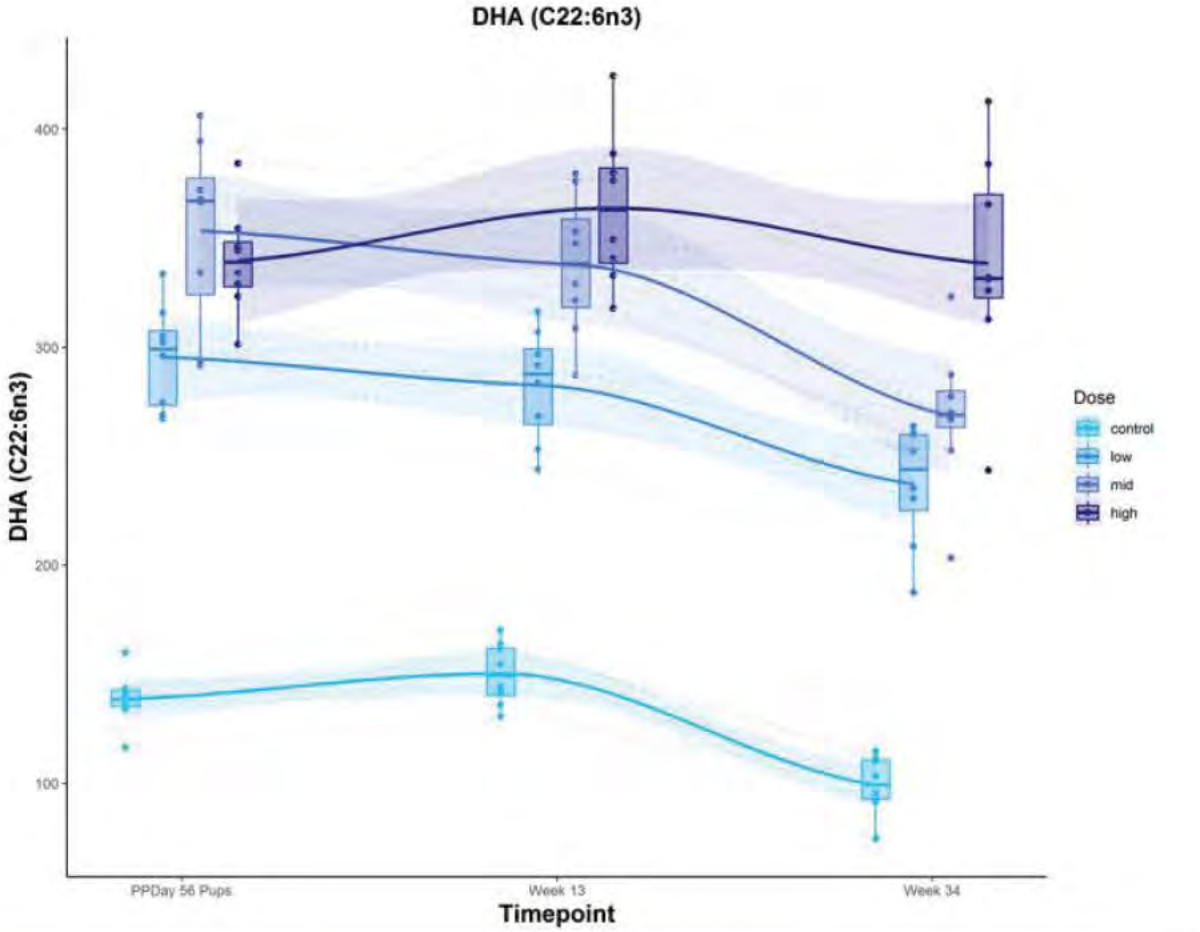


Figure 23 Blood Plasma DHA concentration over time, puppies

Table 37 Blood Plasma EPA concentration, puppies

EPA	Description	PPD 56 F1	Week 13 F1	Week 34 F1
Group 1	Control	14.33 (2.42)	17.55 (1.94)	16.26 (2.06)
Group 2	Low dose	49.08 (9.73)	57.98 (6.95)	59.50 (17.09)
Group 3	Mid dose	101.11(18.42)	115.03 (11.41)	109.59 (17.47)
Group 4	High dose	145.0 (28.9)	182.58 (23.89)	205.9 (32.5)

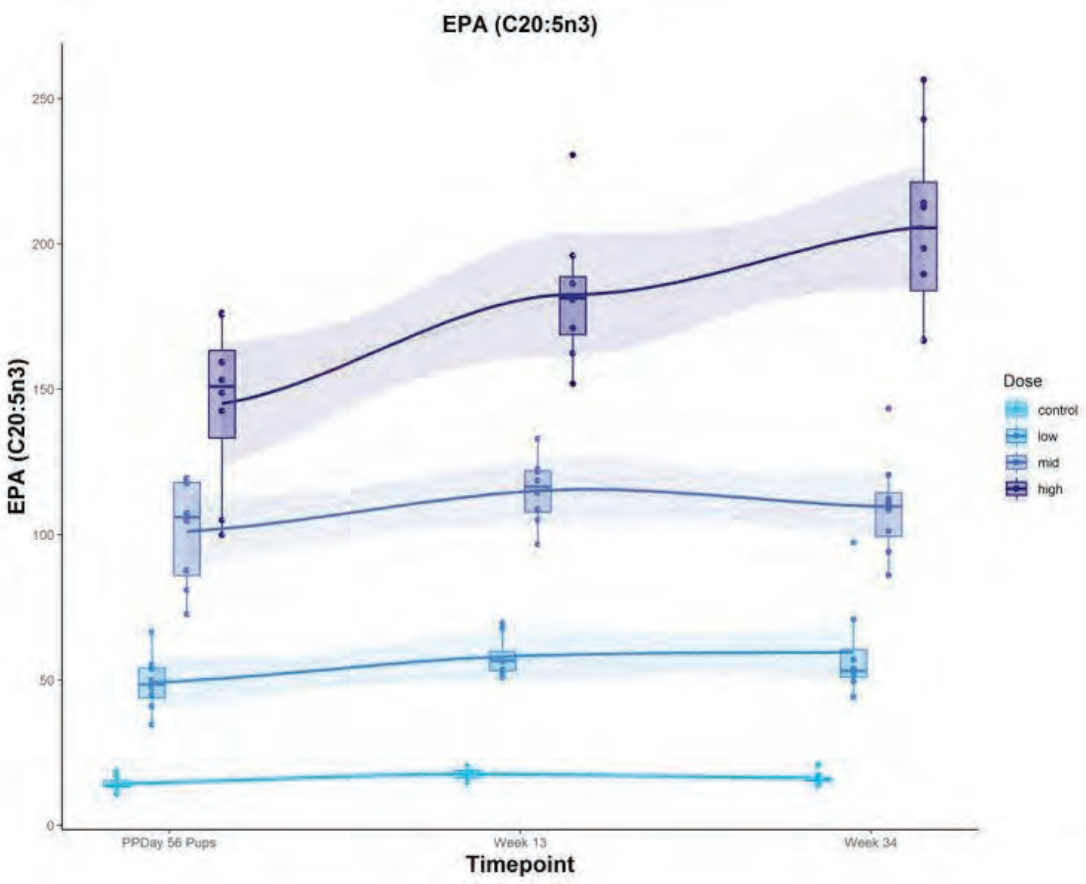


Figure 24 Blood Plasma EPA concentration over time, puppies

7.4.8.4 Statement of compliance with GLP

The GLG study was not conducted in accordance with 21 CFR Part 58, good laboratory practice (GLP) for nonclinical laboratory studies as CVM had been informed during a study protocol review in late 2016. However, the study site was visited and monitored by sponsor personnel familiar with GLP. The study facility works according to standard operating procedures and the study differed from GLP only in that the study did not have a quality assurance unit. Veramaris confirms that the results of the study have not been compromised by the lack of a QA unit.

7.5 Information that may appear to be inconsistent with the GRAS determination

Important potential adverse effects of omega-3 fatty acid supplementation from fish oil include altered platelet function, gastrointestinal adverse effects, detrimental effects on wound healing, lipid peroxidation, potential for nutrient excess and toxin exposure, weight gain, altered immune function, effects on glycemic control and insulin sensitivity, and nutrient-drug interactions. (Lenox and Bauer, 2013) The potential adverse effects noted by the authors in the studies reviewed were typically seen where diets for cats or dogs contained concentrations of EPA and DHA greater than 2.0 gm/Kg of food. The current NRC recommendation for a safe upper limit for EPA plus DHA for dogs is 370 mg/Kg body weight.

AOCED is at a minimum 50% EPA plus DHA, see section 2.5 in this dossier and the lot used to produce the dog food used in the GLG study was (b) (4) with a combined DHA + EPA concentration of 52.5%, see Annex 1. The high dose in the GLG study was 319.4 to 1243.9 mg/Kg BW for the dams and 231.7 to 959.5 for male puppies and 236.6 to 975.8 for female puppies, see table 19 in section 3.1.1 of this dossier.

Consequently, the exposure to the combined EPA and DHA was 167.7 to 653.0 mg/Kg BW for dams and 121.6 to 503.7 mg/Kg BW for male and 124.2 to 512.3 mg/Kg BW for female puppies. These exposures for the high dose, which did not result in any clinical physiological or blood chemistry adverse effects, which were slightly higher than the NRC maximum recommended dose indicates that the mid-dose, the highest expected commercial dose will not induce any adverse effects in dogs.

7.6 Summary

The organism used to produce the substance is not known to be toxic to animals and analysis of parent and sister strain has shown that modifications have not cause the organism to produce known algal toxins. The 90-day rat study and GLG study with Beagle dogs also did not reveal and harmful effects from consumption of the purified oil produced by the *Shizochytrium sp.* Organism within the anticipated use levels. Efficacy studies indicate that the product, AOCED delivers the anticipated effect, elevation of the DHA and EPA concentration in blood plasma.

8 Annexes

Annex 1: Certificates of Analysis for AOCED

Annex 2: Prymnesin analysis

Annex 3: Domoic acid analysis, parent strain

Annex 4: Raw Material Speciifcations

Annex 5: AOCED Stability Report

Annex 6: AOCED Stability Summary 25 and 40 C

Annex 7: Stat-Analysis_1152_Dog_Kibble_Post-extrusion

Annex 8: Stat-Analysis_1309_Dog_Kibble_pre-extrusion

Annex 9: Heavy Metals Analysis

Annex 10: Pesticide Analysis

Annex 11: Dog GLG Final Report

Annex 12: Literature search terms

Annex 13: Domoic Acid analysis, production strain

9 References

Abril, J.R., Barclay, W.R. and Abril, P.G., 2000. Safe use of Microalgae (DHA GOLD™) in Laying Hen Feed for the Production of DHA-Enriched Eggs. CAB International, Egg Nutrition and Biotechnology.eds. J.S. Sim, S. Nakai and W. Guenter.

Bahnweg, G. 2009. Identification of MK27173. Private communication.

Bahnweg, G. 2010. Verification of Identity of (Schizochytrium sp). Private communication.

Barclay,W. and Zeller, S., 1996. Nutritional Enhancement of n-3 and n-6 Fatty Acids in, Rotifers and *Artemia* Nauplii by Feeding Spray-dried *Schizochytrium* sp. J. World Aqua. Soc., 27 (3), 314-322.

Bennett, R.M., Honda, D., Beakes, G.W. and Thines, M., 2017. Labyrinthulomycota, Hanbook of the Protists. 507-542.

Alvarex, R.A., Aguirre, G.D., Acland, G.M. and Anderson, R.E., 1994. Docosapentaenoic Acid Is Converted to Docosahexaenoic Acid in the Retinas of Normal and prcd-Affected Miniature Poodle Dogs. Invest. Opthal. Vis. Sci. 35 (2), 402-408.

Brenna, J.T., Salem, N., Sinclair, A.J., and Cunname, S.C., 2009. α-Linolenic acid supplementation and conversion to n-3 long-chain polyunsaturated fatty acids in humans. Prostaglandins, Leukotrienes and Essential Fatty Acids, 80 (2), 85-91.

Bauer, J.E., McAllister, K.G. and Markwell, P., 1997. Molecular species of cholesteryl esters formed via plasma lecithin: Cholesterol acyltransferase in fish oil supplemented dogs. Nutrition Res., 17 (5), 861-872.

Bauer, J.E., Waldron, M.K., Spencer, A.L. and Hannah, S.S., 2002. Predictive Equations for the Quantitation of Polyunsaturated Fats in Dog Plasma and Neutrophils from Dietary Fatty Acid Profiles. J. Nutrition, 132, 1642S-1645S.

Bauer, J.E., Heinemann, K.M., Bigley, K.E., Lees, G.E. and Waldron, M.K., 2004. Maternal Diet a-Linolenic Acid during Gestation and Lactation Does Not Increase Docosahexaenoic Acid in Canine Milk. J. Nutr. 134: 2035S–2038S.

Brenner, R.R. and Peluffo, P.O., 1966. Effect of Saturated and Unsaturated Fatty Acids on the Desaturation *in Vitro* of Palmitic, Stearic, Oleic, Linoleic, and Linolenic Acids. J. Biological Chem. 241 (20), 5213-5219.

Byrne, K.P., Campbell, K.L., Davis, C.A., Scheaffer, D.J. and Troutt, F., 2000. The effects of dietary n-3 vs. n-6 fatty acids in *ex-vivo* LTB_4 generation by canine neutrophils. Vet. Derm. 11, 123-131.

Cavalier-Smith, T., 2018. Kingdom Chromista and its eight phyla: a new synthesis emphasising periplastid protein targeting, cytoskeletal and periplastid evolution, and ancient divergences. Protoplasma, 255, 297–357.

CFIA, Canadian Food Inspection Agency. Metal Contaminants. www.inspection.gc.ca/animals/feeds/regulatoryguidance/rg8/eng/1347383943203/1347384015909?chap=4

Dahms, I., Bailey-Hall, E. and Salem, N., 2016. Kinetics of docosahexaenoic acid ethyl ester accumulation in dog plasma and brain. Prostaglandins, LeukotrienesandEssentialFattyAcids113, 1–8.

Dahms, I., Belstein, P., Bonnette, K. and Salem, N. 2016. Safety of docosahexaenoic acid (DHA) administered as DHA ethyl ester in a 9-month toxicity study in dogs. Food and Chemical Toxicology 92, 50-57.

Dahms, I., Bailey-Hall, E., Sylvester, E., Parenteau, A., Yo, S, Karagiannis, A., Roos, F and Wilson, J., 2019. Safety of a novel feed ingredient, Algal Oil containing EPA and DHA, in a gestation-lactation- growth feeding study in Beagle dogs. PLoS ONE 14 (6): e0217794. https://doi.org/10.1371/journal.pone.0217794.

deGodoy, M.R.C., Conway, C.E., McLeod, K.R. and Harmon, D.L., 2015. Influence of feeding a fish oil-containing diet to young, lean, adult dogs: effects on lipid metabolites, postprandial glycaemia and body weight. Archives Am. Nutri., 69 (6), 499-514.

deGodoy, M.R.C., McLeod, K.R. and Harmon, D.L., 2018. Influence of feeding a fish oil- containing diet to mature, overweight dogs: Effects on lipid metabolites, postprandial glycaemia and body weight. J Anim Physiol Anim Nutr., 102, e155–e165.

Dunbar, B.L. and Bauer, J.E., 2002. Conversion of Essential Fatty Acids by Delta 6-Desaturase in Dog Liver Microsomes. J. Nutrition, 132 (6) 1701S -1703S.

Dunbar, B.L., Bigley, K.E. and Bauer, J.E., 2010. Early and Sustained Enrichment of Serum n-3 Long Chain Polyunsaturated Fatty Acids in Dogs Fed a Flaxseed Supplemented Diet. Lipids 45,1–10.

Federal Register, 2014. DSM Nutritional Products; Filing of Food Additive Petition (Animal Use). Vol. 79 (200) 62090.

Federal Register, 2018. Food Additives Permitted in Feed and Drinking Water of Animals; Marine Microalgae. Vol. 83 (88) 19934.

FDA GRAS Letter, GRN 533, 2015.

Fritz, L., Quilliam, M.A., Wright, J.L.C., Beale, A.M. and Work, T.M., 1992. An outbreak of domoic acid poisoning attributed to thee pennate diatom *Pseudonitzchia australis*. J. Phycol. 28, 439-442.

Hadley KB, Bauer J, Milgram NW. The oil-rich alga Schizochytrium sp. as a dietary source of docosahexaenoic acid improves shape discrimination learning associated with visual processing in a canine model of senescence. Prostaglandins Leukotrienes and Essential Fatty Acids. 2017;118(Journal Article):10-8.

Houdan, A., Bonnard, A., Fresnel, J., Fouchard, S., Billard, C. and Probert, I., 2004. Toxicity of coastal coccolithophores (Prymnesiophyceae, Haptophyta). J. Plankton Res., 26 (8), 875–883.

Garrison, D.L., Conrad, S.M., Eilers, P.P. and Wldron, E.M., 1992. Confirmation of domoic acid production by *Pseudonitzschia austalis* (Bacillariophyceae) cultures. J. Phycol. 28, 604-607.

Graneli, E. and Johansson, N., 2003. Increase in the production of allelopathic substances by *Prymnesium parvum* cells grown under N- or P-deficient conditions. Harmful Algae, (2), 135–145.

Hall, J.A., Wander, R.C., Gradin, J.L., D, S.H., and Jewell, D.E., 1999. Effect of dietary n-6 to n-3 fatty acid ratio on complete blood and total white blood cell counts, and T-cell subpopulations in aged dogs. American Journal Veterinary Research, 60 (3), 319-326.

Hall, J.A., Tooley, K.A., Gradin, J.L., Jewell, D.E. and Wander, R.C., 2002. Influence of dietary long-chain n-3 fatty acids from Menhaden fish oil on plasma concentrations of α-tocopherol in geriatric Beagles. American Journal Veterinary Research, 63 (1), 104-110.

Hall, J.A., Chinn, R.M., Vorachek, W.R., Gorman, M.E., Greitl, J.L. Joshi, D.K. and Jewell, D.E., 2011a. Influence of dietary antioxidants and fatty acids on neutrophil mediated bacterial killing and gene expression in healthy Beagles. Veterinary Immunology and Immunopathology 139, 217–228.

Hall. J.A., Brockman, J.A. and Jewell, D.E., 2011b. Dietary fish oil alters the lysophospholipid metabolomic profile and decreases urinary 11-dehydro thromboxane B2 concentration in healthy Beagles. Veterinary Immunology and Immunopathology 144, 355– 365.

Hammond, B.G., D.A. Mayhew, M.W. Naylor, F.A. Ruecker, R.W. Mast and W.J. Sander. (2001a). Safety Assessment of DHA-Rich Microalgae from *Schizochytrium* sp.- I. Subchronic Rat Feeding Study. Regulatory Toxicology and Pharmacology 33, 192-204.

Hammond, B.G., D.A. Mayhew, J.F. Holson, M.D. Nemec, R.W. Mast and W.J. Sander (2001b). Safety Assessment of DHA-Rich Microalgae from *Schizochytrium* sp.- II. Developmental Toxicity Evaluation in Rats and Rabbits. Regulatory Toxicology and Pharmacology 33, 205-217.

Hammond, B.G., D.A. Mayhew, K. Robinson, R.W. Mast and W.J. Sander (2001c). Safety Assessment of DHA-Rich Microalgae from *Schizochytrium sp.*- III. Single Generation Rat Reproduction Study. Regulatory Toxicology and Pharmacology 33, 356-362.

Hammond, B.G., D.A. Mayhew, L.D. Kier, R.W. Mast and W.J. Sander (2002). Safety Assessment of DHA-Rich Microalgae from *Schizochytrium sp.*- IV. Mutagenicity Studies. Regulatory Toxicology and Pharmacology 35, 255-265.

Heinemann, K.M., Waldron, M.K., Bigley, K.E., Lees, G.E. and Bauer, J.E., 2005. Long-Chain (n-3) Polyunsaturated Fatty Acids Are More Efficient than α-Linolenic Acid in Improving Electroretinogram Responses of Puppies Exposed during Gestation, Lactation, and Weaning. *Journal of Nutrition,* Vol. 135 (8), 1960-1966.

Hesta, M., Verbrugghe, A., Gulbrandsen, K.E., Christophe, A., Zentek, J., Hellweg, P, and Janssens, G.P.J., 2012. Biological effects of short-term salmon oil administration, using distinct salmon oil sources in healthy dogs. Journal of Small Animal Practice 53, 699–704.

Jamikorn, U. and Yibchok-anun, S., 2014. Effects of Dietary Polyunsaturated Fatty Acid Supplement on Healthy Beagle Dogs. Thai J Vet Med. 44(4): 505-511.

Lands W.E.M., Libelt, B., Morris, A., Kramer, N.C., Prewitt, T.E., Bowen, P., Schmeisser, D., Davidson, M.H., and Burne, J.H., 1992. Maintenance of lower proportions of (n - 6) eicosanoid precursors in phospholipids of human plasma in response to added dietary (n - 3) fatty acids. Biochemica Biophysica Acta., 1180, 147-162.

Larsen, A., Eirkrem, W. and Paasche, Eystein., 1993. Growth and toxicity in *Prymnesium patelliferum* (Prymnesiophyceae) isolated from Norwegian waters. Can. J. Bot. (7), 1357-1362.

LeBlanc, C.J., Dietrich, M.A., Horohov, D.W., Bauer, J.E., Hosgood, G. and Mauldin, G.E., 2007. Effects of dietary fish oil and vitamin E supplementation on canine lymphocyte proliferation evaluated using a flow cytometric technique. Veterinary Immunology and Immunopathology 119 (2007) 180–188.

Lenox CE, Bauer JE. Potential adverse effects of omega-3 fatty acids in dogs and cats. Journal of Veterinary Internal Medicine. 2013;27(2):217-26.

Lundholm, N., Skov, J., Pocklington, R. and Moestrup, O., 1994. Domoic acid, the toxic amino acid responsible for amnesic shellfish poisoning, now in Pseudonitzschia seriata (Bacillariophyceae) in Europe. Phycologia. Vol 33 (6), 475-478.

Liu, M., Bagdade, J.D. and Subbaiah, P.V., 1995. Specificity of lecithin:cholesterol acyltransferase and atherogenic risk: comparative studies on the plasma composition and in vitro synthesis of cholesteryl esters in 14 vertebrate species. J. Lipid Res. 36, 1813-1824.

Mooney, M.A., Vaughn, D.M., Reinhart, G.A., Powers, R.D., Wright, J.C., Hoffman, C.E., Swaim, S.F. and Baker, H.J., 1998. Evaluation of the effects of Omega-3 fatty acid containing diets on the inflammatory stage of wound healing in dogs. American Journal Veterinary Research, 59 (7), 859-863.

Mordenti, A.I., Bonaldo, L.S., Pizzamiglio, V., Brogna, N., Cipollini, I., Tassinari, M. and Zaghini, G., 2010. Influence of marine algae (Schizochytrium spp.) dietary supplementation on doe performance and progeny meat quality. Livestock Science 128, 179–184.

Pawlosky R., Barnes A. and Salem N. Jr.,1994. Essential fatty acid metabolism in the feline: relationship between liver and brain production of long-chain polyunsaturated fatty acids. J. Lipid Res. **35**: 2032–2040.

Pellegrino, F.J., Risso, A., Relling, A. E. and Corrada, Y., 2017. Physical response of dogs supplemented with fish oil during a treadmill training programme. J Anim Physiol Anim Nutr. 1–8.

Ramadeen, A., Connelly, K.A., Leong-Poi, H., Hu, X., Fujii, H., Laurent, G., Domenichiello, A.F., Bazinet, R.P. and Doran, P., 2012. Docosahexaenoic Acid, but Not Eicosapentaenoic Acid, Supplementation Reduces Vulnerability to Atrial Fibrillation. Circ Arrhythm Electrophysiol. 5, 978-983.

Risso, A., Pelligrino, F.J., Relling, A.E. and Corrada, Y., 2016. Effect of Long-Term Fish Oil Supplementation on Semen Quality and Serum Testosterone Concentrations in Male Dogs. International Journal of Fertility and Sterility, 10 (2), 223-231.

Schmitt, D., Tran, N., Peach, J., Bauter, M. and Marone, P. 2012. Toxicologic evaluation of DHA-rich algal oil: Genotoxicity, acute and subchronic toxicity in rats. Food and Chemical Toxicology 50, 3567–3576.

Sparrow, F.K., 1936. Biological observations on the Marine Fungi of Woods Hole Waters. Bio. Bull. Vol70 (2), 236-263.

Stoeckel, K., Nielsen, L.H., Fuhrmann, H. and Bachmann, L., 2011. Fatty acid patterns of dog erythrocyte membranes after feeding of a fish-oil based DHA-rich supplement with a base diet low in n-3 fatty acids versus a diet containing added n-3 fatty acids. Acta Veterinaria Scandinavica, 53-57.

Subbaiah, P.V. and Liu, M. 1996. Comparative studies on the substrate specificity of lecithinxholesterol acyltransferase towards the molecular species of phosphatidylcholine in the plasma of 14 vertebrates. J. Lipid Res. 37, 113-122.

Tsui, C.K.M., Marshall, W., Yokoyama, R., Hond, D, Lippmeier, J.C., Craven, K.D., Peterson, P.D. and Berbee, M.L., 2009. Labyrinthulomycetes phylogeny and its implications for the evolutionary loss of chloroplasts and gain of ectoplasmic gliding. J. Molecular Phylogenetics and Evolution 50, 129–140.

UniProt Taxonomy report. *Schizochytrium sp*. ATCC 20888. Accessed on 9 April 2014. http://www.uniprot.org/taxonomy/368446

Vanhaecke, P., Persoone, G., Claus, C. and Sorgeloos, P., 1981. Proposal for a Short-Term Toxicity Test with Artemia Nauplii. Ecotoxicology and Enviro. Safety (5) 382-387.

Vaughn, D.M., Reinhart, G.A>, Swaim, S.F., Lauten, S.D>, Garner, C.A., Boudreaux, M.K., Spano, J.S., Hoffman, C.E. and Conner, B., 1994. Evaluation of Effects of Dietary n-6 to n-3 Fatty Acid Rarios on Leukotriene B Synthesis in Dog Skin and Neutrophils. Vet Derm 5, 163-173.

Villac, M.C. Roelke, D.L., Villareal, T.A. and Fryxell, G.A., 1993. Comparison of two domoic acid-producing diatoms : a review. Hydrobiologia (269/270), 213-224.

Waldron, M.K., Hannah, S.S. and Bauer, J.E.,

Walters, J.M, Hackett, T.B>, Ogilvie, G.K. and Fettman, M.J., 2010. Polyunsaturated Fatty Acid Dietary Supplementation Induces Lipid Peroxidation in Normal Dogs. Veterinary Medicine International, Vol 2010, 1-4.

Westgarth, S., Blois, S.L., Wood, R.D>, Verbrugghe, A. and Ma, D.W., 2018. Effects of omega-3 polyunsaturated fatty acids and aspirin, alone and combined, on canine platelet function. Journal of Small Animal Practice 59, 272–280.

10 Expert Panel Statement

GRAS Panel Consensus Statement on the Generally Recognized as Safe (GRAS) Determination of the Use of Algal Oil produced by *Schizochytrium* sp.

for use as a source of DHA and EPA in Food for Dogs

September 18, 2019

The undersigned, an independent panel of experts, qualified by their scientific training and national and international experience to evaluate the safety of food and food ingredients (the "GRAS Panel"), was specially convened by DSM Nutritional Products ("DSM") on behalf of Veramaris LLC to conduct a critical and comprehensive evaluation of the available pertinent data and information, and determine whether, under the conditions of intended use as a nutritive additive in the food of dogs, algal oil produced by *Schizochytrium* sp. as an oil soluble liquid, is safe and "generally recognized as safe" ("GRAS") based on scientific procedures as stated under FDA's GRAS Notification Pilot Program in Animal Feed (proposed 21 CFR §570.36(c)(1) (U.S. FDA, 2010). For purposes of this evaluation, "safe" or "safety" as it relates to GRAS within the terms of the Federal Food, Drug, and Cosmetic Act means that there is a reasonable certainty of no harm under the intended conditions of use of the ingredient in foods, as stated in 21 CFR §170.3(i) (U.S. FDA, 2012a).

DSM Nutritional Products ("DSM") performed a comprehensive search of the scientific literature, through May, 2019, relating to the safety of algal products. DSM summarized the results of the literature search and prepared a safety dossier, **"The Safety and Generally Recognized as Safe (GRAS) Status of Algal Oil produced by Schizochytrium sp. As a Source of DHA and EPA in Food for Dogs"** for consideration by the GRAS Panel.

The GRAS Panel consisted of the following individuals: Michael Pariza, Ph.D. (Emeritus Professor, University of Wisconsin-Madison, Food Research institute), Michael Carakostas, DVM, Ph.D. (Consultant) and Stanley M. Tarka Jr., Ph.D., F.A.T.S. (The Pennsylvania State University College of Medicine, Tarka Group, Inc. and Panel Chair). The GRAS Panel critically evaluated the safety documentation (the dossier), and other

available data and information that the members of the GRAS Panel believed to be pertinent to the safety of the algal oil preparation and its intended use as a nutritive additive in the food of dogs.

On September 18, 2019, the GRAS Panel convened via teleconference, and independently, jointly, and unanimously concluded that algal oil, internally referenced as AOCED (algal oil containing EPA and DHA) for use as a nutritive additive in the food of dogs, produced consistent with current good manufacturing practice ("cGMP") and meeting the stated specifications, is safe for its intended use as a nutritive additive in the food of dogs. The GRAS Panel further concluded unanimously that the intended use of the algal oil from *Schizochytrium sp.*, and internally referenced as AOCED, is GRAS based on scientific procedures. It is also the unanimous consensus opinion of this GRAS Panel that other qualified experts would concur with these conclusions.

Summarized below are the data, information, and interpretive analysis supporting the GRAS Panel's conclusions.

Summary and Basis for GRAS Determination

Algal oil (AOCED) produced by *Schizochytrium sp.* is intended for use as a nutritive additive in food for dogs. The product contains over 50% by weight of the omega-3 fatty acids EPA (Eicosapentaenoic Acid) and DHA (Docosahexaenoic Acid) in a ratio of at least 1:2.5. The balance of the product is other saturated and unsaturated fatty acids with the majority (~25%) being palmitic acid.

EPA and DHA are found predominately in marine products, flax seed oil and borage seed oil, the concentration and ratio produced by the production strain of *Schizochytrium sp.* closely resembles that of fish oil. EPA and DHA have been added to dog food via fish meal for decades and via the dried *Shizochytrium sp.* Algal for over 10 years.

AOCED (Algal oil) is manufactured following cGMP in a multistep process starting with the fermentation by the *Schizochytrium sp.* organism followed by enzymatic hydrolysis, de-emulsification and separation by centrifugation. Any remaining water is removed by drying with nitrogen under vacuum. The fermentation was previously described in Animal Food Additive Petition Federal Register /Vol. 83, No. 88, pg. 19934 (21 CFR §573.615). Raw materials used in the fermentation medium are acceptable for use in animal food. The purified final product is a clear, orange-to-golden brown, mobile fluid that can be incorporated into both dry and canned dog food products.

Process Flow for Manufacture of Algal Oil from Marine Microalgae



Four pre-production lots were evaluated and found to meet the specification necessary for use in food for dogs. Lot (b) (4) was used in the manufacture of the food used in the target animal study.

Specification		Method	Lot Number (b) (4)
DHA + EPA content (mg/g)	Min. 500	AOCS Ce 1b-89	
DHA content (mg/g)	Min. 250	AOCS Ce 1b-89	
EPA content (mg/g)	Min. 100	AOCS Ce 1b-89	
Free fatty acids (%)	Max. 5	AOCS Ca 5a-40	
Moisture (%)	Max. 0.75	AOAC 930.15	
Crude Fat (%)	Min. 92	AOAC 954.02	

Schizochytrium sp. are thraustochytrids that belong to the Chromista kingdom (Bennett et al., 2017). The genus *Schizochytrium* is characterized by multiple binary cell divisions leading to clusters of sporangia. *Schizochytrium* spores are biflagellate at discharge and the number of spores discharged can range from two-to-one hundred. Thraustochytrids are microscopic, unicellular algae. The earliest research of thraustochytrids placed them in the fungi because of their heterotrophic nature and superficial resemblance to chytrids (Sparrow, 1936). Current analysis using molecular biology techniques have demonstrated that thraustochytrids are not fungi, but are related to the heterokont algae (Cavalier-Smith, 2018) and as a result are now considered microalgae. Current phylogenic analysis indicates that the members of the Chromista are all photosynthetic, but some groups such as the Thraustochytridae have lost their chloroplast and the capability of photosynthesis and as a result, are exclusively heterotrophic (Tsui et al. 2009).

Veramaris has developed an improved strain from the patented wild-type parent strain using a classical mutagenesis screening program. This program utilized well-accepted techniques commonly used in industrial strain improvement programs. No recombinant DNA technology was employed. The parent, ATCC PTA-10208, underwent three successive mutagenesis steps using a standard UV exposure procedure. The production strain was selected as a single colony out of the surviving population after screening for oil production ability and DHA to EPA ratio. The selected strain has consistent DHA and EPA content, and high biomass density under large scale fermentation conditions. Further manipulation of the fermentation media composition, pH and temperature led to an optimal oil production level without adversely affecting the DHA to EPA ratio.

Although some members of the Chromista are known to produce toxins, domoic acid and prymnesin, there are no literature reports of this organism producing toxins or being pathogenic nor does the sponsor have any data indicating the initially isolated strains nor the daughter after over 30 years of strain improvement have produced toxins under the conditions of large-scale fermentation. Analysis of related and parent strains in the DSM collection used for the manufacture of algal oil for human consumption did not reveal the presence of domoic acid (Annex 3). Toxicology studies with the production strain confirmed the absence of toxins. The production strain was also evaluated for domoic acid production and found

The AOCED was shown to be stable in commercial packaging for up to 12 months at 25° C and 6 months at 40° C.

The intended conditions of use are as follows:

The algal oil will be applied to dry, extruded kibble or in canned food at a level of no more than 1.5 % wt/wt of dry matter. AOCED will be used as a replacement for fish oil in dog food. The algal oil will be added to the food of dogs at no more than what is necessary following good animal feeding practices, NRC recommendations. When added to a model canned dog food, the concentrations of EPA and DHA remained stable for 12 months at 25° C and at 40° C. When applied topically to extruded kibble, the EPA and DHA levels fell slowly over two years and indicated a shelf life of at least 12 months. However, when AOCED is added to the mash before extrusion, shelf life is reduced to 9 months at 40° C.

The safety evaluation of the algal oil included the assessment of detailed literature including pivotal published safety studies conducted with the oil from parent and sister strains. These included studies addressing *In Vitro* Genotoxicity, (Ames test and Chromosomal Aberration) *In Vivo* Genotoxicity (mammalian chromosome aberration) and short-term acute and repeated-dose toxicity, 90-day rat and Reprotoxicity (rat) and Developmental toxicity with the rat and rabbit. The results of these investigations were previously provided in human GRAS Notices for the use of algal oil in infant formula.

Algal oil from the production strain was evaluated in a combined target animal and efficacy study, a Gestation-Lactation-Growth study with the preferred model breed for dogs, Beagles, utilizing three doses of algal oil, ½ x, 1x and 2x of the anticipated highest amount to be added to commercial dog food. Clinical observations were made twice daily on the dams and one a day with the litters; no adverse effects were noted. Detailed clinical evaluations of the puppies starting at one-week post-weaning revealed no adverse effects. The body weight of the animals was measured in weekly intervals as well as the feed intake. All puppies in the four groups (control plus treatments) gained weight continually; no growth depression could be recognized.

Achieved AOCED intake in mg/Kg body weight/ day

Dietary group	Dams Gestation (GD 0-62)	Dams Lactation (PPD 0-55)	Puppies Combined Post-weaning Weeks 1-2	Puppies Males Post-weaning Weeks 3-26	Puppies Females Post-weaning Weeks 3-26
Low dose AOCED	138.3	319.4	314.0	231.7	236.6
Mid dose AOCED	248.6	638.6	568.5	435.5	440.2
High dose AOCED	474.9	1243.9	1310.0	959.5	975.8

The purpose of adding the Algal oil to dog food is to act as a replacement for fish oil/meal in the diet. The monitoring of blood lipid profile was performed and revealed an increase in DHA and EPA content compared to control in the dams beginning at four weeks after initiation of the study. Treatment puppies

also had elevated levels of EPA and DHA following the same pattern as the dams indicating that AOCED is effective as a source of EPA and DHA in the diet of dogs. Other clinical blood chemistry parameters were not affected in an adverse manner.

Blood Plasma DHA concentration, Dams

DHA	Description	Pretreat F0	GD28 F0	PPD56 F0
Group 1	Control	61.14 (8.63)	90.34 (6.85)	75.29 (11.43)
Group 2	Low-dose	83.78 (9.25)	223.5 (45.4)	319.7 (36.6)
Group 3	Mid-dose	75.14 (17.74)	313.9 (116.2)	359.6 (92.4)
Group 4	High-dose	73.96 (17.87)	318.7 (32.3)	391.03 (14.40)

Blood Plasma EPA concentration, Dams

EPA	Description	Pretreat F0	GD28 F0	PPD56 F0
Group 1	Control	20.62 (3.37)	15.47 (4.11)	27.66 (4.41)
Group 2	Low-dose	23.79 (5.67)	36.15 (5.16)	79.53 (19.80)
Group 3	Mid-dose	27.91 (1.76)	94.20 (49.8)	173.6 (44.4)
Group 4	High-dose	24.39 (2.69)	116.1 (42.5)	267.2 (57.9)

Blood Plasma DHA concentration, puppies

DHA	Description	PPD 56 F1	Week 13 F1	Week 34 F1
Group 1	Control	138.61 (12.02)	150.31 (14.22)	99.28 (13.34)
Group 2	Low-dose	295.52 (23.68)	282.6 (25.58)	237.35 (27.52)
Group 3	Mid-dose	353.40 (42.9)	337.9 (32.3)	268.6 (33.70)
Group 4	High-dose	339.65 (24.37)	363.8 (34.9)	338.5 (51.0)

Blood Plasma EPA concentration, puppies

EPA	Description	PPD 56 F1	Week 13 F1	Week 34 F1
Group 1	Control	14.33 (2.42)	17.55 (1.94)	16.26 (2.06)
Group 2	Low-dose	49.08 (9.73)	57.98 (6.95)	59.50 (17.09)
Group 3	Mid-dose	101.11(18.42)	115.03 (11.41)	109.59 (17.47)
Group 4	High-dose	145.0 (28.9)	182.58 (23.89)	205.9 (32.5)

Based upon this collection of data, AOCED (Algal oil) produced by a strain of *Schyzochytrium sp.* and its marketed forms are safe and efficacious as a GRAS food ingredient for use as a nutritive additive in the food for dogs. The proposed uses of Veramaris' AOCED as a nutritive additive in food for dogs is safe and "generally recognized as safe" (GRAS) based on scientific procedures as stated under FDA's GRAS Notification Pilot Program in Animal Feed (proposed 21 CFR §570.36(c)(1) (U.S. FDA, 2010) as the pivotal data and information are generally available, satisfying the "common knowledge" element of a GRAS determination.

The use of AOCED as a nutritive additive in food for dogs is also supported by years of use of the dried algae itself in food for dogs, small mammals and chickens. It is therefore reasonable to conclude that the proposed use of AOCED is safe within the meaning of the FD&C Act, i.e., meets the standard of reasonable certainty of no harm.

CONCLUSION

We, the undersigned independent qualified members of the GRAS Panel, have individually and collectively critically evaluated the data and information summarized above, as well as other data and information that we deemed pertinent to the safety of the intended conditions of use of Algal oil containing EPA and DHA, referred to in this document and accompanying GRAS dossier as AOCED, in diets of dogs. We unanimously conclude that the proposed use of this algal oil referred to as AOCED, produced via fermentation by a strain of *Schizochytrium sp.* in a manner that is consistent with current Good Manufacturing Practice (cGMP) and meeting appropriate established specifications as presented in the supporting dossier *["The Safety and Generally Recognized as Safe (GRAS) Status of Algal Oil produced by Schizochytrium sp. As a Source of DHA and EPA in Food for Dogs"]* is safe for consumption at the maximum use levels specified in diets of dogs. The AOCED will be present in the diet of dogs at no more that 1.5% of the diet in both extruded (dry) food and canned (wet) food.

We, the members of the GRAS Panel, further unanimously conclude that the intended use of this algal oil referred to as AOCED, produced via fermentation by a strain of *Schizochytrium sp.* in a manner that is consistent with current Good Manufacturing Practice (cGMP) and meeting appropriate established specifications as presented in the supporting dossier is Generally Recognized as Safe (GRAS) based on scientific procedures, under the intended conditions of use in the diet of dogs at no more that 1.5% of the diet in both extruded (dry) food and canned (wet) food.

It is our opinion that other qualified experts would concur with this conclusion.

(b) (4), (b) (6)

Michael Pariza, Ph.D.
(Panel Member)
Professor Emeritus, Univ. Wisconsin

October 10, 2019
Date

(b) (4), (b) (6)

Michael Carakostas., DVM, Ph.D.
(Panel Member)

10 - Oct. 2019
Date

(b) (4), (b) (6)

The Tarka Group, Inc.(Chair), The Pennsylvania State University College of Medicine

10 October 2019
Date

Annex 1
CoA Lots of AOCED

(b) (4)

Person in charge
Client Support

(b) (6)

DSM NUTRITIONAL PRODUCTS/MARTEK
(b) (4), (b) (6)

Reporting Date 11/08/2018

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Sample Code (b) (4)

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Client Sample Code: VY00014962

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REPORT OF ANALYSIS

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REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result

Respectfully Submitted

(b) (4)

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(b) (4) Analytical Service Manager

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

ACCREDITED

TESTING CERT (b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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Person in charge
Client Support

(b) (4), (b) (6)

DSM NUTRITIONAL PRODUCTS/MARTEK
(b) (4), (b) (6)

Reporting Date 11/08/2018

(b) (4)

REPORT OF ANALYSIS

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REPORT OF ANALYSIS

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REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result

Respectfully Submitted,

(b) (4)

(b) (4), (b) (6)

(b) (4), (b) (6) Analytical Service Manager

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Uncertainty can be obtained upon request.

ACCREDITED

TESTING CERT (b) (4)

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Person in charge
Client Support

(b) (4), (b) (6)

DSM NUTRITIONAL PRODUCTS/MARTEK

(b) (4), (b) (6)

[redacted]

Reporting Date 11/08/2018

(b) (4)

[redacted]

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Sample Code (b) (4)

(b) (4)

[redacted]

(b) (4)

(b) (4)

Client Sample Code: VY00015465

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation

(b) (4)

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(b) (4)

Client Sample Code: VY00015465

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results **Result**

(b) (4)

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(b) (4)

Client Sample Code: VY00015465

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

(b) (4)

(b) (4)

Client Sample Code: VY00015465

(b) (4)

REPORT OF ANALYSIS

(b) (4)

This analytical report supersede

Test Results

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(b) (4)

Client Sample Code: VY00015465

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

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(b) (4)

Client Sample Code: VY00015465

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result

Respectfully Submitted,

(b) (4)

(b) (4), (b) (6)

(b) (4), (b) (6) Analytical Service Manager

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

ACCREDITED

TESTING CERT

(b) (4)

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(b) (4), (b) (6)

Person in charge
Client Support

DSM NUTRITIONAL PRODUCTS/MARTEK
(b) (4)

Reporting Date 11/08/2018

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Sample Code (b) (4)

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(b) (4)

Client Sample Code: VY00015572

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

(b) (4)

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(b) (4)

Client Sample Code: VY00015572

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

(b) (4)

(b) (4)

Client Sample Code: VY00015572

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results Result

(b) (4)

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Client Sample Code: VY00015572

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results Result

(b) (4)

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(b) (4)

Client Sample Code: VY00015572

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results Result

(b) (4)

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(b) (4)

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(b) (4)

Client Sample Code: VY00015572

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results **Result**

Respectfully Submitted,

(b) (4)

(b) (4), (b) (6)

(b) (4), (b) (6) Analytical Service Manager

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

ACCREDITED

TESTING CERT

(b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation

(b) (4)

Annex 2
Prymnesin Analysis

From: [redacted] (b) (4), (b) (6)

To:

Subject: Toxicity Study on Orca using *Artemia nauplii* to Detect Presence/Absence of Prymnesin Toxin

Date: December 21, 2009

Summary

Orca strain is a new species of Schizochytrium. While no evidence from the literature indicates prymnesin toxin potential Schizochytrium sp, artemia bioassay was performed to confirm absence of prymnesin toxin by Orca. Multiple experiments using different fermentation broths were performed and it was concluded that Orca strain exhibited no evidence of prymnesin toxin production.

Introduction

Prymnesin toxins are acidic polar phosphor-proteolipids limited to two species of *Prymnesium* (*P. parvum* and *P. patelliferum*). These toxins exhibit a broad spectrum of activity including lethal effects on gill breathing animals, cytotoxic effects on erythrocytes, mammalian cells, protozoa and bacteria. The major economic impact of prymnesin toxins to humans to date has been related to fish kills in aqua-culture ponds. All gill breathing animals tested to date have proved sensitive to prymnesin toxin. As a result, a sensitive toxicity test for prymnesin toxin has been developed using nauplii of the brine shrimp *Artemia* (Larsen et. al. 1993).

According to taxonomic system of Cavalier-Smith (1981, 1983, 1993), in Chromista kingdom, Thraustochytriales (including *Schizochytrium* sp.) are found in separate division (Heterokonka) than the known prymnesin toxic producers (found in the Prymnesiophyta division). Furthermore, in the four orders of Prymnesiophyta, all known toxin producers are found in only one order, Prymnesiales. Orca strain was identified as a new species of *Schizochytrium* and no evidence from the literature indicates prymnesin toxin potential in *Schizochytrium* sp. However, the artemia bioassay was performed to confirm absence of prymnesin toxin.

Methods

The overall experiment and more precisely the cells/ml were based on two previously published papers:
1) Levels Toxicity of coastal coccolithophores (Prymnesiophyceae, Haptophyta)
A. HOUDAN*, A. BONNARD, J. FRESNEL, S. FOUCHARD, C. BILLARD AND I. PROBERT
JOURNAL OF PLANKTON RESEARCH 26: 875–883 (2004)
2) Increase in the production of allelopathic substances by *Prymnesium parvum* cells grown under N- or P-deficient conditions; Edna Granéli , Niclas Johansson; Harmful Algae 2: 135–145 (2003)

Orca Preparation

- [redacted] (b) (4)
-
-

(b) (4)

Toxicity Test

- A volume of 10 mL 25 ppt Instant Ocean was added to a 60x15 mm sterile petri dish.
- 10 artemia nauplii were added to each petri dish.
- For each condition, a target number of cells were added while the control contained only the artemia in the 25 ppt Instant Ocean and did not include any Orca cells. Each condition was run in five replicates and the plates were randomized to avoid bias.
- The plates were incubated at 25°C and observed after approximately 24 hours and 48 hours. The number of dead artemia were counted and tabulated.
- The 25°C was chosen as the experimental temperature based on 1) This was the growth condition stated in the Increase in the production of allelopathic substances by *Prymnesium parvum* cells grown under N- or P-deficient conditions; Edna Granéli , Niclas Johansson; Harmful Algae 2: 135–145 (2003) 2) It was believed best to keep the nauplii growth conditions the same as used to hatch the cysts. A temperature of 17°C was used in "Levels Toxicity of coastal coccolithophores (Prymnesiophyceae, Haptophyta)", Houdan et. al., sited earlier.

Results and Discussion

Three different Orca fermentation broths were used for toxicity studies and some broths were retested to confirm the results. Each study contained a control with no Orca broth addition and each control exhibited numberous deaths. The most basic explanation is starvation. As cysts are hatched they rely on a yolk sac to sustain them for the first 48 hours. After 48 hours the newly hatched artemia begin to consume outside nutrients for substance. If food has not been provided within the 48 hour allotment of the experiment it is not unreasonable for the artemia to begin dying. As each artemia hatches and matures at a slightly different pace it would also follow that they will die at differing times. The mortality of each experimental condition was compared to the experimental control. If an experimental condition had mortality comparable to or lower than the control, the condition would be considered non-toxic. The experimental results are discussed below.

1. Artemia Feeding Trial using 10L Fermentation Broth NBS1- Nx1020et09(1-4)

A broth sample from the 10L fermentation run NBS1 Nx1020et09(1-4) was obtained from th (b) (4) (b) (4) The cell concentrations for each condition and the experimental results are summarized below.

10/28/09 Artemia Feeding Trial

Fermentation broth from lab fermentation lot #Nx 1020et09 (1-4) was tested on 10/28/09 using the procedures described in the Methods section. The cell concentrations and results are summarized in the table below.

24 hr

	1	2	3	4	5	Total dead	avg	
Control	0	0	2	0	1	3	0.6	control
A	(b) (4)						1.4	0.025ml in 10ml= $9*10^4$ cells/ml
D							2.8	0.05ml in 10ml= $1.8*10^5$ cells/ml
E							4.8	0.1 ml in 10ml= $3.6*10^5$ cells/ml
C							2.8	0.25 ml in 10 ml= $9*10^5$ cells/ml
B							0.8	0.5 ml in 10 ml= $1.8*10^6$ cells/ml

48 hr

	1	2	3	4	5	Total dead	avg	
Control	4	3	3	1	2	13	2.6	control
A	(b) (4)						3	0.025ml in 10ml= $9*10^4$ cells/ml
D							4.4	0.05ml in 10ml= $1.8*10^5$ cells/ml
E							5.4	0.1 ml in 10ml= $3.6*10^5$ cells/ml
C							3.4	0 25 ml in 10 ml= $9*10^5$ cells/ml
B							2.2	0 5 ml in 10 ml= $1.8*10^6$ cells/ml

Based on the experimental results, there was no clear correlation between Orca cell concentrations and average artemia death. Therefore, the experiment yielded inconclusive results. Additional experiments were performed to determine the Orca toxicity to artemia.

2. Artemia Feeding Trials Using Production Run F884 (Pasteurized Broth)

A frozen pasteurized broth sample from production run #F884 was obtained from (b) (4) he broth was thawed in hot water and then used for the experiments on 11/4/09. The broth was refrozen and retested on 11/11/09. The cell concentrations for each condition and the experimental results are summarized below.

11/04/09 Artemia Feeding Trial

-ORCA cell count- $3.97x\ 10^8$ cells/ml

		dH2O added
Control-	No ORCA adds.	
E	0.45 ml in 10 ml= $1.8*10^7$ cells/ml	
B	0.225 ml in 10 ml= $9*10^6$ cells/ml	225ul
D	0.09 ml in 10ml= $3.6*10^6$ cells/ml	360ul
A	0.045ml in 10ml= $1.8*10^6$ cells/ml	405ul
C	0.0225ml in 10ml= $9*10^5$ cells/ml	449ul

5-Nov	1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
Control	1	2	0	0	2	5	1	0
C	(b) (4)						0.4	0.0225 ml
A							1	0.045 ml
D							0	0.09 ml
B							0.2	0.225 ml
E							0.6	0.45 ml

6-Nov							Avg dead per plate	Volume of ORCA add
Control	1	4	0	0	4	9	1.8	0
C	(b) (4)						1	0.0225 ml
A							1	0.045 ml
D							1	0.09 ml
B							0.8	0.225 ml
E							0.8	0.45 ml

This feeding trial shows no adverse effects on artemia at a wide range of ORCA concentrations.

11/11/09 Artemia Feeding Trial

The above experiment was repeated using the same broth on 11/11/09, Fermentation lot #F-884. The cell concentrations and results are summarized in the tables below.

-ORCA cell count- 2.81x 10^8 cells/ml

Control- No ORCA adds.

E 0.03ml in 10ml= 9*10^5 cells/ml

A 0.064ml in 10ml= 1.8*10^6 cells/ml

B 0.128 ml in 10ml= 3.6*10^6 cells/ml

C 0.32 ml in 10 ml= 9*10^6cells/ml

D 0.64 ml in 10 ml= 1.8* 10^7cells/ml

12-Nov	1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
Control	1	0	0	0	0	1	0.2	na
E	(b) (4)						0.8	0.03 ml
A							0.8	0.064ml
B							0	0.128 ml
C							0.5	0.32 ml
D							0.2	0.64 ml

13-Nov	1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
Control	1	0	1	2	1	5	1	na
E	(b) (4)						0.8	0.03 ml
A							1	0.064ml
B							0.6	0.128 ml
C							1	0.32 ml
D							0.5	0.64 ml

The results obtained were similar to those found in the 11/4/09 experiment.
Based on the two trials, broth from production run F884 exhibited no adverse effects on artemia at a wide range of ORCA concentrations.

3. Artemia Feeding Trials Using 10L Fermentation Broth NBS1 Nx1105et09(1-4)

A broth sample from the 10L fermentation run NBS1 1 Nx1105et09(1-4) was obtained from the [redacted] (b) (4) The broth was used for the artemia feeding trials on 11/18/09, 11/23/09 and 12/09/09, and the broth was frozen in between test dates. The cell concentrations for each condition and the experimental results are summarized below.

Artemia Feeding Trial- ORCA Strain- 11/18/09

- Fermentation lot #Nx1105et09(1-2) [NBS1] was tested on 11/18/09.

-ORCA cell count- 2.2x 10^7 cells/ml

Control- No ORCA adds.
E 0.04ml in 10ml= $9*10^4$ cells/ml
A 0.08ml in 10ml= $1.8*10^5$ cells/ml
B 0.16 ml in 10ml= $3.6*10^5$cells/ml
C 0.41 ml in 10 ml= $9*10^5$ cells/ml

No dH2O was added to normalize the total volume added to each plate.

19-Nov	1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
Control	2	1	1	1	2	7	1.4	
E	[redacted] (b) (4)						1	0.04 ml
A							0.6	0.08 ml
B							1.4	0.16 ml
C							1.2	0.41 ml
D							1.4	0.81 ml

20-Nov	1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
Control	4	4	1	2	3	14	2.8	
E	[redacted] (b) (4)						2.2	0.04 ml
A							0.8	0.08 ml
B							2.4	0.16 ml
C							2.2	0.41 ml
D							1.8	0.81 ml

*** At 4:30 pm on 11/19/09 I came in and found the incubator power turned off and the temperature was down to 21.5 C.***

This feeding trial shows no adverse effects on artemia at a wide range of ORCA concentrations.

Artemia Feeding Trial- ORCA Strain- 11/23/09

- Fermentation lot #Nx1105et09(1-4) [NBS1] was tested on 11/23/09.

-ORCA cell count- 2.03x 10^7 cells/ml

Control- No ORCA adds.

B 0.91ml in 10 ml= 1.8* 10^6 cells/ml

E 0.44ml in 10 ml= 9*10^5 cells/ml

C 0.18 ml in 10ml= 3.6*10^5cells/ml

D 0.09ml in 10ml= 1.8*10^5 cells/ml

A 0.04ml in 10ml= 9*10^4 cells/ml

No dH2O was added to normalize the total volume added to each plate.

24-Nov	1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
Control						(b) (4)	0.2	
A							0.4	40 ul
B							0.2	910 ul
C							0	180 ul
D							0.2	90 ul
E							0	440 ul

25-Nov	1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
Control						(b) (4)	0.6	
A							0.2	40 ul
B							0.8	910 ul
C							0.6	180 ul
D							1.2	90 ul
E							1.2	440 ul

*** At 4:30 pm on 11/19/09 I came in and found the incubator power turned off and the temperature was down to 21.5 C.***

Based on the experimental results, there was no clear correlation between Orca cell concentrations and average artemia death. Also to be noted is a lower than usual number of the control artemia died makes for a questionable experiment. Therefore, the experiment yielded inconclusive results. A third repeat of this broth is planned for the week of 12/07/09.

Artemia Feeding Trial- ORCA Strain- 12/09/09

- Fermentation lot #Nx1105et09(1-4) [NBS1] was tested on 12/09/09.

-ORCA cell count- 4.51x 10^7 cells/ml		
	Control-	No ORCA adds.
	C	0.02ml in 10ml= 9*10^4 cells/ml (20uL)
	E	0.04ml in 10ml= 1.8*10^5 cells/ml (40uL)
	A	0.08 ml in 10ml= 3.6*10^5cells/ml (80 uL)
	D	0.20 ml in 10 ml= 9*10^5 cells/ml (200 uL)
	B	0.4ml in 10 ml= 1.8* 10^6 cells/ml (400uL)

Note: No dH2O was added to normalize the total volume added to each plate.

10-Dec		1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
	Control	0	2	0	2	1	5	1	
	C	(b) (4)						0.2	20uL
	E							1.2	40 uL
	A							1.6	80 uL
	D							0.6	200 uL
	B							1.6	400 uL

11-Dec		1	2	3	4	5	Total dead	Avg dead per plate	Volume of ORCA add
	Control	1	4	2	3	3	13	2.6	
	C	(b) (4)						0.4	20uL
	E							1.6	40 uL
	A							1.8	80 uL
	D							1.2	200 uL
	B							1.8	400 uL

This feeding trial shows no adverse effects on artemia at a wide range of ORCA concentrations.

Based on the three trials, broth from run Nx1105et09(1-4) exhibited no adverse effects on artemia at a wide range of ORCA concentrations. The inconclusive results observed in the 11/23/09 experiment were not dose responsive, hence points to experimental variability.

Statistical Analysis

Statistcal analysis was performed using the artemia testing results above (see report " Results of Toxicity Study" (b) (4) dated Jaunuary 15, 2010). ANOVA and Dunnett's Comparison was used to determine if the mean number of dead Artemia in the Control plates was statistically different than the mean number of dead Artemia in the plates containing Orca. Analysis was conducted for all trials at 24 hours and 48 hours with a 5% risk. The conclusions are summarized below.

- Results from the trial performed October 28th indicate conditions C, D and E are statistically different than the Control at 24 hours. At 48 hours, condition E is statistically different than the Control.
- Results from the trials performed November 4th, November 11th and November 23rd indicate all conditions are statistically equal to the corresponding Control at 24 hours and 48 hours.
- Results from the trial performed November 18th indicate all conditions are statistically equal to the Control at 24 hours. At 48 hours, condition A is statistically different than the Control. Although statistically significant, condition A has a lower average compared to the Control (0.8 vs. 2.8), indicating Orca did not have an adverse affect on the Artemia.
- Results from the trial performed December 9th indicate all conditions are statistically equal to the Control at 24 hours. At 48 hours, condition C is statistically different than the Control. Although statistically significant, condition C has a lower average compared to the Control (0.4 vs. 2.6), indicating Orca did not have an adverse affect on the Artemia

Conclusion

Based on the results and discussion above, it was concluded that Orca strain exhibited no evidence of prymnesin toxin production.

Annex 3
Domoic Acid Analysis

(b) (4)

Domoic Acid Data Report

Project: (b) (4)

Date: 1/15/2010
Report Prepared by: (b) (4)
Samples Submitted by: (b) (4)

Sample Identification:

NB61105et09
NBx1220dt09

Toxins: Domoic Acid (DA)

Toxin extraction: Vials received 1/7/2010 were stored in the fridge at 20°C until they were emptied into weigh boats and mixed in preparation of extraction. Dried material was extracted in 1.0 gram subsets. The sample NBx1220dt09 was less dense than the material from NB61105et09, so extraction solution volumes were doubled for NBx1220dt09. NB61105et09 was extracted with10 mL of acidified methanol-water solution (75%-25%) while NBx1220dt09 was extracted with 20 mL. Duplicate spiked samples were also prepared prior to extraction with the addition of a Domoic Acid certified standard provided by the National Research Council of Canada. A spiked sample for NB61105et09 was prepared with the addition of 0.01 µg Domoic Acid (DA) to the dried material and NBx1220dt09 was spiked with 0.1 µg DA. After the addition of acidified MeOH, samples were vortexed then sonicated via water bath for 25 minutes. The samples were then centrifuged @ 3,000 RPM for 10 minutes and the supernatant retained. Extraction on the pellet was repeated two additional times with 75% acidified methanol. The pooled supernatant was filtered through GF/C and blown to dryness under a stream of nitrogen at 60°C. Samples and spiked samples were then reconstituted at a concentration of 1g/mL in 10% acetonitrile.

An initial extraction of NBx1220dt09 resulted in a positive response (~40 ng/g DA) with the Domoic Acid Enzyme Linked Immunosorbent Assay (ELISA). This could not be confirmed with Liquid Chromatography-Mass Spectrometry, so the sample was re-extracted as detailed above, and further cleanup using Solid Phase Extraction was employed. Strata-X 200 mg Polymeric Reversed Phase SPE (Phenomenex) was conditioned and equilibrated with methanol and DI water, loaded, rinsed and eluted with 100% MeOH. The resultant eluant was blown to dryness, reconstituted in 10% acetonitrile and diluted appropriately for analysis. Samples were analyzed via ELISA (Biosense) in duplicate after sufficient dilutions of extract were made using the kit protocol.

(b) (4)

[redacted] (b) (4)

Analytical Methodology: A Domoic Acid ELISA (Biosense) was utilized for the quantitative detection of DA. The current assay is sensitive down to a detection/quantification limit of 0.5 ng/g for DA as determined from spike recoveries, dilution factors, and kit sensitivity. The standard recoveries were 88% and 97%.

Summary of Results

Sample	DA levels (ng/g)
NB61105et09	ND
NBX1220dt09	ND

ND = Not detected above the detection limit
Detection/Quantification Limit = 0.5 ng/g
Sample Spikes = 10 & 100 ng/g
Standards = 0.5 & 1.0 ng/mL

Data Interpretation: Although an initial extraction of NBx1220dt09 resulted in a positive response with ELISA, an additional extraction employing Solid Phase Extraction resulted in acceptable spike recovery (76%) and a non-detect when re-analyzed. The initial results appear to be due to matrix interference, as indicated by the inability to detect domoic acid via LC/MS. Domoic acid was not detected in either sample above our detection limit of 0.5 ng/g.

Submitted by: [redacted] (b) (4) Ph.D.

Date: 1/15/10

[redacted] (b) (4)

(b) (4)

To: (b) (4) Jan 12, 2010

Cc:

From:

Subject: Domoic Acid Analysis of Orca Biomass by Monsanto Method

Summary

Previously, we determined the amount of domoic acid in Orca oils with an independent method using LC-MS (see report from (b) (4) "Domoic Acid in Bell and Orca" on 12/4/2009). Here, the domoic acid was quantified in one Orca biomass (NB61105et09) using Monsanto Corporate Research's method (code (b) (4) (b) (4) which was derived from AOAC official Method 991.26 using HPLC/diode array detector. The Orca biomass sample was found to have less than 0.5 ppm domoic acid.

Experimental

Reagent preparation and standard calibration

Domoic Acid Stock Solution: 5 mg of domoic acid (90%) was dissolved in 100 mL volumetric flask with 0.1 N HCl. The stock concentration is 0.045 mg/mL = 45 ppm.

Domoic Acid Standard Calibration: Using stock solution to make 5, 4, 2, 1, 0.5, 0.05 ppm domoic acid for standard calibration. Each sample was injected into the HPLC system to get the area reading.

Sample preparation

A) Hexane Wash:
About sixty grams of Orca biomass were treated with 10 mL/g hexane wash in a 1 L beaker. The sample was ultrasonicated for 10 minutes followed by filtration. The hexane filtrate was discarded and the biomass powder was dried under vacuum overnight for the neat biomass extraction.
B) Biomass Spike recoveries:
Five grams of biomass was spiked with 0.5 ppm of domoic acid by adding 250 µL of 10 ppm domoic acid stock solution. The sample is rolled to mix the domoic acid uniformly and dried overnight under vacuum for the neat biomass extraction step.
C) Neat Biomass Extraction:
Two portions of 2.5 grams of biomass (regular and spiked) were weighed into two 25 mL glass tubes and heated to 80-90ûC in the heating block for 5 minutes with 10 mL of 0.1N HCl. Transfer the extract into a 50 mL volumetric flask with 0.1 N HCl and cooled in an ice bath. Each of the samples was then transferred into 50 mL Falcon tube for 2500 rpm centrifugation for 10 minutes. The supernatants were filtered through 0.45 µm syringe filters into autosampler vials for HPLC analysis. All samples were prepared in duplicate and labeled as Orca, Orca-spiked, Orca Dup, and Orca Dup-spiked.

HPLC instrumental parameters

System: Waters Acquity UPLC®
Column: Waters Atlantis dC18 (part # 186001346), 4.6×250 mm, 5µm, ambient temperature

Flow rate: 1 mL/min
Injection volume: 20 µL
Detection: Waters Photodiode Array Detector, 235-245 nm, UV.
Mobile phase: A. 100% water with 0.2% phosphoric acid
B. 100% acetonitrile with 0.2% phosphoric acid

Gradient

Time (min)	% A	% B
0	100	0
5	100	0
20	88	12
30	88	12
31	10	90
35	10	90
35.1	100	0
45	100	0

Results and Discussion

The linear regressions for the calibration curve have exceeded 0.999. The instrument detection limit was 0.05ppm; since the sample was diluted 10-fold during the extraction, the method detection limit for domoic acid was 0.5ppm.

Under this condition, domoic acid eluted out from the column at around 27 min. From the HPLC chromatogram, there was no peak observed for un-spiked Orca sample (Figure 1). We concluded that domoic acid was not detected in Orca NB61105et09 at the method detection limit of 0.5 ppm.

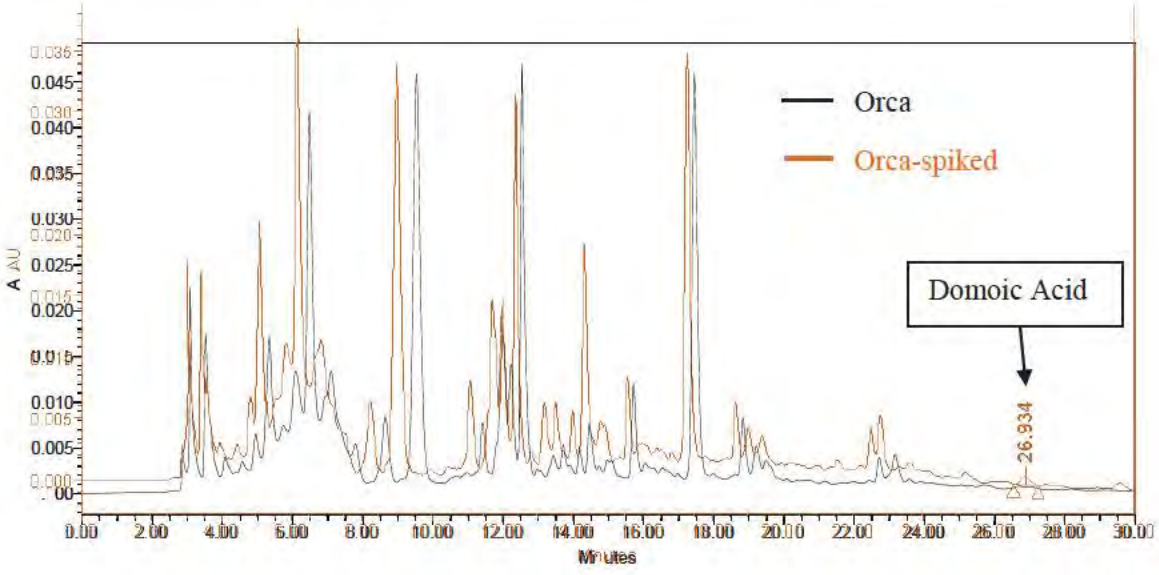

Figure 1. The Orca sample showed no domoic acid above method detection limit (0.5 ppm). The peak for Orca was too small to be integrated and quantitated.

Annex 4
Raw Material Specifications

DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Sodium Chloride Granular - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- o (b) (4) Part Number N/A: Description: Sodium Chloride
- o (b) (4) Part Number N/A: Description: Sodium Chloride

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 50 b. bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep in a tightly closed container, stored in a cool, dry, ventilated area. (per Manufacturer's instructions)
	Product Shelf Life:	2 years from date of manufacture

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APPROVED Printed on 4/21/2015 - Valid for 72 hours from print date

Mon Oct 10 13:57:13 CDT 2016

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	N/A	Attach COA	9.0 – 100.5%	
Identification • Sodium • Chloride		USP		Passes Test	
Acidity/Alkalinity				Passes Test	
Loss on drying		N/A		Max. 0.5%	
Bromides				Max. 0.010%	
Phosphates				Max. 0.0025%	
Potassium				Max. 0,05%	
Iodides		USP		Passes Test	
Aluminum		N/A		Max. 0.2 ppm	
Mg/Alkaline Earth Metals				Max. 100 ppm	
Arsenic		USP		Max. 1 ppm	
Iron		N/A		Max. 2 ppm	
Barium		USP		Passes Test	
Ferrocyanides				Passes Test	
Sulfate		N/A		Max. 0.020%	
Nitrites (absorbance 0.01 max.)		USP		Passes Test	
Heavy Metals		N/A		Max. 5 ppm	
Grade		COA or Letter on File		Record	

o **Pass** o **Fail** — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o **Unrestricted** o **Restricted**
o **Blocked**

QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

o **Update Status in SAP**

QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 08/31/12	New document	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 12/12/12	Revised expiration to match DSM defined expiration		NA	NA	NA	
03: 01/06/15	Biennial Review; no changes necessary		NA	NA	NA	

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Potassium Phosphate Monobasic - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- (b) (4) Part Number 5111: Description : MonoPotassium Phosphate
- (b) (4) Part Number N/A: Description: MonoPotassium Phosphate
- (b) (4) Part Number 5111: Description: MonoPotassium Phosphate

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 50 b. bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Cool and dry (per Manufacturer's instructions)
	Product Shelf Life:	18 months from production date

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	NA	Attach COA	Min. 98.0%	
Arsenic				Max. 3 mg/kg	
Fluoride				Max. 10 mg/kg	
Insoluble Substances				Max. 0.2%	
Lead				Max. 2 mg/kg	
Loss on drying				Max. 1%	
Grade		COA or Letter on File		Record	
o Pass o Fail	QA/QC Signature and Date:				

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted o Restricted o Blocked	QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

o Update Status in SAP	QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 08/31/12	New document	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 11/29/12	Revised expiration period to match DSM defined expiration from 24 to 18 months.		NA	NA	NA	
03: 01/05/15	Biennial Review; no changes necessary		NA	NA	NA	

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Ammonium Sulfate - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

o (b) Part Number 515518: Description : Ammonium Sulfate

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 22.7 kg bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Cool, dry area
	Product Shelf Life:	2 years from production date

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Moisture	Manufacturer	NA	Attach COA	≤ 0.15%	
Assay-Ammonium Sulfate				≥ 99.0%	
Water Insoluble				≤ 0.3%	
Residue on Ignition				≤ 0.25%	
Iron as Fe				≤ 15 ppm	
Lead				≤ 3 ppm	
Selenium				≤ 5 ppm	
Arsenic				≤ 0.5 ppm	
Grade		COA or Letter on File		Record	

o **Pass** o **Fail** — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o **Unrestricted**
o **Restricted**
o **Blocked**

QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

o **Update Status in SAP**

QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 08/31/12	New document	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 11/29/12	Revised expiration period to match DSM defined expiration (from 3 to 2 years).		NA	NA	NA	
03: 01/06/15	Biennial Review; no changes necessary		NA	NA	NA	

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DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) - MCS

Owner: Janes, Ken
Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	09-Jun-2015 14:07:14 UTC	3.4
413100	(b) (4), (b) (6)	08-Jul-2015 11:34:59 UTC	3.4

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	09-Jul-2015 19:41:12 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4), (b) (6)	13-Jul-2015 12:36:17 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Phosphoric Acid (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 4.0, CURRENT Effective Date: 14/Jul/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION	
Approved Manufacturer(s): ☐ (b) (4) Part Number N/A: Description: Phosphoric Acid 75% Bulk ☐ (b) (4) Part Number N/A: Description: Phosphoric Acid 75% Bu k ☐ (b) (4) Part Number N/A: Description: Phosphoric Acid 75% Bulk ☐ (b) (4) Part Number N/A: Description: Phosphoric Acid 75% Bulk	
Date Received:	**Quantity Received:** / **Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL				
Sample Use	**Sample Quantity**	**Packaging**	**Storage**	**Shipped To**
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION	
Manufacture Date:	**Expiration Date:**

Mon Oct 10 14:15:03 CDT 2016

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** Bulk	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store in an area that is cool, dry, and well-ventilated (per Manufacturer's instructions)
	Product Shelf Life:	24 months from date of production

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Concentration	Manufacturer	N/A	Attach COA	≥75%	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked — **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ Update Status in SAP — **QA/QC Signature and Date:**

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 08/31/12	New document	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 11/29/12	Revised expiration to match DSM defined expiration		NA	NA	NA	
03; 01/06/15	Biennial Review; no changes necessary		NA	NA	NA	
04: 06/08/15	Scheduled review - no changes		NA	(b) (4), (b) (6)	NA	

DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Dextrose Bulk Liquid DE 95 (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	09-Jul-2015 19:48:49 UTC	4.3

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	15-Jul-2015 17:19:30 UTC	Approve	Kingstree Quality Assurance

DSM Nutritional Products

Title/Product Name: (b) (4) Dextrose Bulk Liquid DE 95 (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 5.0, CURRENT Effective Date: 16/Jul/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- ☐ (b) (4) Part Number: N/A, Description : Corn Syrup, Clearsweet 95% DE
- ☐ (b) (4) Part Number: N/A, Description: Corn Syrup
- ☐ (b) (4) Part Number: N/A, Description: Corn Syrup
- ☐ (b) (4) Part Number: N/A, Description: Corn Syrup
- ☐ (b) (4) (b) (4) Part Number: N/A, Description: 95 DE Corn Syrup

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 4 (Obtain wash certificate for tanker truck deliveries. Documentation on file with QA for railcars) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
QC Sample	1 x 125 ml	125 ml Nalgene Sample Cup	N/A	Internal QC

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

DSM Nutritional Products

Title/Product Name: (b) (4) Dextrose Bulk Liquid DE 95 (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 5.0, CURRENT Effective Date: 16/Jul/2015

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** Bulk	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Note: The recommended storage temperature for liquefied syrup is 110-140°F[1] Syrups stored for extended periods (over 6 months) should be evaluated periodically for fitness of use [1]Internal Specification
	Product Shelf Life:	6 months from date of manufacture

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
ID Test	Site QC	Visual	Attach COA	Clear to light straw liquid	
pH	Manufacturer	N/A		Record	
Composition		COA		Monosaccharides (Dextrose + Fructose) >95%	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked	**QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ Update Status in SAP	**QA/QC Signature and Date:**

Revision History

Version No.	Date	Author	Summary of Changes
	08/October/2012	(b) (4), (b) (6)	New document - transferred from MiSys as 1002440
	12/December/2012		Revised expiration period to match DSM defined expiration
	06/January/2015		Biennial Review; no changes necessary

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DSM Nutritional Products

Title/Product Name: (b) (4) extrose Bulk Liquid DE 95 (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 5.0, CURRENT Effective Date: 16/Jul/2015

Version No.	Date	Author	Summary of Changes
	17/June/2015	(b) (4), (b) (6)	Revised Kosher section per External Audit Finding 116637
			Revised Kosher section per External Audit Finding 116637 again to correct

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Magnesium Sulfate USP (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
413100	(b) (4), (b) (6)	17-Nov-2015 17:06:14 UTC	3.9
699805		18-Nov-2015 16:45:08 UTC	3.9

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
699805	(b) (4), (b) (6)	19-Nov-2015 16:35:18 UTC	Approve	Kingstree Quality Assurance
413100		01-Dec-2015 18:24:54 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Magnesium Sulfate US (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 4.0, CURRENT Effective Date: 02/Dec/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION		
Approved Manufacturer(s): ☐ (b) (4), Part Number N/A: Description : Epsom Salt, Magnesium Sulfate Heptahydrate (Epsom Salt) ☐ (b) (4) Part Number N/A: Description: Epsom Salt, Magnesium Sulfate Heptahydrate (Epsom Salt) ☐ (b) (4), a division of Premier Magnesia, LLC., Part Number N/A: Description: Magnesium Sulfate Heptahydrate (Epsom Salt)		
Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO		**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A		**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO		**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A		**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A		**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:		**Date:**

Section 2. SAMPLE CONTROL				
Sample Use	**Sample Quantity**	**Packaging**	**Storage**	**Shipped To**
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION	
Manufacture Date:	**Expiration Date:**

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DSM Nutritional Products

Title/Product Name: (b) (4) Magnesium Sulfate USP (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 4.0, CURRENT Effective Date: 02/Dec/2015

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 22.7 kg bag or 25 kg bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep containers closed. Protect from extremes of temperature and humidity during storage. Recommended storage conditions 68-110°F and 54-87% relative humidity (per Manufacturer's instructions)
	Product Shelf Life:	3 years from date of manufacture

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Chloride	Manufacturer	N/A	Attach COA	0.00 - 0.014%	
Heavy metals as Pb				Max. 0.001%	
Loss on Ignition				40.00 - 52.00%	
$MgSO_4$ (Anhydrous wt. %)				99.0 - 100.5%	
Selenium				Max. 0.0030%	
Grade		COA or Letter on File		Record	
☐ Pass ☐ Fail	QA/QC Signature and Date:				
Remarks:					

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked	QA/QC Signature and Date:
Remarks/Conditions:	

Section 7. QUALITY STATUS

☐ Update Status in SAP	QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
01	31/Aug/2012	(b) (4), (b) (6)	New document
02	12/Dec/2012		Revised expiration period to match DSM defined expiration

Mon Oct 10 13:55:23 CDT 2016

DSM Nutritional Products

Title/Product Name: (b) (4) Magnesium Sulfate USP (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 4.0, CURRENT Effective Date: 02/Dec/2015

Version No.	Date	Author	Summary of Changes
03	06/Jan/2015	(b) (4), (b) (6)	Biennial Review; no changes necessary
04	04/Nov/2015		Added new supplier per MOC123829

DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Caustic Soda 50% Liquid - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- o (b) (4) Part Number N/A: Description : Caustic Soda 50% FG Kosher (Sodium Hydroxide Solution)
- o (b) (4) Part Number N/A: Description : 105016 Caustic 50% Rayon grade
- o (b) (4) Part Number N/A: Description : Caustic Soda
- o (b) (4) Part Number N/A: Description : Caustic Soda 50%
- o (b) (4) Part Number N/A: Description : LIQ CAU SODA – ET50
- o (b) (4) Number N/A: Description : DIA 50% LIQ CAUS SODA - BULK

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 55 gallon drums	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep away from heat, sparks, and flames. Store in a cool dry place.
	Product Shelf Life:	1 year from date of manufacture

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Sodium Hydroxide (NaOH) wt.	Manufacturer	NA	Attach COA	48.50 – 51.00%	
Iron				Max. 9 ppm	
Grade		COA or Letter on File		Record	
o Pass o Fail	QA/QC Signature and Date:				

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted o Restricted o Blocked	QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

o Update Status in SAP	QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 08/31/12	New document	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 12/12/12	Revised expiration period to match DSM defined expiration		NA	NA	NA	
03: 01/05/14	Biennial Review; no changes necessary		NA	NA	NA	

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Alcalase 2.4 Food Grade

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

o (b) (4) Part Number NA: Description : Alcalase 2.4

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 3 (Kosher Marking Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 25 kg pails or 225 kg drums	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Dry and protected from sun at 0 - 10°C (32° - 50°F)
	Product Shelf Life:	2 years from date of manufacture

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Protease Units AU-A	Manufacturer	NA	Attach COA	≥2.4 g	
Total Viable Count				≤50000 g	
Coliform Bacteria				≤30 g	
Enteropathogenic E. Coli				Not detected in 25 g	
Salmonella				Not detected in 25 g	
Grade		COA or Letter on File		Record	
o Pass o Fail	QA/QC Signature and Date:				

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted o Restricted o Blocked	QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

1. Update Status in SAP	QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 12/15/12	New document; transferred for SAP	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 01/06/15	Biennial review only; No changes		NA	NA	NA	

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Ammonia, Anhydrous

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

o (b) (4) a division of Tanner Industries, Inc. Part Number NA: Description : Ammonia, Anhydrous

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** Tanker	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store in cool dry area out of direct sunlight
	Product Shelf Life:	Indefinite, per Manufacturer (5 year re-evaluation per DSM)

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay (% NH_3)	Manufacturer	NA	Attach COA	Min. 99.9965%	
Water (ppm)				Max. 33 ppm	
Oil				Max. 2 ppm	
Grade		COA or Letter on File		Record	
o Pass o Fail	QA/QC Signature and Date:				

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted o Restricted o Blocked	QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

1. Update Status in SAP	QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 12/15/12	New document; transferred for SAP	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 01/06/15	Biennial review only; No changes		NA	NA	NA	K. Janes

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DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Calcium Pantothenate 0AQ (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
413100	(b) (4), (b) (6)	08-Jul-2015 12:41:06 UTC	2.4
191665	Janes, Ken	08-Jul-2015 13:36:23 UTC	2.4

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	09-Jul-2015 19:42:04 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4), (b) (6)	21-Jul-2015 19:46:51 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Calcium Pantothenate 0AQ (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 3.0, CURRENT Effective Date: 22/Jul/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

☐ (b) (4) a division of (b) (4) Part Number: CA159, Description : Calcium Pantothenate

☐ (b) (4) Part Number: 1443, Description: Calcium Pantothenate

☐ (b) (4) Part Number: 379422, Description: Calcium Pantothenate

☐ (b) (4) Part Number: 0412678, Description: Calcium D- Pantothenate

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**

Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

DSM Nutritional Products

Title/Product Name: (b) (4) Calcium Pantothenate 0AQ (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 3.0, CURRENT Effective Date: 22/Jul/2015

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 25 kg pail, 1 kg jar, 12 kg jar, or 50 kg jar	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep in a tightly closed container, stored in a cool, dry, ventilated area. Protect against physical damage. Isolate from any source of heat or ignition. Containers of this material may be hazardous when empty since they retain product residues (dust, solids); observe all warnings and precautions listed for the product. Store below 25°C, per manufacturer's instructions
	Product Shelf Life:	3 years from date of manufacture

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Alkalinity	Manufacturer	NA	Attach COA	Passes Test	
Specific Rotation				+ 25.0 - + 27.5°	
Nitrogen Content				5.7 – 6.0%	
Calcium Content				8.2 – 8.6%	
Loss on Drying				Max. 5.0%	
Heavy Metals (as Pb)				Max. 0.002%	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

1. Update Status in SAP **QA/QC Signature and Date:**

Mon Oct 10 14:09:52 CDT 2016

DSM Nutritional Products

Title/Product Name: (b) (4) Calcium Pantothenate 0AQ (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 3.0, CURRENT Effective Date: 22/Jul/2015

Revision History

Version No.	Date	Author	Summary of Changes
	04/February/13	(b) (4), (b) (6)	New document - transferred from MiSys as 1001560
	13/March/14		Added DSM Nutritional Products as new supplier - per MOC 42160. Updated section 5 specifications accordingly
	22/Jul/2015		Scheduled Review - no changes

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

DNP

DNP OPS Americas Full Lifecycle

Specification

(b) (4) Cerelose 2001 (Dextrose) FG (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b)

Reviewed By

Aurora ID	User Name	Date	Version
251334	(b) (4), (b) (6)	23-Mar-2016 17:05:45 UTC	3.5
699805		12-Apr-2016 13:43:41 UTC	3.5

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
699805	(b) (4), (b) (6)	19-Jun-2016 01:54:00 UTC	Approve	Kingstree Quality Assurance
251334		17-Jun-2016 19:09:34 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Cerelose 2001 (Dextrose) FG (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 4.0, CURRENT Effective Date: 20/Jun/2016

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION	
Approved Manufacturer(s): ☐ (b) (4) Part Number: Cerelose 2001, Description: Cerelose Dextrose 2001	
Date Received: / **Quantity Received:**	**Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 3 (Kosher Marking Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

DSM Nutritional Products

Title/Product Name: (b) (4) Cerelose 2001 (Dextrose) FG (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 4.0, CURRENT Effective Date: 20/Jun/2016

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 22.7 kg bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Clean, dry area
	Product Shelf Life:	In bags, material will keep indefinitely when not exposed to high (>90°F/32°C), prolonged temperature per manufacturer (5 year re-evaluation per DSM)

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Moisture	Manufacturer	NA	Attach COA	8.0 - 9.0%	
Color				0.0 - 2.5 color units	
Clarity				> 92.0%	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

1. Update Status in SAP **QA/QC Signature and Date:**

Revision History

Version No.	Date	Author	Summary of Changes
01	04/Feb/2013	(b) (4), (b) (6)	New document - transferred from MiSys as 10002040
02	24/Apr/2013		Changed container size in Section 4 to 22.7 kg per Materials Control
03	13/Jun/2013		Changed name of supplier to Ingredion (formally Corn Products) per supplier notification
04	21/Mar/2016		Scheduled Review - No changes

DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Cupric Sulfate, 5AQ, ACS (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b)

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	17-Jun-2015 19:29:32 UTC	1.4
413100	(b) (4), (b) (6)	08-Jul-2015 12:45:39 UTC	1.4

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	09-Jul-2015 19:43:33 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4), (b) (6)	21-Jul-2015 19:50:19 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Cupric Sulfate, 5AQ, ACS (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 22/Jul/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

☐ (b) (4) a Division of (b) (4), Part Number: N/A, Description: Cupric Sulfate

☐ (b) (4), Part Number: N/A, Description: Cupric Sulfate

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**

Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Mon Oct 10 14:07:43 CDT 2016

DSM Nutritional Products

Title/Product Name: (b) (4) Cupric Sulfate, 5AQ, ACS (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 22/Jul/2015

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 45 kg pail	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep container tightly closed. Keep container in a cool, well-ventilated area. Per Manufacturer's instruction
	Product Shelf Life:	Indefinite per Manufacturer (5 year re-evaluation per DNP)

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	N/A	Attach COA	98.0 – 102.0%	
Insoluble Matter				Max. 0.005%	
Chloride				Max. 0.001%	
Nitrogen Compounds				Max. 0,002%	
Calcium				Max. 0.005%	
Iron				Max. 0.003%	
Nickel				Max. 0.005%	
Potassium				Max. 0.01%	
Sodium				Max. 0.02%	
Grade		COA or Letter on File		Record	

☐ **Pass** ☐ **Fail** **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ **Unrestricted** ☐ **Restricted** ☐ **Blocked**	**QA/QC Signature and Date:**
Remarks/Conditions:	

Section 7. QUALITY STATUS

☐ **Update Status in SAP**	**QA/QC Signature and Date:**

DSM Nutritional Products

Title/Product Name: (b) (4) Cupric Sulfate, 5AQ, ACS (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 22/Jul/2015

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 02/04/13	New document – transferred from MiSys as 1002520	(b) (4), (b) (6)	NA	NA	NA	(b) (4),
02: 06/16/15	Scheduled Review - no changes		NA	A. McCutcheon	NA	K. Janes

Mon Oct 10 14:07:43 CDT 2016

DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) D-Biotin USP (b) (4) MCS

Owner: Janes, Ken

Authors: Duke, Dennie

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	17-Jun-2015 19:30:13 UTC	1.4
413100	(b) (4), (b) (6)	08-Jul-2015 12:47:57 UTC	1.4

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	09-Jul-2015 19:44:02 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4), (b) (6)	21-Jul-2015 19:50:54 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) D-Biotin USP (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 22/Jul/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION	
Approved Manufacturer(s): ☐ (b) (4) Part Number: N/A, Description: D-Biotin ☐ (b) (4) Part Number: N/A, Description: D-Biotin	
Date Received:	**Quantity Received:** / **Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Mon Oct 10 14:10:30 CDT 2016

DSM Nutritional Products

Title/Product Name: (b) (4) D-Biotin USP (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 22/Jul/2015

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 1 kg container	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store at temperature below 25°C, per Manufacturer's instructions
	Product Shelf Life:	38 months from the date of manufacture

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Appearance	Manufacturer	N/A	Attach COA	White Powder	
Identification				Corresponds	
Specific Rotation				89 - 93°	
Assay				97.5 – 100.5%	
Organic Volatile Impurities				To Meet USP requirements	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked — **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ Update Status in SAP — **QA/QC Signature and Date:**

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 02/04/13	New document – transferred from MiSys as 1002600	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 06/16/15	Scheduled Review - no changes		NA	(b) (4), (b) (6)	NA	K. Janes

DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) 20 percent Silicone Anti-foam - MCS

Owner: Janes, Ken

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	09-Jun-2015 14:09:28 UTC	10.5

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	11-Jun-2015 15:45:13 UTC	Approve	Kingstree Quality Assurance

DSM Nutritional Products

Title/Product Name: (b) (4) 20 percent Silicone Anti-foam - MCS

Product Code:

SPE #: (b) (4) Version: 11.0, CURRENT Effective Date: 12/Jun/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

☐ (b) (4), Part Number: N/A, Description: Xiameter AFE-1520 Antifoam Emulsion

Date Received:	Quantity Received:	Manufacturer Lot / Run Number:

Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO ☐ N/A
Shipping Criteria: ☐ Acceptable ☐ Damaged	**Temperature abuse evident?** ☐ YES ☐ NO
Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)? ☐ YES ☐ NO ☐ N/A	**Kosher Group 3 (Kosher Marking Required)** ☐ YES ☐ NO **N/A** (For DNP Manufactured, not required)

Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?
☐ YES ☐ NO If YES, explain:_____

Note: if one of the above is nonconforming, initiate nonconformance and forward to QA.

Inspected By:	Date:

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Lot Number: N/A	**Container or Packaging Instructions:** 200 kg drum
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:** Store at or below 350C (per Manufacturer's instructions).
	Product Shelf Life: 23 months from date of manufacture

Section 5. QUALITY CONTROL

Mon Oct 10 14:45:02 CDT 2016

DSM Nutritional Products

Title/Product Name: (b) (4) 20 percent Silicone Anti-foam - MCS

Product Code:

SPE #: (b) (4) Version: 11.0, CURRENT Effective Date: 12/Jun/2015

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
pH	Manufacturer	N/A	Attach COA	3.00 – 4.00	
Viscosity				3500 – 8500 cP	
Appearance				Pass	
Appearance spec				Free from extraneous matter; creamy liquid	
Nonvolatile Content[1]/% Solids[2]				23.0 – 29.0%	
Grade		COA or Letter on File		Record[1,2]	
☐ Pass ☐ Fail	QA/QC Signature and Date:				
Note: Footnotes above in relation to manufacturers referenced on page 1 section 1.					
Remarks:					

Section 6. PRODUCT RELEASE CONTROL

☐ Batch Record Review Completed ☐ N/A	QA/QC Signature and Date:
☐ COA Completed	QA/QC Signature and Date:
☐ Unrestricted ☐ Restricted ☐ Blocked	QA/QC Signature and Date:
Remarks/Conditions:	

Section 7. QUALITY STATUS

☐ Update Status in SAP	QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
07: 04/13/10	Added new approved manufacturer and specifications	(b) (4), (b) (6)				(b) (4), (b) (6)
08: 9/3/10	Deleted Emerald as approved Manufacturer. Clarified specifications.					
09: 8/28/12	Biennial Review only, no changes necessary.					
10: 1/22/13	Transferred from MiSys as 1003040 Changed description in section 1		NA	NA	NA	(b) (4), (b) (6)
11:6/1/15	Scheduled Review - No Changes		NA	NA	NA	K. Janes

Mon Oct 10 14:45:02 CDT 2016

DNP

DNP OPS Americas Full Lifecycle

Specification

(b) (4) Monosodium Glutamate, 1AQ, FCC (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
413100	(b) (4), (b) (6)	21-Jul-2015 20:01:12 UTC	1.5
191665	Janes, Ken	22-Jul-2015 13:31:49 UTC	1.5

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
413100	(b) (4), (b) (6)	22-Jul-2015 17:33:54 UTC	Approve	Kingstree Production
191665	Janes, Ken	29-Jul-2015 19:14:33 UTC	Approve	Kingstree Quality Assurance

DSM Nutritional Products

Title/Product Name: (b) (4) Monosodium Glutamate, 1AQ, FC (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 30/Jul/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

☐ (b) (4) Part Number: N/A, Description: Monosodium Glutamate

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO		**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 3 (Kosher Marking Required) ☐ YES ☐ NO ☐ N/A		**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO		**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A		**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A		**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:		**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 22.7 kg bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store in a cool, dry place Per manufacturer's instructions
	Product Shelf Life:	5 years or more from date of manufacturing

DSM Nutritional Products

Title/Product Name: (b) (4) onosodium Glutamate, 1AQ, FCC (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 30/Jul/2015

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	N/A	Attach COA	99 – 101.5%	
LOD				NMT 0.5%	
pH				6.7 – 7.2	
Bu k Density				1.15 – 1.35 ml/g	
Arsenic				NMT 2 mg/kg	
Lead				NMT 1 mg/kg	
Heavy Metals				NMT 10 mg/kg	
Micro				Max. 100/gram	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail — QA/QC Signature and Date:

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked — QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ Update Status in SAP — QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
	01/March/2013	(b) (4), (b) (6)	New document - transferred from MiSys as 1005440
	22/July/2015		Scheduled review - No changes

DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Nickel Sulfate, 6AQ (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	09-Jul-2015 19:49:16 UTC	1.4
413100	(b) (4), (b) (6)	21-Jul-2015 20:01:43 UTC	1.4

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
413100	(b) (4), (b) (6)	22-Jul-2015 17:34:29 UTC	Approve	Kingstree Production
191665	Janes, Ken	22-Jul-2015 13:28:18 UTC	Approve	Kingstree Quality Assurance

DSM Nutritional Products

Title/Product Name: (b) (4) Nickel Sulfate, 6AQ (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 23/Jul/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

☐ (b) (4) Part Number: 2808, Description: Nickel II Sulfate, 6-Hydrate Crystal

☐ (b) (4) Part Number: 227676, Description: Nickel II Sulfate Hexahydrate

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO		**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A		**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO		**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A		**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A		**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:		**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 500 g jar	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep tightly closed, per manufacturer's instructions
	Product Shelf Life:	Indefinite, per manufacturer (5 year re-evaluation per DNP)

DSM Nutritional Products

Title/Product Name: (b) (4) Nickel Sulfate, 6AQ (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 23/Jul/2015

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	NA	Attach COA	98.0 – 102.0% (confirms Nickel and Sulfur components	
Insoluble Matter				Max. 0.005%	
Chloride				Max. 0.001%	
Nitrogen compounds				Max. 0.002%	
Calcium				Max. 0.005%	
Copper				Max. 0.005%	
Iron				Max. 0.001%	
Magnesium				Max. 0.005%	
Manganese				Max. 0.002%	
Potassium				Max. 0.01%	
Sodium				Max. 0.05%	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail — QA/QC Signature and Date:

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted
☐ Restricted
☐ Blocked

QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ Update Status in SAP

QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
1	1/March/2013	(b) (4), (b) (6)	New document – transferred from MiSys as 1005560
			Scheduled Review - No changes

Mon Oct 10 14:08:17 CDT 2016

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

DNP

DNP OPS Americas Full Lifecycle

Specification

(b) (4) Novozymes 37071 - MCS

Owner: Ketcham, Kim

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
413100	(b) (4), (b) (6)	21-Mar-2016 14:55:44 UTC	1.6
699805	Ketcham, Kim	12-Apr-2016 13:44:04 UTC	1.6

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
699805	Ketcham, Kim	26-Apr-2016 21:20:26 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4)	15-Apr-2016 17:52:23 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Novozymes 37071 - MCS

Product Code: (b) (4)

SPE #: (b) (4) 4 Version: 2.0, CURRENT Effective Date: 27/Apr/2016

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION	
Approved Manufacturer(s): ☐ (b) (4) Part Number: 37071, Description: Food grade enzyme	
Date Received: / Quantity Received: / Manufacturer Batch Number:	
Packing List Received matches PO and material identification ☐ YES ☐ NO	COA Received? ☐ YES -- Attach to MCS ☐ NO
Kosher Group 2 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	Shipping Criteria: ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)? ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern? ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	Note: if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	Date:

Section 2. SAMPLE CONTROL				
Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION	
Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE		
Batch Number: N / A	Container or Packaging Instructions: 181 kg drum	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	Storage Condition:	Keep tightly closed in a dry, cool place between 0 - 10°C (32 - 50°F) per manufacturer's instruction
	Product Shelf Life:	24 months from date of production

DSM Nutritional Products

Title/Product Name: (b) (4) Novozymes 37071 - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 27/Apr/2016

Section 5. QUALITY CONTROL					
Test	**Responsible Party**	**Method No.**	**Result**	**Specification**	**Initial / Date**
Protease unit AU-A	Manufacturer	N/A	Attach COA	Min. 4/g	
Total viable count				Max. 10,000/g	
Coliform bacteria				Max. 30/g	
E. Coli				Not Detected/25g	
Salmonella				Not Detected/25g	
Grade		COA or Letter on File		Record	
☐ Pass ☐ Fail	QA/QC Signature and Date:				
Remarks:					

Section 6. PRODUCT RELEASE CONTROL	
☐ Unrestricted ☐ Restricted ☐ Blocked	QA/QC Signature and Date:
Remarks/Conditions:	

Section 7. QUALITY STATUS	
☐ Update Status in SAP	QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
01	20/May/2013	(b) (4), (b) (6)	New document - Per MOC 47659
02	21/Mar/2016		Scheduled review - No changes

DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Potassium Chloride FCC (b) (4) - MCS

Owner: Janes, Ken

Authors: (b) (4), (b) (6)

Reviewed By

Aurora ID	User Name	Date	Version
413100	(b) (4), (b) (5)	22-Jul-2015 17:35:19 UTC	1.4
191665	Janes, Ken	29-Jul-2015 19:20:43 UTC	1.4

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	03-Aug-2015 15:17:14 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4), (b) (6)	11-Aug-2015 17:10:28 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Potassium Chloride FCC (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 12/Aug/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION	
Approved Manufacturer(s): ☐ (b) (4), Part Number: 452883, Description: Potassium Chloride ☐ (b) (4), Part Number: 6838, Description: Potassium Chloride	
Date Received:	**Quantity Received:** / **Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL				
Sample Use	**Sample Quantity**	**Packaging**	**Storage**	**Shipped To**
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION	
Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE		
Batch Number: N / A	**Container or Packaging Instructions:** 113.4 kg drums	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep in a tightly closed container, stored in a cool, dry, ventilated area. Per manufacturer's instructions
	Product Shelf Life:	Stable for five (5) years from the date of release in their original, unopened container

DSM Nutritional Products

Title/Product Name: (b) (4) Potassium Chloride FC (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 12/Aug/2015

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Identification • Potassium • Chloride	Manufacturer	N/A	Attach COA	Passes test	
Assay				99 – 100.5%	
Acidity/Alkalinity				Passes test	
Loss on Drying				Max. 1.0%	
Iodide or Bromide				Passes test	
Aluminum				Max. 1 ppm	
Calcium and Magnesium				Passes test	
Sodium				Passes test	
Heavy Metals				Max. 0.001%	
Organic volatile impurities				Meets requirements	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail QA/QC Signature and Date:

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ Update Status in SAP QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
1.0	01/March/2013	(b) (4), (b) (6)	New document – transferred from MiSys as 1006240
2.0	30/July/2015		Scheduled for review - No changes

Mon Oct 10 13:53:54 CDT 2016

DNP

DNP OPS Americas Full Lifecycle Specification

[redacted] Sodium Molybdate, ACS, 2AQ [redacted] - MCS

Owner: Janes, Ken

Authors: [redacted]

Reviewed By

Aurora ID	User Name	Date	Version
413100	[redacted]	28-Jul-2015 15:36:55 UTC	1.6
191665	Janes, Ken	29-Jul-2015 19:26:33 UTC	1.6

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	07-Aug-2015 17:04:52 UTC	Approve	Kingstree Quality Assurance
413100	[redacted]	11-Aug-2015 17:16:52 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Sodium Molybdate, ACS, 2AQ (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 12/Aug/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION	
Approved Manufacturer(s): ☐ (b) (4), a Division of (b) (4) Part Number: N/A, Description: Sodium Molybdate, Dihydrate ☐ (b) (4) Part Number: N/A, Description: Sodium Molybdate, Dihydrate	
Date Received:	**Quantity Received:** / **Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Mon Oct 10 14:07:05 CDT 2016

DSM Nutritional Products

Title/Product Name: (b) (4) Sodium Molybdate, ACS, 2AQ (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 12/Aug/2015

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 12 kg pail	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep in tightly close container. Store in cool, dry, ventilated area away from sources of heat, moisture, and incompatibilities, per manufacturer's instructions.
	Product Shelf Life:	Stable for five (5) years from the date of release in original, unopened container

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	N/A	Attach COA	99.5 – 103.0%	
pH of 5% solution at 25°C				7.0 – 10.5	
Insoluble Matter				Max. 0.005%	
Chloride (Cl)				Max. 0.005%	
Phosphate (PO_4)				Max. 5 ppm	
Sulfates (SO_4)				Max. 0.015%	
Ammonium (NH_4)				Max. 0.001%	
Heavy Metals (as Pb)				Max. 5 ppm	
Iron (Fe)				Max. 0.001%	
Grade		COA or Letter on File		Record	

☐ **Pass** ☐ **Fail** **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ **Unrestricted** ☐ **Restricted** ☐ **Blocked** **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ **Update Status in SAP** **QA/QC Signature and Date:**

Revision History

Version No.	Date	Author	Summary of Changes
1.0	01/March/2013	(b) (4), (b) (6)	New document – transferred from MiSys as XP51007400
2.0	04/August/2015		Scheduled Review. No changes

Mon Oct 10 14:07:05 CDT 2016

DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Sodium Sulfate FCC Grade - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

o (b) (4) a Division of (b) (4) Part Number: N/A, Description: Sodium Sulfate, Anhydrous; Disodium Salt

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 50 b. bags	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep from contact with oxidizing materials. Isolate from incompat ble materials. Material is hygroscopic.
	Product Shelf Life:	Indefinite, if kept dry – Per manufacturer's instructions

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APPROVED

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Purity (% Na_2SO_4)	Manufacturer	NA	Attach COA	Min. 99.7	
NaCl (%)				Max. 0.3	
Water Insoluble (%)				Max. 0.02	
Mg, ppm				Max. 60	
Ca, ppm				Max. 30	
Fe, ppm				Max. 3	
HCO_3, ppm				Max. 250	
CO_3, ppm				Max. 30	
pH (5% solution, 27°C)				Max. 7.5	
Moisture (%)				Max. 0.02	
Grade		COA or Letter on File		Record	
o Pass o Fail	QA/QC Signature and Date:				

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted o Restricted
o Blocked

QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

o Update Status in SAP

QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 3/20/13	New document – transferred from MiSys as 1007500	(b) (4), (b) (6)	N/A	N/A	N/A	(b) (4), (b) (6)
02: 1/27/14	Changed purity specification per MOC 71591		NA	NA	NA	
03: 8/15/14	Changed sodium chloride spec per MOC 71591. Correct Kosher status		NA	NA	NA	K. Janes

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Tastone 154 Yeast - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

o (b) (4) Part Number: TT15MTK-40-AG, Description: Tastone 154

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 3 (Kosher Marking Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 40 b. bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store under cool and dry conditions, per manufacturer's instructions
	Product Shelf Life:	24 months

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Protein (TN x 6.25)	Manufacturer	N/A	Attach COA	61 – 74%	
Total Nitrogen				Record	
AN/TN				26 – 40%	
Moisture				Max. 6.0%	
Ash				Max. 22%	
Salt				Max. 1.5%	
pH				5.4 – 6.3	
Salmonella				Negative	
Standard Plate Count				Max. 15000/g	
Coliform				Max. 10/g	
Viable Yeast				Max. 50/g	
Mold				Max. 50/g	
Biotin				Record	
Phosphorus				Record	
Grade		COA or Letter on File		Record	

o Pass o Fail — QA/QC Signature and Date:

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted
o Restricted
o Blocked

QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

o Update Status in SAP

QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 03/01/13	New document – transferred from MiSys as 1008440	(b) (4)	N/A	N/A	N/A	(b) (4)
02: 1//23/14	Revised per Customer COA modifications and MOC 57077		NA	NA	NA	

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DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Thiamine HCl Crystalline, USPG (b) (4) MCS

Owner: Janes, Ken

Authors: (b) (4)

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	29-Jul-2015 19:29:28 UTC	1.4
413100	(b) (4), (b) (6)	11-Aug-2015 17:27:48 UTC	1.4

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	17-Aug-2015 13:03:07 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4), (b) (6)	24-Aug-2015 17:00:13 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name (b) (4) Thiamine HCl Crystalline, USP (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 25/Aug/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

☐ (b) (4) Part Number: N/A, Description: Thiamine Hydrochloride

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**

Packing List Received matches PO and material identification ☐ YES ☐ NO	**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 1 (Kosher Marking Not Required) ☐ YES ☐ NO ☐ N/A	**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 25 kg drum	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Below 25°C, per manufacturer's instructions
	Product Shelf Life:	3 years from the date of manufacture

DSM Nutritional Products

Title/Product Name: (b) (4) Thiamine HCl Crystalline, USPG (b) (4) - MCS

Product Code (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 25/Aug/2015

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Appearance	Manufacturer	N/A	Attach COA	Powder	
Color				White or almost white	
Clarity of solution 5% in water				Practically clear and colorless	
pH of solution 2.5% in water				2.7 – 3.3	
Identity				Corresponds	
Absorbance of a solution 10% in water at 400 nm				Max. 0.025	
Water				Max. 5.0%	
Sulphated ash (residue on ignition)				Max. 0.1%	
Heavy metals				Max. 10 ppm	
Nitrates				Passes test (USP)	
Sulphate				Max. 300 ppm	
Organic volatile impurities				Meets USP requirements	
Assay				98.5 – 101.0%	
Related substances				Corresponds	
Lead				Max. 2 ppm	
Grade		COA or Letter on File		Record	

☐ Pass ☐ Fail | QA/QC Signature and Date:

Remarks:

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked | QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

☐ Update Status in SAP | QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
1.0	01/March/2013	(b) (4)	New document – transferred from MiSys as 1008640
2.0	12/August/2015		Scheduled Review. No changes

Mon Oct 10 14:08:46 CDT 2016

DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 3
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Tocoblend L70 IP

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- o (b) (4) Part Number: N/A, Description: A natural food grade antioxidant containing natural mixed tocopherols in sunflower oil.
- o (b) (4), Part Number: 50210254, Description: Natural mixed tocopherols concentrate (Covi-ox T-70)

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 3 (Kosher Marking Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Visual Inspection Plan: Sample Plan: $\sqrt{n}$ + 1 = **Note 1: n= number of containers Note 2: n < 10, inspect 100%**	**Total Number of Containers to be Inspected:**
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
QC Release testing	1 x 50 g	50 ml centrifuge tube	N/A	Internal QC
Sensory Testing	1 x 100 g	125 ml PETG Nalgene bottle	Ambient	Columbia Sensory
QC Retention	1 x 100 g	125 ml PETG Nalgene bottle	Refrigerated	Internal QC

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 20 kg pail	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store at 15 - 25°C (per manufacturer's instructions)
	Product Shelf Life:	[1]24 months from date of production when stored at above conditions in original unopened packaging/[2]36 months

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Identity Testing	Internal QC	QCL.00109	Attach Report	Min. 90%	
Total Tocopherol	Manufacturer	N/A	Attach COA	[1]Min. 70%/[2]Min. 700 mg/g	
Non alpha tocopherols				[1]Min. 56%/[2]583 mg/g – 850 mg/g	
Acidity				[1]Passes test/[2]Max. 1.00	
Heavy Metals				Max. 10 ppm	
Specific Rotation				Min. 20°	
Sensory (Aroma)					
Overall Intensity	Columbia Sensory	DEV.00018	Attach Report	Record	
Fishy Marine Complex				Max. 0	
Green Complex				Record	
Herbaceous				Record	
Nutty Roasted				Record	
Egg Complex				Record	
Painty				Max. 0	
Other				Max. 0	
Sensory (Aromatics)					
Overall Intensity	Columbia Sensory	DEV.00018	Attach Report	Record	
Fishy Marine Complex				Max. 0	
Green Complex				Record	
Herbaceous				Record	
Nutty Roasted				Record	
Egg Complex				Record	
Painty				Max. 0	
Other				Max. 0	
Grade	Manufacturer	COA or Letter on File		Record	

o **Pass** o **Fail** — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o **Unrestricted** o **Restricted**
o **Blocked** — **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

o **Update Status in SAP** — **QA/QC Signature and Date:**

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Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 10/08/12	New document – transferred from MiSys as 1008760	(b) (4)	NA	NA	NA	(b) (4)
02: 10/07/14	Biennial Review; No changes necessary		NA	NA	NA	K. Janes
03: 03/04/15	Updated specifications due to manufacturer change notification		NA	NA	NA	K. Janes

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DNP

DNP OPS Americas Full Lifecycle Specification

(b) (4) Vitamin B12 Crystalline (b) (4) MCS

Owner: Janes, Ken

Authors: (b) (4)

Reviewed By

Aurora ID	User Name	Date	Version
191665	Janes, Ken	07-Aug-2015 17:06:50 UTC	1.5
413100	(b) (4)	11-Aug-2015 17:28:50 UTC	1.5

Electronically Approved By

Aurora ID	User Name	Date	Signature Justification	Department
191665	Janes, Ken	17-Aug-2015 13:04:42 UTC	Approve	Kingstree Quality Assurance
413100	(b) (4)	24-Aug-2015 17:01:15 UTC	Approve	Kingstree Production

DSM Nutritional Products

Title/Product Name: (b) (4) Vitamin B12 Crystalline (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 25/Aug/2015

Location: US Kingstree, US Winchester

Material Type: ☒ Raw Material ☐ Finished Goods ☐ Resale ☐ Intermediate ☐ Packaging Component

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

☐ (b) (4) Part Number: 0429155, Description: A red purplish-red, crystalline powder

Date Received:	**Quantity Received:**	**Manufacturer Batch Number:**
Packing List Received matches PO and material identification ☐ YES ☐ NO		**COA Received?** ☐ YES -- Attach to MCS ☐ NO
Kosher Group 3 (Kosher Marking Required) ☐ YES ☐ NO ☐ N/A		**Shipping Criteria:** ☐ Acceptable ☐ Damaged
Temperature abuse evident? ☐ YES ☐ NO		**Truck seals intact & match Truck Bill (Fwd. seals to Lab with COA)?** ☐ YES ☐ NO ☐ N/A
Shortage of more than 1% (Bulk only)? ☐ YES ☐ NO ☐ N/A		**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** ☐ YES ☐ NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? ☐ YES ☐ NO ☐ N/A		**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:		**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	**Expiration Date:**

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 1 kg jug	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store at a temperature below 25°C, per manufacturer's instructions
	Product Shelf Life:	60 months from the date of manufacture

DSM Nutritional Products

Title/Product Name: (b) (4) Vitamin B12 Crystallin (b) (4) - MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 25/Aug/2015

Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Appearance	Manufacturer	N/A	Attach COA	Red to purplish-red powder	
Identity				Corresponds	
Ratio of the absorbencies in water					
A361 – A278	Manufacturer	N/A	Attach COA	1.70 – 1.90	
A361/Amax (548-552)				3.15 – 3.40	
Loss on drying				Max. 3%	
Assay				96.0 – 100.5%	
Grade		COA or Letter on File		Record	
☐ Pass ☐ Fail	QA/QC Signature and Date:				
Remarks:					

Section 6. PRODUCT RELEASE CONTROL

☐ Unrestricted ☐ Restricted ☐ Blocked	QA/QC Signature and Date:
Remarks/Conditions:	

Section 7. QUALITY STATUS

☐ Update Status in SAP	QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
1.0	01/March/2013	(b) (4), (b) (6)	New document – transferred from MiSys as 1009040
2.0	14/August/2015		Scheduled Review. No Changes

DSM Nutritional Products

Title/Product Name (b) (4) Vitamin B12 Crystallin (b) (4) MCS

Product Code: (b) (4)

SPE #: (b) (4) Version: 2.0, CURRENT Effective Date: 25/Aug/2015

Section 5. QUALITY CONTROL					
Test	**Responsible Party**	**Method No.**	**Result**	**Specification**	**Initial / Date**
Appearance	Manufacturer	N/A	Attach COA	Red to purplish-red powder	
Identity				Corresponds	
Ratio of the absorbencies in water					
A361 – A278	Manufacturer	N/A	Attach COA	1.70 – 1.90	
A361/Amax (548-552)				3.15 – 3.40	
Loss on drying				Max. 3%	
Assay				96.0 – 100.5%	
Grade		COA or Letter on File		Record	
☐ Pass ☐ Fail	QA/QC Signature and Date:				
Remarks:					

Section 6. PRODUCT RELEASE CONTROL	
☐ Unrestricted ☐ Restricted ☐ Blocked	QA/QC Signature and Date:
Remarks/Conditions:	

Section 7. QUALITY STATUS	
☐ Update Status in SAP	QA/QC Signature and Date:

Revision History

Version No.	Date	Author	Summary of Changes
1.0	01/March/2013	(b) (4), (b) (6)	New document – transferred from MiSys as 1009040
2.0	14/August/2015		Scheduled Review. No Changes

DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Zinc Sulfate, 7AQ, ACS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- o (b) (4) Part Number: 4382, Description: Zinc Sulfate
- o (b) (4) Part Number: Z1095, Description: Zinc Sulfate

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO **If YES, explain:**_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 100 lb. drum	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep in a tightly closed container, stored in a cool, dry, ventilated area, per manufacturer's instructions
	Product Shelf Life:	5 years from manufacturing date

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	N/A	Attach COA	99.0 – 103.0%	
Insoluble Matter				Max. 0.01%	
pH of 5% solution at 25°C				4.4 – 6.0	
Nitrate (NO_3)				Max. 0.002%	
Ammonium (NH4)				Max. 0.001%	
Calcium (Ca)				Max. 0.005%	
Lead (Pb)				Max. 0.003%	
Magnesium (Mg)				Max. 0.005%	
Potassium (K)				Max. 0.01%	
Sodium (Na)				Max. 0.05%	
Trace Impurities (in ppm)					
Chloride (Cl)				Max. 5 ppm	
Manganese (Mn)				Max. 3 ppm	
Grade		COA or Letter on File		Record	

o **Pass** o **Fail** — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o **Unrestricted** o **Restricted** o **Blocked** — **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

o **Update Status in SAP** — **QA/QC Signature and Date:**

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 03/01/13	New document – transferred from MiSys as 1009240	D. Duke	N/A	N/A	N/A	C. Panker
02: 6/6/13	Removed Sigma as a supplier for this material	D. Duke	NA	R. Bergman	NA	C. Panker
03: 7/28/14	Added Spectrum Chemical as a supplier	D. Duke		NA	NA	K. Janes

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Calcium Chloride 0AQ, FCC

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- o (b) (4) Part Number: 229423, Description: Calcium Chloride [1](See section 4 shelf life)
- o (b) (4) art Number: 42059, Description: Calcium Chloride [1](See section 4 shelf life)
- o (b) (4) art Number: NA, Description: Calcium Chloride anhydrous pellets [2](See section 4 shelf life)

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A

Container or Packaging Instructions: 50 b. bag

Labeling Instructions:

1. Label as "Quality Inspection, as needed"

Storage Condition:	Store in a covered, clean and dry container away from incompat ble materials
Product Shelf Life:	[1]Indefinte, per Manufacturer (5 year re-evaluation per DNP) [2]24 months from date of manufacture

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay ($CaCl_2$)	Manufacturer	NA	Attach COA	93.0 – 100.5%	
Acid-Insoluble Substances				Max. 0.02%	
Arsenic				Max. 3 mg/kg	
Fluoride				Max. 0.004%	
Lead				Max. 5 mg/kg	
Magnesium and Alkali Salts				Max. 5.0%	
Grade		COA or Letter on File		Record	
o Pass o Fail	QA/QC Signature and Date:				

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted o Restricted o Blocked	QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

1. Update Status in SAP	QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
02/04/13	New document – transferred from MiSys as 1001520	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 04/28/14	Corrected product code, which was changed during SAP integration, but information was not relayed to QA		(b) (4), (b) (6)	NA	NA	K. Janes

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Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

- o (b) (4) Part Number N/A: Description : Citric Acid
- o (b) (4) Number 510102106: Citric Acid

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 3 (Kosher Marking Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
NA	NA	NA	NA	NA

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 50 b. bag	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Store below 75°F and 55% relative humidity in tightly sealed container (per Manufacturer's instructions)
	Product Shelf Life:	3 years from date of manufacture

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Identification	Manufacturer	N/A	Attach Report of Analysis	Passes test	
Assay				99.5 – 100.5%	
Water				Max. 0.5%	
Residue on Ignition				Max. 0.05%	
Heavy Metals				Max. 5 mg/kg	
Lead				Max. 0.5%	
Sulfate				Max. 0.015%	
On USS 30 mesh				Max. 3%	
Mesh, % through #100				Max. 5%	
Color of solution				Passes test	
Grade		COA or Letter on File		Record	

o **Pass** o **Fail** — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o **Unrestricted** o **Restricted** o **Blocked** — **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

o **Update Status in SAP** — **QA/QC Signature and Date:**

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 10/08/12	New document – transferred from MiSys as 1002160 and SAP as XP10865001	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 4/1/14	Added new supplier and updated specifications per MOC 75532		NA	NA	K. Janes	

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Ferrous Sulfate, 7AQ USP - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

o (b) (4) a Division o (b) (4) Part Number: FE110, Description:

o (b) (4) Part Number: NA, Description: Ferrous Sulfate 7-Hydrate

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 12 kg or 50 kg jug	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep container tightly closed. Keep container in a cool, well-ventilated area
	Product Shelf Life:	[1]3 years [2]Retest after twelve months

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	NA	Attach COA	99.5 – 104.5%	
Appearance				Bluish-green crystals	
Arsenic				Max. 3 ppm	
Lead				Max. 0.001%	
Mercury				Max. 3 ppm	
Identification				To pass test (conforms)	
Grade		COA or Letter on File		Record	

o Pass o Fail — QA/QC Signature and Date:

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o Unrestricted o Restricted o Blocked — QA/QC Signature and Date:

Remarks/Conditions:

Section 7. QUALITY STATUS

o Update Status in SAP — QA/QC Signature and Date:

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 02/04/13	New document – transferred from MiSys as 1003370	(b) (4), (b) (6)	NA	NA	NA	(b) (4), (b) (6)
02: 7/31/14	Corrected item number which was changed without QA notification during SAP implementation		NA	NA	NA	K. Janes

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DSM BRIGHT SCIENCE. BRIGHTER LIVING.	MATERIAL CONTROL SPECIFICATION	Page 1 of 2
	Document Name: (b) (4)	Product Code: (b) (4)

Raw Material: Manganese Chloride, 4 AQ, ACS - MCS

Section 1. RECEIVING / RECEIVING INSPECTION

Approved Manufacturer(s):

o (b) (4), Part Number: 2540, Description: Manganous Chloride, 4-Hydrate, Crystal

Date Received:	Quantity Received:	Manufacturer Batch Number:

Packing List Received matches PO and material identification o YES o NO	**COA Received?** o YES -- Attach to MCS o NO
Kosher Group 1 (Kosher Marking Not Required) o YES o NO o N/A	**Shipping Criteria:** o Acceptable o Damaged
Temperature abuse evident? o YES o NO	**Truck seals intact & match Truck Bill (Fwd seals to Lab with COA)?** o YES o NO o N/A
Shortage of more than 1% (Bulk only)? o YES o NO o N/A	**Evidence of moisture, insects, rodents, spillage, foreign odors, or other concern?** o YES o NO If YES, explain:_____
Materials require allergen labeling according to plant Allergen Control Policy. Labels applied? o YES o NO o N/A	**Note:** if one of the above is nonconforming, initiate nonconformance and forward to QA.
Inspected By:	**Date:**

Section 2. SAMPLE CONTROL

Sample Use	Sample Quantity	Packaging	Storage	Shipped To
N/A	N/A	N/A	N/A	N/A

Section 3. MANUFACTURE DATE & EXPIRATION

Manufacture Date:	Expiration Date:

Section 4. PRODUCT PACKAGING, LABELING & STORAGE

Batch Number: N / A	**Container or Packaging Instructions:** 200 lb. drum	
Labeling Instructions: 1. Label as "Quality Inspection, as needed"	**Storage Condition:**	Keep in tightly closed container, stored in a cool, dry ventilated area. Per manufacturer's instructions
	Product Shelf Life:	Non-shelf life item, per manufacturer (5 year re-evaluation per DNP)

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Section 5. QUALITY CONTROL

Test	Responsible Party	Method No.	Result	Specification	Initial / Date
Assay	Manufacturer	N/A	Attach COA	98.0 – 101.0%	
Insoluble Matter				Max. 0.005%	
pH of 5% solution at 25°C				3.5 – 6.0	
Sulfate				Max. 0.005%	
Calcium				Max. 0.005%	
Magnesium				Max. 0.005%	
Potassium				Max. 0.01%	
Sodium				Max. 0.05%	
Zinc				Max. 0.005%	
Heavy Metals				Max. 5 ppm	
Iron				Max. 5 ppm	
Grade		COA or Letter on File		Record	

o **Pass** o **Fail** — **QA/QC Signature and Date:**

Remarks:

Section 6. PRODUCT RELEASE CONTROL

o **Unrestricted** o **Restricted** o **Blocked** — **QA/QC Signature and Date:**

Remarks/Conditions:

Section 7. QUALITY STATUS

o **Update Status in SAP** — **QA/QC Signature and Date:**

Section 8. DOCUMENT APPROVALS & CHANGE CONTROL

Revision: Approval Date	Change Control History	Author	Materials	Operations	QC	QA
01: 03/01/13	New document – transferred from MiSys as 1004880	(b) (4), (b) (6)	N/A	N/A	N/A	(b) (4), (b) (6)
02: 05/06/14	Item number changed to match SAP		NA	NA	NA	K. Janes

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Annex 5
Algal Oil Containing EPA and DHA (AOCED) Stability Report

AOCED Stability in Aluminum Bottles Stored at -20 C, 4 C, 25 C and 40 C

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL unlined aluminum bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in unlined aluminum at 40C.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** 40 ± 2ºC, no humidity control	**Shelf Life:** To Be Determined

Stability Tests		**Appearance**[1]	**Potency**[1]	**Free Fatty Acid**[1]	**Peroxide Value**[1]	**Anisidine Value**[1]	**Tocopherols**[4]	**Sensory**[1]	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	W	W	W	W	W	W	W	(b) (4)
	1 month	W			W	W			
	2 month	W	W		W	W			
	3 month	W		W	W	W		W	
	4 month	W	W		W	W			
	5 month	W			W	W			
	6 month	W	W	W	W	W	W	W	
Reserve Samples									
Total (per lot)									

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments (b) (4) method QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00800 Green Ocean AOCED in Aluminum - 40C Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance

	Launch Date	0	1	2	3	4	5	6
VY-14962	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15240	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15465	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15572	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS

Potency, DHA mg/g, Record

	0	1	2	4	6
VY-14962	447				
VY-15240	424				
VY-15465	445				
VY-15572	406				

(b) (4)

Potency, EPA mg/g, Record

	0	1	2	4	6
VY-14962	123				
VY-15240	127				
VY-15465	118				
VY-15572	125				

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0	1	2	4	6
VY-14962	447				
VY-15240	424				
VY-15465	445				
VY-15572	406				

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6
VY-14962	0.6						
VY-15240	0.6						

(b) (4)

VY-15465	0.2	[redacted]
VY-15572	0.2	

Anisidine Value, Record

	0	1	2	3	4	5	6
VY-14962	3	[redacted]					
VY-15240	7						
VY-15465	2						
VY-15572	1						

TOTOX Value, <35

	0	1	2	3	4	5	6
VY-14962	4	[redacted]					
VY-15240	8						
VY-15465	2						
VY-15572	1						

Tocopherols, Record ppm

	0	6
VY-14962	1996	[redacted]
VY-15240	1730	
VY-15465	1757	
VY-15572	1663	

Tocopherols, Record ppm [redacted] method QQ188-1)

	0	6
VY-14962	1050	[redacted]
VY-15240	1120	
VY-15465	1160	
VY-15572	1070	

Free Fatty Acid, Record, % as Oleic Acid

	0	1	3	6
VY-14962	3.0	[redacted]		
VY-15240	2.3			
VY-15465	1.7			
VY-15572	3.3			

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL unlined aluminum bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in unlined aluminum at controlled room temperature.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** 25 ± 2°C, no humidity control	**Shelf Life:** To Be Determined

Stability Tests		**Appearance**[1]	**Potency**[1]	**Free Fatty Acid**[1]	**Peroxide Value**[1]	**Anisidine Value**[1]	**Tocopherols**[4]	**Sensory**[1]	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	X	X	X	X	X	X	X	(b) (4)
	1 month	X			X	X			
	2 month	X	X		X	X			
	3 month	X		X	X	X		X	
	4 month	X	X		X	X			
	5 month	X			X	X			
	6 month	X	X	X	X	X		X	
	9 month	X	X	X	X	X		X	
	12 month	X	X	X	X	X	X	X	
Reserve Samples									
Total (per lot)									

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments: (b) (4) method QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00801 Green Ocean AOCED in Aluminum - Room Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance

	Launch Date	0	1	2	3	4	5	6	9	12
VY-14962	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15240	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15465	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15572	1/24/2017	PASS	PASS	PASS	*PASS	*PASS	*PASS	*PASS	*PASS	*PASS

* Contains dark particles

Potency, DHA mg/g, Record

	0	1	2	4	6	9	12
VY-14962	447						
VY-15240	424						
VY-15465	445						
VY-15572	406						

(b) (4)

Potency, EPA mg/g, Record

	0	1	2	4	6	9	12
VY-14962	123						
VY-15240	127						
VY-15465	118						
VY-15572	125						

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0	1	2	4	6	9	12
VY-14962	570						
VY-15240	551						
VY-15465	563						
VY-15572	531						

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6	9	12
VY-14962	0.6								

(b) (4)

VY-15240	0.6	
VY-15465	0.2	
VY-15572	0.2	

(b) (4)

Anisidine Value, Record

	0	1	2	3	4	5	6	9	12
VY-14962	3								
VY-15240	7								
VY-15465	2								
VY-15572	1								

(b) (4)

TOTOX Value, <35

	0	1	2	3	4	5	6	9	12
VY-14962	4								
VY-15240	8								
VY-15465	2								
VY-15572	1								

(b) (4)

Tocopherols, Record ppm

	0	12
VY-14962	1996	
VY-15240	1730	
VY-15465	1757	
VY-15572	1663	

(b) (4)

Tocopherols, Record ppm (b) (4) method QQ188-1)

	0	12
VY-14962	1050	
VY-15240	1120	
VY-15465	1160	
VY-15572	1070	

(b) (4)

*Tocopherol HPLC down at 12 mos

Free Fatty Acid, Record, % as Oleic Acid

	0	1	3	6	9	12
VY-14962	3.0					
VY-15240	2.3					
VY-15465	1.7					
VY-15572	3.3					

(b) (4)

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL unlined aluminum bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in unlined aluminum at controlled refrigerated temperature.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** 4 ± 2°C	**Shelf Life:** To Be Determined

Stability Tests		**Appearance[1]**	**Potency[1]**	**Free Fatty Acid[1]**	**Peroxide Value[1]**	**Anisidine Value[1]**	**Tocopherols[4]**	**Sensory[1]**	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	Y	Y	Y	Y	Y	Y	Y	(b) (4)
	1 month	Y			Y				
	2 month	Y	Y		Y				
	3 month	Y		Y	Y	Y			
	4 month	Y	Y		Y				
	5 month	Y			Y				
	6 month	Y	Y	Y	Y	Y		Y	
	9 month	Y	Y	Y	Y	Y			
	12 month	Y	Y	Y	Y	Y	Y	Y	
Reserve Samples									
Total (per lot)									

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments (b) (4) method QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00802 Green Ocean AOCED in Aluminum - Refrigerated Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance, Brown Oil

	Launch Date	0	1	2	3	4	5	6	9	12
VY-14962	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15240	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15465	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15572	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS

Slightly lighter in color, almost a frothy appearance

Contains dark particles

Potency, DHA mg/g, Record

	0	2	4	6	9	12
VY-14962	447					
VY-15240	424					
VY-15465	445					
VY-15572	406					

(b) (4)

Potency, EPA mg/g, Record

	0	2	4	6	9	12
VY-14962	123					
VY-15240	127					
VY-15465	118					
VY-15572	125					

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0	2	4	6	9	12
VY-14962	570					
VY-15240	551					
VY-15465	563					
VY-15572	531					

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6	9	12

VY-14962	0.6
VY-15240	0.6
VY-15465	0.2
VY-15572	0.2

(b) (4)

Anisidine Value, Record

	0	1	2	3	4	5	6	9	12
VY-14962	3								
VY-15240	7								
VY-15465	2								
VY-15572	1								

(b) (4)

(b) (4)

TOTOX Value, <35

	0	1	2	3	4	5	6	9	12
VY-14962	4								
VY-15240	8								
VY-15465	2								
VY-15572	1								

(b) (4)

(b) (4)

Tocopherols, Record ppm

	0	12
VY-14962	1996	
VY-15240	1730	
VY-15465	1757	
VY-15572	1663	

Tocopherols, Record ppm (b) (4) method QQ188-1)

	0
VY-14962	1050
VY-15240	1120
VY-15465	1160
VY-15572	1070

(b) (4)

*Tocopherol HPLC down at 12 mos

Free Fatty Acid, Record, % as Oleic Acid

	0	3	6	9	12
VY-14962	3.0				
VY-15240	2.3				
VY-15465	1.7				
VY-15572	3.3				

(b) (4)

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL unlined aluminum bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in unlined aluminum at controlled frozen temperature.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** -20 ± 2°C	**Shelf Life:** To Be Determined

Stability Tests		**Appearance[1]**	**Potency[1]**	**Free Fatty Acid[1]**	**Peroxide Value[1]**	**Anisidine Value[1]**	**Tocopherols[4]**	**Sensory[1]**	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	Z	Z	Z	Z	Z	Z	Z	(b) (4)
	1 month	Z			Z				
	2 month	Z			Z				
	3 month	Z	Z	Z	Z	Z			
	4 month	Z			Z				
	5 month	Z			Z				
	6 month	Z	Z	Z	Z	Z		Z	
	9 month	Z	Z	Z	Z	Z			
	12 month	Z	Z	Z	Z	Z	Z	Z	
Reserve Samples									
Total (per lot)									

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments (b) (4) method QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00803 Green Ocean AOCED in Aluminum -Frozen Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance

	Launch Date	0	1	2	3	4	5	6	12	18	24
VY-14962	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS		
VY-15240	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS		
VY-15465	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS		
VY-15572	1/24/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS		

Slightly lighter in color, almost a frothy appearance

Contains dark particles

Potency, DHA mg/g, Record

	0	3	6	12	18	24
VY-14962	447					
VY-15240	424					
VY-15465	445					
VY-15572	406					

(b) (4)

Potency, EPA mg/g, Record

	0	3	6	12	18	24
VY-14962	123					
VY-15240	127					
VY-15465	118					
VY-15572	125					

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0	3	6	12	18	24
VY-14962	570					
VY-15240	551					
VY-15465	563					
VY-15572	531					

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6	12	18	24

VY-14962	0.6									
VY-15240	0.6									
VY-15465	0.2									
VY-15572	0.2									

(b) (4)

Anisidine Value, Record

	0	1	2	3	4	5	6	12	18	24
VY-14962	3									
VY-15240	7									
VY-15465	2									
VY-15572	1									

(b) (4) (b) (4)

TOTOX Value, <35

	0	1	2	3	4	5	6	12	18	24
VY-14962	4									
VY-15240	8									
VY-15465	2									
VY-15572	1									

(b) (4) (b) (4)

Tocopherols, Record ppm

	0	12	24
VY-14962	1996		
VY-15240	1730		
VY-15465	1757		
VY-15572	1663		

*Tocopherol HPLC down at 12 mos

Tocopherols, Record ppm (b) (4) method QQ188-1)

	0	12	24
VY-14962	1050		
VY-15240	1120		
VY-15465	1160		
VY-15572	1070		

(b) (4)

Free Fatty Acid, Record, % as Oleic Acid

	0	3	6	12	18	24
VY-14962	3.0					
VY-15240	2.3					
VY-15465	1.7					
VY-15572	3.3					

(b) (4)

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

AOCED Stability in HDPE Bottles Stored at -20 C, 4 C, 25 C and 40 C

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL Nalgene HDPE bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in HDPE at 40C.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** 40 ± 2°C, no humidity control	**Shelf Life:** To Be Determined

Stability Tests		**Appearance**[1]	**Potency**[1]	**Free Fatty Acid**[1]	**Peroxide Value**[1]	**Anisidine Value**[1]	**Tocopherols**[4]	**Sensory**[1]	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	(b) (4)
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	W	W	W	W	W	W	W	
	1 month	W			W	W			
	2 month	W	W		W	W			
	3 month	W		W	W	W		W	
	4 month	W	W		W	W			
	5 month	W			W	W			
	6 month	W	W	W	W	W	W	W	
								Reserve Samples	
								Total (per lot)	

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments: (b) (4) method QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00804 Green Ocean AOCED in HDPE - 40C Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance (Record)

	Launch Date	0	1	2	3	4	5	6
VY-14962	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15240	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15465	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15572	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS
oil contains a large amount of dark particles								

Potency, DHA mg/g, Record

	0	1	2	4	6
VY-14962	447				
VY-15240	424				
VY-15465	445				
VY-15572	406				

(b) (4)

Potency, EPA mg/g, Record

	0	1	2	4	6
VY-14962	123				
VY-15240	127				
VY-15465	118				
VY-15572	125				

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0				6
VY-14962	570				
VY-15240	551				
VY-15465	563				
VY-15572	531				

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6
VY-14962	0.6						

(b) (4)

VY-15240	0.6	(b) (4)
VY-15465	0.2	
VY-15572	0.2	

Anisidine Value, Record

	0	1	2	3	4	5	6
VY-14962	3	(b) (4)					
VY-15240	6						
VY-15465	3						
VY-15572	2						

TOTOX Value, <35

	0	1	2	3	4	5	6
VY-14962	4	(b) (4)					
VY-15240	8						
VY-15465	4						
VY-15572	3						

Tocopherols, Record ppm

	0	6
VY-14962	1917	(b) (4)
VY-15240	1672	
VY-15465	1784	
VY-15572	1666	

Tocopherols, Record ppm (b) (4) (method QQ188-1)

	0	6
VY-14962	1280	(b) (4)
VY-15240	1110	
VY-15465	1260	
VY-15572	1120	

Free Fatty Acid, Record, % as Oleic Acid

	0	1	3	6
VY-14962	3.0	(b) (4)		
VY-15240	2.3			
VY-15465	1.6			
VY-15572	3.3			

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL Nalgene HDPE bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in HDPE at controlled room temperature.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** 25 ± 2ºC, no humidity control	**Shelf Life:** To Be Determined

Stability Tests		**Appearance[1]**	**Potency[1]**	**Free Fatty Acid[1]**	**Peroxide Value[1]**	**Anisidine Value[1]**	**Tocopherols[4]**	**Sensory[1]**	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	X	X	X	X	X	X	X	(b) (4)
	1 month	X			X	X			
	2 month	X	X		X	X			
	3 month	X		X	X	X		X	
	4 month	X	X		X	X			
	5 month	X			X	X			
	6 month	X	X	X	X	X		X	
	9 month	X	X	X	X	X		X	
	12 month	X	X	X	X	X	X	X	
Reserve Samples									
Total (per lot)									

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments: (b) (4) method QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00805 Green Ocean AOCED in HDPE - Room Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance

	Launch Date	0	1	2	3	4	5	6	9	12
VY-14962	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15240	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15465	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15572	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS

oil contains a large amount of dark particles

Potency, DHA mg/g, Record

	0	1	2	4	6	9	12
VY-14962	447						
VY-15240	424						
VY-15465	445						
VY-15572	406						

(b) (4)

Potency, EPA mg/g, Record

	0	1	2	4	6	9	12
VY-14962	123						
VY-15240	127						
VY-15465	118						
VY-15572	125						

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0	1	2	4	6	9	12
VY-14962	570						
VY-15240	551						
VY-15465	563						
VY-15572	531						

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6	9	12

VY-14962	0.6									
VY-15240	0.6									
VY-15465	0.2									
VY-15572	0.2									

(b) (4)

Anisidine Value, Record

	0	1	2	3	4	5	6	12	18	24
VY-14962	3									
VY-15240	6									
VY-15465	3									
VY-15572	2									

(b) (4)

(b) (4)

TOTOX Value, <35

	0	1	2	3	4	5	6	12	18	24
VY-14962	4									
VY-15240	8									
VY-15465	4									
VY-15572	3									

(b) (4)

(b) (4)

Tocopherols, Record ppm

	0	12	24
VY-14962	1917		
VY-15240	1672		
VY-15465	1784		
VY-15572	1666		

*Tocopherol HPLC down at 12 mos

Tocopherols, Record ppm (b) (4) method QQ188-1)

	0	12	24
VY-14962	1280		
VY-15240	1110		
VY-15465	1260		
VY-15572	1120		

(b) (4)

Free Fatty Acid, Record, % as Oleic Acid

	0	3	6	12	18	24
VY-14962	3.0					
VY-15240	2.3					
VY-15465	1.6					
VY-15572	3.3					

(b) (4)

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL Nalgene HDPE bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in HDPE at controlled refrigerated temperature.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** 4 ± 2°C	**Shelf Life:** To Be Determined

Stability Tests		**Appearance[1]**	**Potency[1]**	**Free Fatty Acid[1]**	**Peroxide Value[1]**	**Anisidine Value[1]**	**Tocopherols[4]**	**Sensory[1]**	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	Y	Y	Y	Y	Y	Y	Y	(b) (4)
	1 month	Y			Y				
	2 month	Y	Y		Y				
	3 month	Y		Y	Y	Y			
	4 month	Y	Y		Y				
	5 month	Y			Y				
	6 month	Y	Y	Y	Y	Y		Y	
	9 month	Y	Y	Y	Y	Y			
	12 month	Y	Y	Y	Y	Y	Y	Y	
Reserve Samples									
Total (per lot)									

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments (b) (4) ethod QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00806 Green Ocean AOCED in HDPE - Refrigerated Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance

	Launch Date	0	1	2	3	4	5	6	9	12
VY-14962	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15240	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15465	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS
VY-15572	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS

Slightly lighter in color, almost a frothy appearance

Contains dark particles

Potency, DHA mg/g, Record

	0	2	4	6	9	12
VY-14962	447					
VY-15240	424					
VY-15465	445					
VY-15572	406					

(b) (4)

Potency, EPA mg/g, Record

	0	2	4	6	9	12
VY-14962	123					
VY-15240	127					
VY-15465	118					
VY-15572	125					

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0	2	4	6	9	12
VY-14962	570					
VY-15240	551					
VY-15465	563					
VY-15572	531					

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6	9	12

VY-14962	0.6	(b) (4)
VY-15240	0.6	
VY-15465	0.2	
VY-15572	0.2	

Anisidine Value, Record

	0	1	2	3	4	5	6	9	12
VY-14962	3								
VY-15240	6								
VY-15465	3								
VY-15572	2								

(b) (4)

(b) (4)

TOTOX Value, <35

	0	1	2	3	4	5	6	9	12
VY-14962	4								
VY-15240	8								
VY-15465	4								
VY-15572	3								

(b) (4)

(b) (4)

Tocopherols, Record ppm

	0	12
VY-14962	1917	
VY-15240	1672	
VY-15465	1784	
VY-15572	1666	

Tocopherols, Record ppm (b) (4) **(method QQ188-1)**

	0	12
VY-14962	1280	
VY-15240	1110	
VY-15465	1260	
VY-15572	1120	

(b) (4)

*Tocopherol HPLC down at 12 mos

Free Fatty Acid, Record, % as Oleic Acid

	0	3	6	9	12
VY-14962	3.0				
VY-15240	2.3				
VY-15465	1.6				
VY-15572	3.3				

(b) (4)

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

Product: Green Ocean AOCED	**Strength/Size:** Min 500 mg/g total (DHA+EPA)	**Container / Closure System:** 125mL Nalgene HDPE bottles w/ screw cap
Batch Type: Production	**Department:** Quality	**Number of Lots Tested:** 4, Base w/MNT
Purpose of Study: To evaluate the stability of Green Ocean AOCED when stored in HDPE at controlled frozen temperature.		
Lot No.: VY-14962, VY-15240, VY-15465, VY-15772	**Storage Conditions:** -20 ± 2°C	**Shelf Life:** To Be Determined

Stability Tests		**Appearance**[1]	**Potency**[1]	**Free Fatty Acid**[1]	**Peroxide Value**[1]	**Anisidine Value**[1]	**Tocopherols**[4]	**Sensory**[1]	**Number of Samples**
Test Method		QCL.00123	QCL.00028	QCL.00029	QCL.00086	QCL.00082	3rd party*	DEV.00018	(b) (4)
Expected Result		Record	Min 500 mg/g (DHA+EPA)	Record	Record, meq/kg	Record	Record, ppm	Record, Aroma only	
Test Interval	Initial	Z	Z	Z	Z	Z	Z	Z	
	1 month	Z			Z				
	2 month	Z			Z				
	3 month	Z	Z	Z	Z	Z			
	4 month	Z			Z				
	5 month	Z			Z				
	6 month	Z	Z	Z	Z	Z		Z	
	9 month	Z	Z	Z	Z	Z			
	12 month	Z	Z	Z	Z	Z	Z	Z	
Reserve Samples									
Total (per lot)									

Testing Location: 1 = MD 2 = KY 3 = SC 4 = CAL-LA

Storage Condition: W = 40C X = 25C Y = 4C Z = -20C

Comments: (b) (4) method QQ188-1, (AOAC 971.30) with HPLC quantification modification

STA.00807 Green Ocean AOCED in HDPE -Frozen Temperature

All test intervals in months

NOTE: Retain all tested samples in the walk-in -20C freezer. A bin is labeled on the front shelf.

Appearance

	Launch Date	0	1	2	3	4	5	6	12	18
VY-14962	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	
VY-15240	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	
VY-15465	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	
VY-15572	1/25/2017	PASS	PASS	PASS	PASS	PASS	PASS	PASS	PASS	

Slightly lighter in color, almost a frothy appearance

Contains dark particles

Potency, DHA mg/g, Record

	0	3	6	12	18	24
VY-14962	447					
VY-15240	424					
VY-15465	445					
VY-15572	406					

(b) (4)

Potency, EPA mg/g, Record

	0	3	6	12	18	24
VY-14962	123					
VY-15240	127					
VY-15465	118					
VY-15572	125					

(b) (4)

Potency, Min. 500 mg/g (DHA+EPA)

	0	3	6	12	18	24
VY-14962	570					
VY-15240	551					
VY-15465	563					
VY-15572	531					

(b) (4)

Peroxide Value, Record

	0	1	2	3	4	5	6	12	18	24

VY-14962	0.6	(b) (4)
VY-15240	0.6	
VY-15465	0.2	
VY-15572	0.2	

Anisidine Value, Record

	0	1	2	3	4	5	6	9	12
VY-14962	3	(b) (4)							
VY-15240	6								
VY-15465	3								
VY-15572	2								

TOTOX Value, <35

	0	1	2	3	4	5	6	9	12
VY-14962	4	(b) (4)							
VY-15240	8								
VY-15465	4								
VY-15572	3								

Tocopherols, Record ppm

	0	12
VY-14962	1917	
VY-15240	1672	
VY-15465	1784	
VY-15572	1666	

Tocopherols, Record ppm (b) (4) **method QQ188-1)**

	0	12
VY-14962	1280	(b) (4)
VY-15240	1110	
VY-15465	1260	
VY-15572	1120	

*Tocopherol HPLC down at 12 mos

Free Fatty Acid, Record, % as Oleic Acid

	0	1	3	6	9	12
VY-14962	3.0	(b) (4)				
VY-15240	2.3					
VY-15465	1.6					
VY-15572	3.3					

Rancimat, Record, Hours

	0
VY-14962	12
VY-15240	8
VY-15465	11
VY-15572	18

Product Information

Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Summary
The stability studies reported in this document are outlined in the table below.

The stability studies were conducted on production scale batches manufactured according to standard conditions.

Batch Number	Packaging	Conditions	Time
VY00014962	Aluminum bottle	Long term (25°C +/- 2°C)	12 months
VY00015240	Aluminum bottle	Long term (25°C +/- 2°C)	12 months
VY00015465	Aluminum bottle	Long term (25°C +/- 2°C)	12 months
VY00015572	Aluminum bottle	Long term (25°C +/- 2°C)	12 months
VY00014962	High density polyethylene bottle (HDPE)	Long term (25°C +/- 2°C)	12 months
VY00015240	High density polyethylene bottle (HDPE)	Long term (25°C +/- 2°C)	12 months
VY00015465	High density polyethylene bottle (HDPE)	Long term (25°C +/- 2°C)	12 months
VY00015572	High density polyethylene bottle (HDPE)	Long term (25°C +/- 2°C)	12 months
VY00014962	Aluminum bottle	Accelerated (40°C +/- 2°C)	6 months
VY00015240	Aluminum bottle	Accelerated (40°C +/- 2°C)	6 months
VY00015465	Aluminum bottle	Accelerated (40°C +/- 2°C)	6 months
VY00015572	Aluminum bottle	Accelerated (40°C +/- 2°C)	6 months
VY00014962	High density polyethylene bottle (HDPE)	Accelerated (40°C +/- 2°C)	6 months
VY00015240	High density polyethylene bottle (HDPE)	Accelerated (40°C +/- 2°C)	6 months
VY00015465	High density polyethylene bottle (HDPE)	Accelerated (40°C +/- 2°C)	6 months
VY00015572	High density polyethylene bottle (HDPE)	Accelerated (40°C +/- 2°C)	6 months

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Conclusion
The stability data in long term conditions (25°C ± 2°C) confirms the product specifications are met when packaged in both aluminum bottles and high density polyethylene bottles. The product is stable when stored under the specified conditions for at least 12 months.

In addition, the stability study carried out under accelerated conditions (40°C ± 2°C) packaged in both aluminum bottles and high density polyethylene bottles shows that the product is stable under these conditions for at least 6 months.

Stability data
The stability data in long term conditions and accelerated conditions are provided in the tables hereafter.

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00014962							
Batch size	(4) (b) kg							
Date of manufacture	July 02, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00015240							
Batch size	(4) (b) kg							
Date of manufacture	July 31, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00015465							
Batch size	[redacted] kg							
Date of manufacture	August 25, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms	[redacted]						
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00015572							
Batch size	(b) (4) kg							
Date of manufacture	September 04, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00014962							
Batch size	(4) (b) kg							
Date of manufacture	July 02, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00015240							
Batch size	(b) (4) kg							
Date of manufacture	July 31, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00015465							
Batch size	(b) (4) kg							
Date of manufacture	August 25, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Long term storage condition: 25°C ± 2°C

Lot No	VY00015572							
Batch size	[redacted]kg							
Date of manufacture	September 04, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms	[redacted]						
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							
9 months	Conforms							
12 months	Conforms							(b) (4)

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40°C ± 2°C

Lot No	VY00014962							
Batch size	(4) (b) kg							
Date of manufacture	July 02, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40°C ± 2°C

Lot No	VY00015240							
Batch size	(b) (4) kg							
Date of manufacture	July 31, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40 °C ± 2 °C

Lot No	VY00015465							
Batch size	(b) (4) kg							
Date of manufacture	August 25, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40°C ± 2°C

Lot No	VY00015572							
Batch size	[redacted] kg							
Date of manufacture	September 04, 2016							
Packaging	Aluminum bottle							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms	[redacted]						
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40°C ± 2°C

Lot No	VY00014962							
Batch size	(b) (4) kg							
Date of manufacture	July 02, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40°C ± 2°C

Lot No	VY00015240							
Batch size	(b) (4) g							
Date of manufacture	July 31, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40 °C ± 2 °C

Lot No	VY00015465							
Batch size	(4) (b) kg							
Date of manufacture	August 25, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms							
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Algal Oil Containing EPA+DHA (AOCED)

Stability Data

Accelerated storage condition: 40°C ± 2°C

Lot No	VY00015572							
Batch size	[redacted] kg							
Date of manufacture	September 04, 2016							
Packaging	High density polyethylene bottle (HDPE)							
	Appearance	Potency, EPA [mg/g oil]	Potency, DHA [mg/g oil]	Potency, EPA + DHA [mg/g oil]	Peroxide value [meq/kg]	Anisidine value	TOTOX [2x Peroxide Value + Anisidine Value]	Free Fatty Acid [%]
Specification	Record	Min. 100	Min. 250	Min. 500	Record	Record	Max. 35	Max. 5
Start	Conforms	[redacted]						
1 month	Conforms							
2 months	Conforms							
3 months	Conforms							
4 months	Conforms							
5 months	Conforms							
6 months	Conforms							

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Annex 7
Stat-Analysis 1309
Dog Kibble post-extrusion

Visualisation and statistical analysis of stability trial data Trial 1152, post extrusion application of AOCED

Dr. (b) (4), (b) (6) Senior Biostatistician, NIC-RD/HN, DSM Nutritional Products

01 Juli, 2019

Table of Contents

1 Visualisation of raw data 1

1.1 Visualisation of stability trial data in % FA Dry Matter (DM) 2

1.2 Visualisation of stability trial data in retention percent (reference: average of 8 samples per lot at baseline) 3

2 Statistical Analysis 4

2.1 Statistical Analysis of DHA, 25°C 4

2.2 Statistical Analysis of EPA, 25°C 7

2.3 Statistical Analysis of DHA, 40°C 11

2.4 Statistical Analysis of EPA, 40°C 15

3 Summary of results 20

4 Database used 20

5 Source code 20

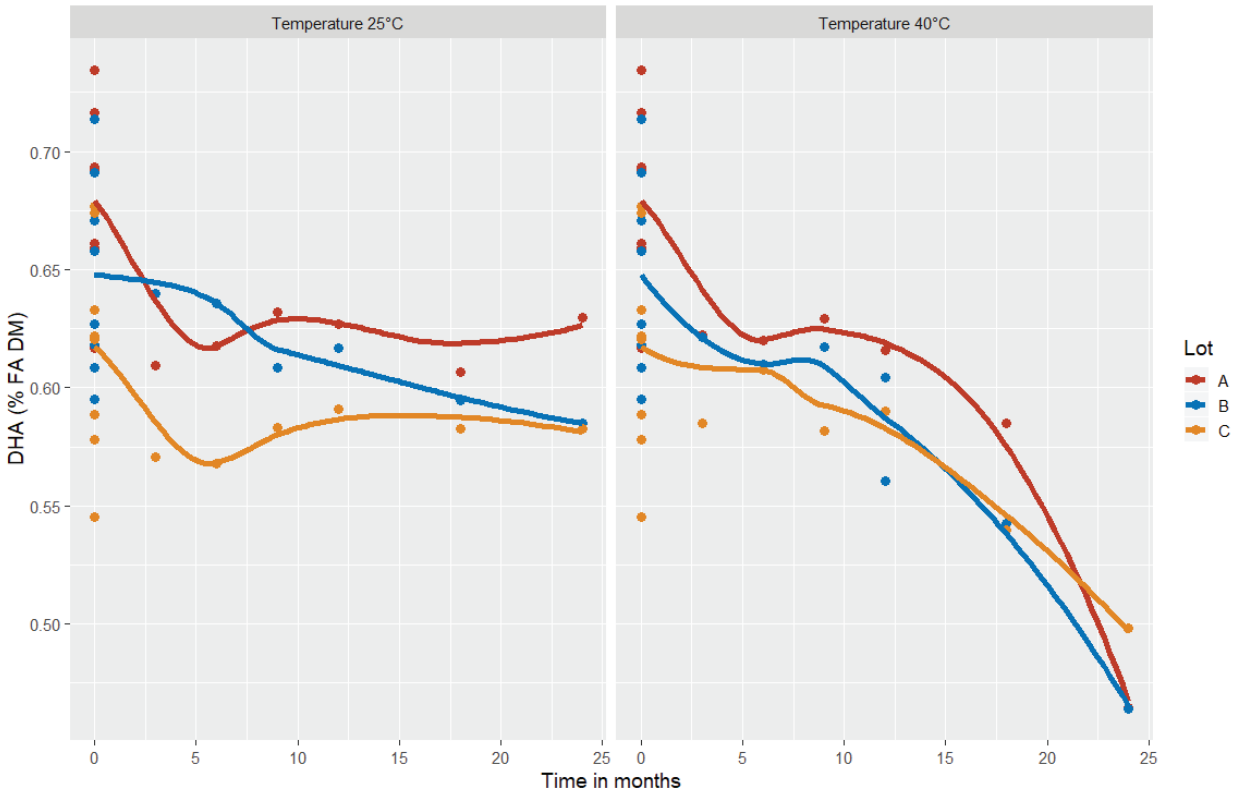
6 Appendix: Reproducibility information 20

1 Visualisation of raw data

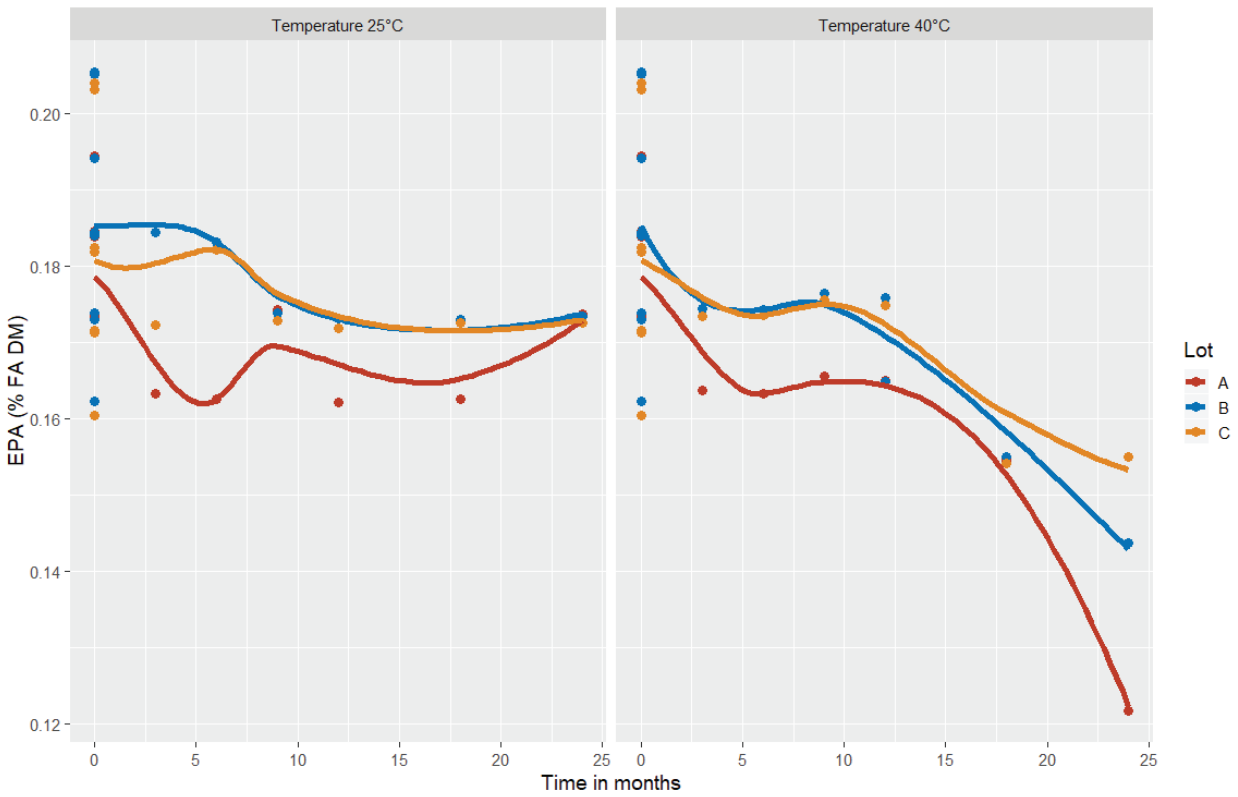
Data are plotted by temperature and coloured by lot. A data-driven regression (loess smoother, which is a local polynomial regression fitting) is displayed to visualize the evolution of the mean values by lot and time point.

1.1 Visualisation of stability trial data in % FA Dry Matter (DM)

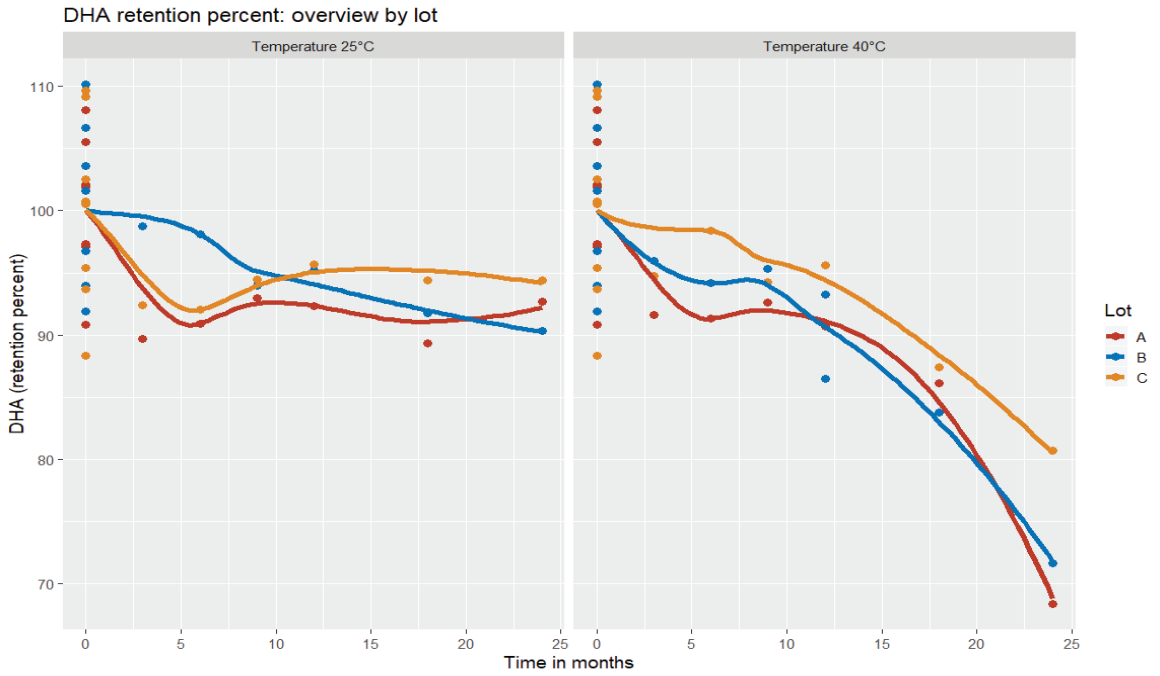
DHA content: overview by lot

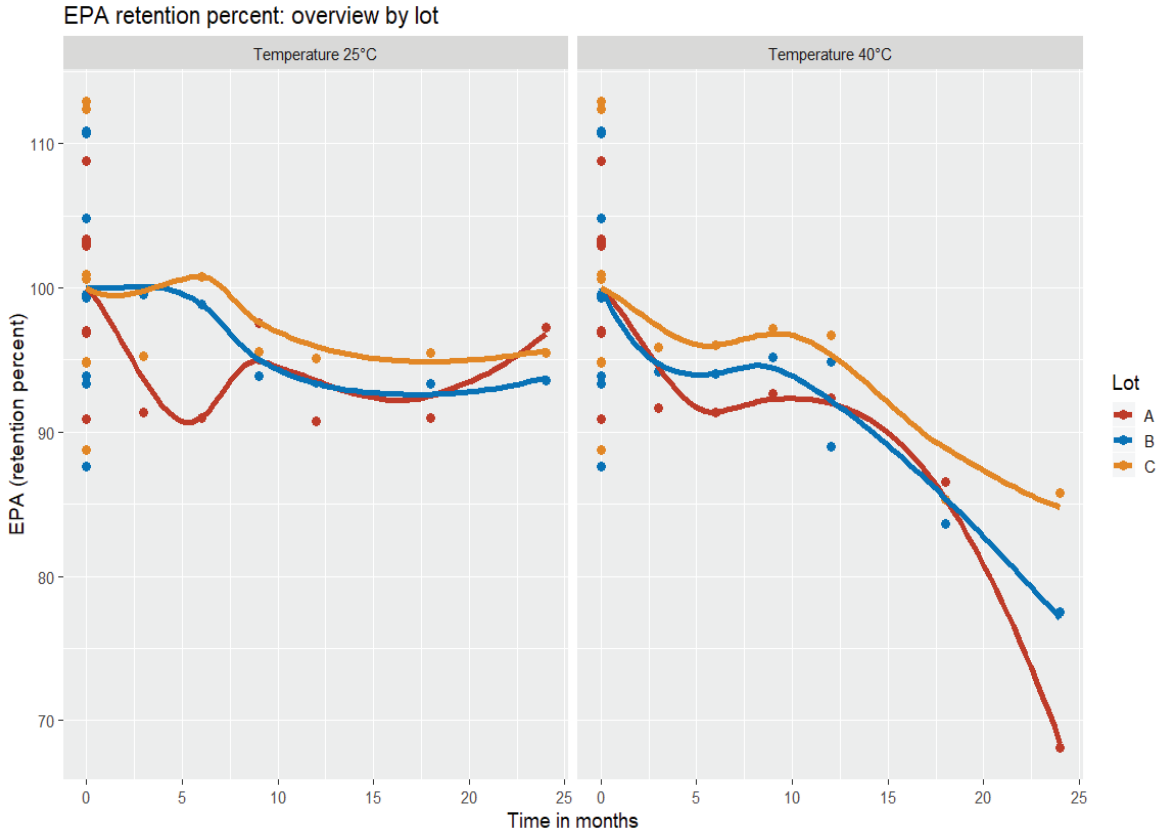


EPA content: overview by lot



1.2 Visualisation of stability trial data in retention percent (reference: average of 8 samples per lot at baseline)





2 Statistical Analysis

Each endpoint (DHA/EPA) and temperature (25°C/40°C) combination is analysed separately.

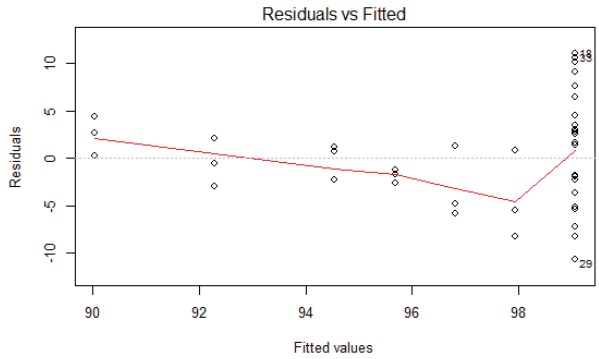
Each statistical analysis follows a two-step regression approach. Step 1 tests the poolability of lots. At first, a separate slope and intercept is fit for each lot. The slopes are tested against each other, and if not significant, they are removed. The intercepts of the lots are then tested against each other, and if not significant, they are removed as well. Step 2 performs a pooled regression using all lots.

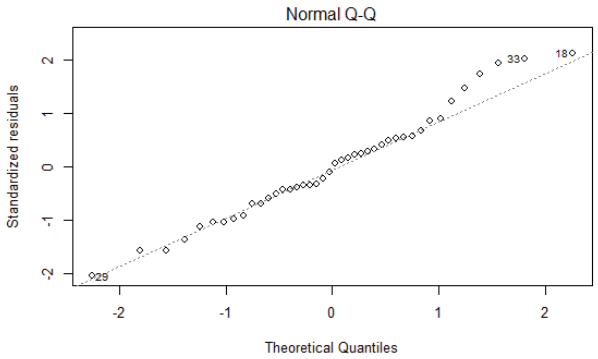
This analysis follows the recommendations of FDA Guidance GFI # 221 and ICCF Guidance # 01.

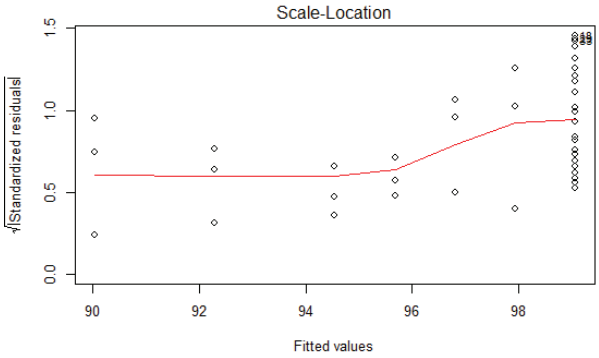
2.1 Statistical Analysis of DHA, 25°C

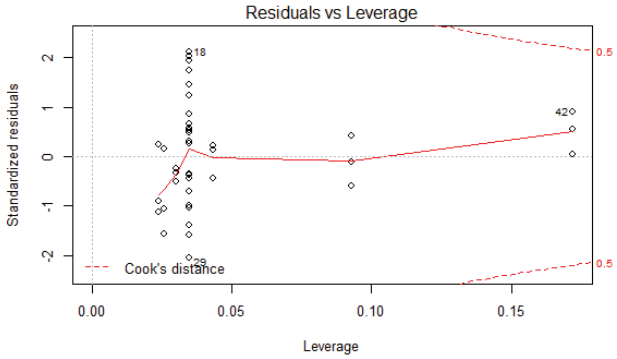
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 25°C
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -10.4296  -3.3353  -0.1484   3.0802  10.8321
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## Time      -0.425598   0.195174  -2.181   0.0358 *
## LotA      98.471122   1.784228  55.190   <2e-16 ***
## LotB      99.935752   1.784228  56.011   <2e-16 ***
## LotC      98.798331   1.784228  55.373   <2e-16 ***
## Time:LotB -0.004056   0.276017  -0.015   0.9884
## Time:LotC  0.150820   0.276017   0.546   0.5882
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.519 on 36 degrees of freedom
## Multiple R-squared:  0.9972, Adjusted R-squared:  0.9968
## F-statistic:  2170 on 6 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error
## Time:LotB = slope.B - slope.A == 0             -0.004056   0.276017
## Time:LotC = slope.C - slope.A == 0              0.150820   0.276017
## Time:LotC - Time:LotB = slope.C - slope.B == 0  0.154876   0.276017
##                                                t value Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0              -0.015    1.000
## Time:LotC = slope.C - slope.A == 0               0.546    0.849
## Time:LotC - Time:LotB = slope.C - slope.B == 0   0.561    0.841
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
```

```
## Residuals:
##      Min       1Q   Median       3Q      Max
## -10.9536  -3.6602  -0.6236   3.4547  10.4708
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.3767     0.1103  -3.415  0.00153 **
## LotA  98.2195     1.5513  63.313  < 2e-16 ***
## LotB  99.6633     1.5513  64.244  < 2e-16 ***
## LotC  99.3224     1.5513  64.024  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.403 on 38 degrees of freedom
## Multiple R-squared:  0.9972, Adjusted R-squared:  0.9969
## F-statistic:  3397 on 4 and 38 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0   1.4438     2.0420   0.707
## LotC - LotA = intercept.C - intercept.A == 0   1.1029     2.0420   0.540
## LotC - LotB = intercept.C - intercept.B == 0  -0.3409     2.0420  -0.167
##                                               Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.761
## LotC - LotA = intercept.C - intercept.A == 0    0.852
## LotC - LotB = intercept.C - intercept.B == 0    0.985
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -10.6996  -3.4755  -0.1165   2.7591  11.0657
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  99.0684     0.9898 100.085  < 2e-16 ***
## Time         -0.3767     0.1083  -3.479  0.00123 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.304 on 40 degrees of freedom
## Multiple R-squared:  0.2323, Adjusted R-squared:  0.2131
## F-statistic:  12.1 on 1 and 40 DF,  p-value: 0.00123

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```










```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                  2.5 %      97.5 %
## (Intercept) 97.0678634 101.0689393
## Time        -0.5955123  -0.1578412

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

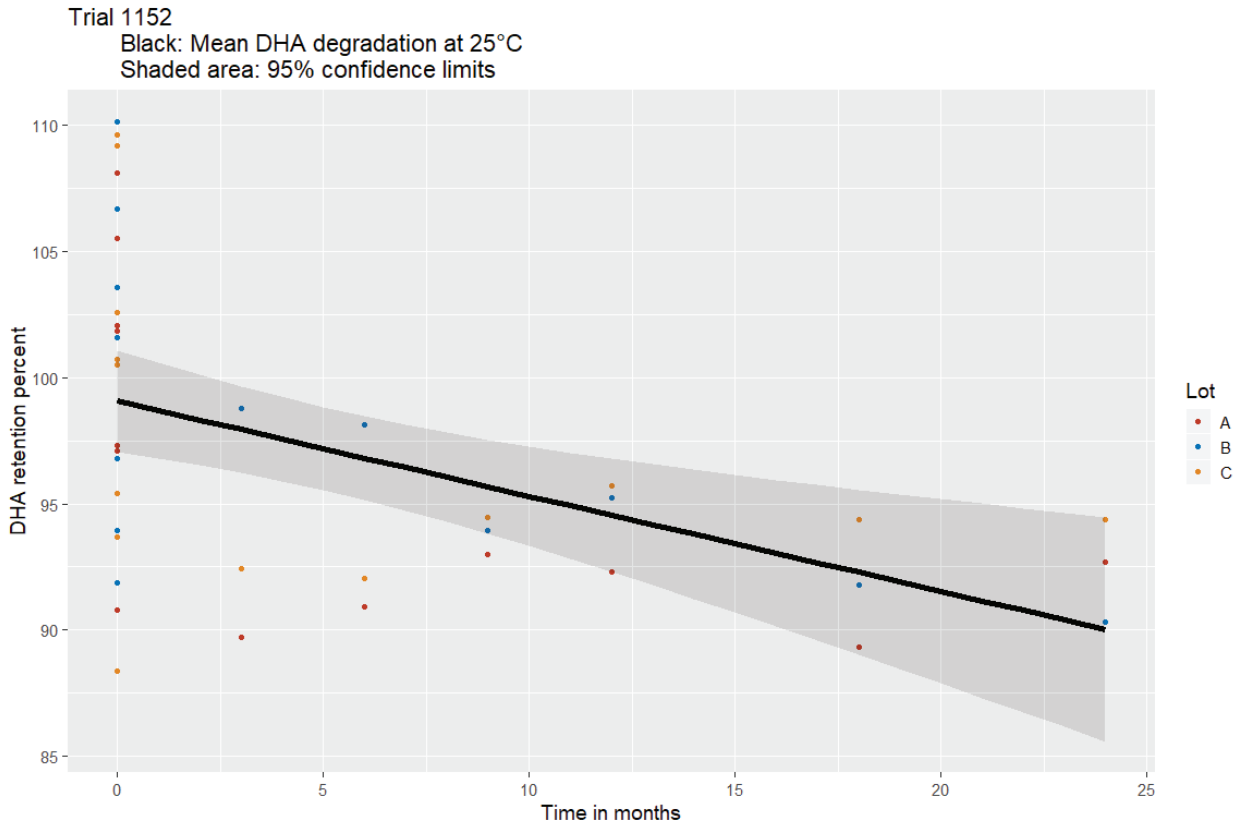
Temp	Time	DHA.estimated.mean	DHA.lower.CI	DHA.upper.CI
25	0	99.06840		
25	1	98.69172		
25	2	98.31505		
25	3	97.93837		
25	4	97.56169		
25	5	97.18502		
25	6	96.80834		
25	7	96.43166		
25	8	96.05499		
25	9	95.67831		
25	10	95.30163		
25	11	94.92496		
25	12	94.54828		

(b) (4)

(b) (4)

```
25          13              94.17160
25          14              93.79493
25          15              93.41825
25          16              93.04157
25          17              92.66490
25          18              92.28822
25          19              91.91154
25          20              91.53487
25          21              91.15819
25          22              90.78151
25          23              90.40484
25          24              90.02816
```

```
##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

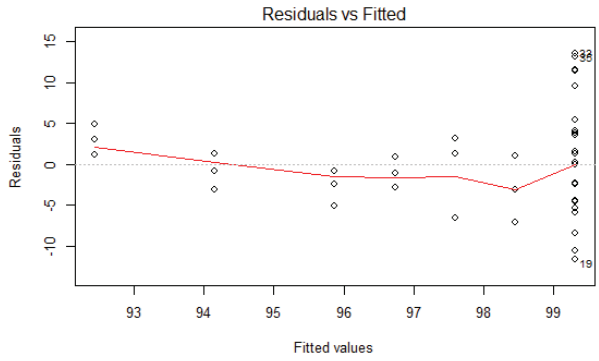


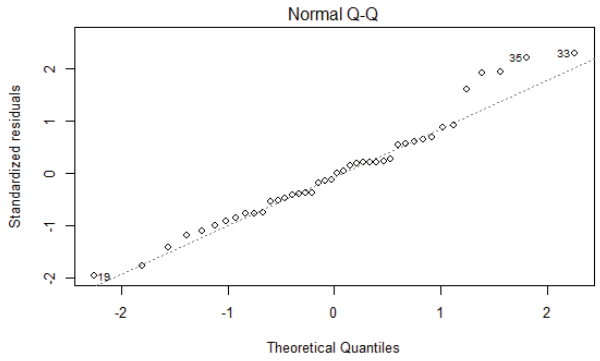
2.2 Statistical Analysis of EPA, 25°C

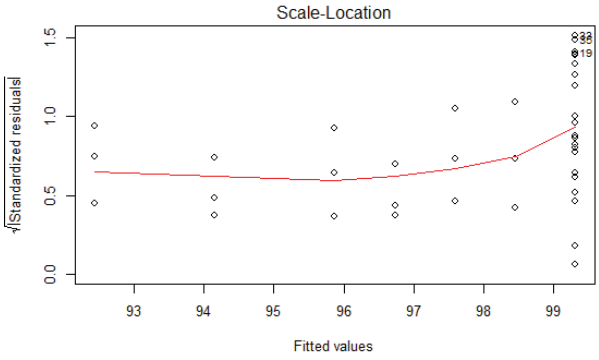
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES FOR EACH LOT AND TEST, 25°C
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
```

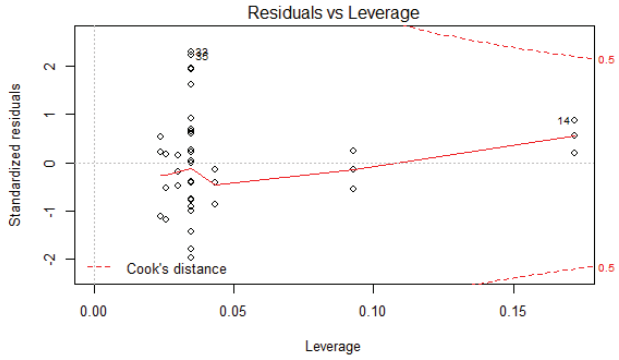
```
## Residuals:
##     Min      1Q  Median      3Q     Max
## -12.203  -4.141  -0.414   2.445  13.318
##
## Coefficients:
##           Estimate Std. Error t value Pr(>|t|)
## Time      -0.28678    0.22346  -1.283    0.208
## LotA      98.54453    2.04278  48.240   <2e-16 ***
## LotB      99.81400    2.04278  48.862   <2e-16 ***
## LotC      99.58657    2.04278  48.751   <2e-16 ***
## Time:LotB -0.05782    0.31601  -0.183    0.856
## Time:LotC  0.05789    0.31601   0.183    0.856
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6.319 on 36 degrees of freedom
## Multiple R-squared:  0.9964, Adjusted R-squared:  0.9958
## F-statistic:  1679 on 6 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0             -0.05782    0.31601  -0.183
## Time:LotC = slope.C - slope.A == 0              0.05789    0.31601   0.183
## Time:LotC - Time:LotB = slope.C - slope.B == 0  0.11570    0.31601   0.366
##                                                 Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                 0.982
## Time:LotC = slope.C - slope.A == 0                 0.982
## Time:LotC - Time:LotB = slope.C - slope.B == 0     0.929
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -11.9057  -4.1722  -0.6143   2.6016  13.0208
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.2868     0.1258  -2.279   0.0283 *
## LotA  98.5444     1.7694  55.693   <2e-16 ***
## LotB  99.5165     1.7694  56.243   <2e-16 ***
## LotC  99.8842     1.7694  56.450   <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6.162 on 38 degrees of freedom
## Multiple R-squared:  0.9964, Adjusted R-squared:  0.996
## F-statistic:  2648 on 4 and 38 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                          Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0   0.9721     2.3290   0.417
## LotC - LotA = intercept.C - intercept.A == 0   1.3397     2.3290   0.575
## LotC - LotB = intercept.C - intercept.B == 0   0.3676     2.3290   0.158
```

```
##                                            Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.909
## LotC - LotA = intercept.C - intercept.A == 0    0.834
## LotC - LotB = intercept.C - intercept.B == 0    0.986
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -11.7042  -4.1238  -0.4094   3.1707  13.5899
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  99.3150     1.1262  88.189   <2e-16 ***
## Time         -0.2868     0.1232  -2.328   0.0251 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6.034 on 40 degrees of freedom
## Multiple R-squared:  0.1193, Adjusted R-squared:  0.09729
## F-statistic: 5.419 on 1 and 40 DF,  p-value: 0.02507

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```









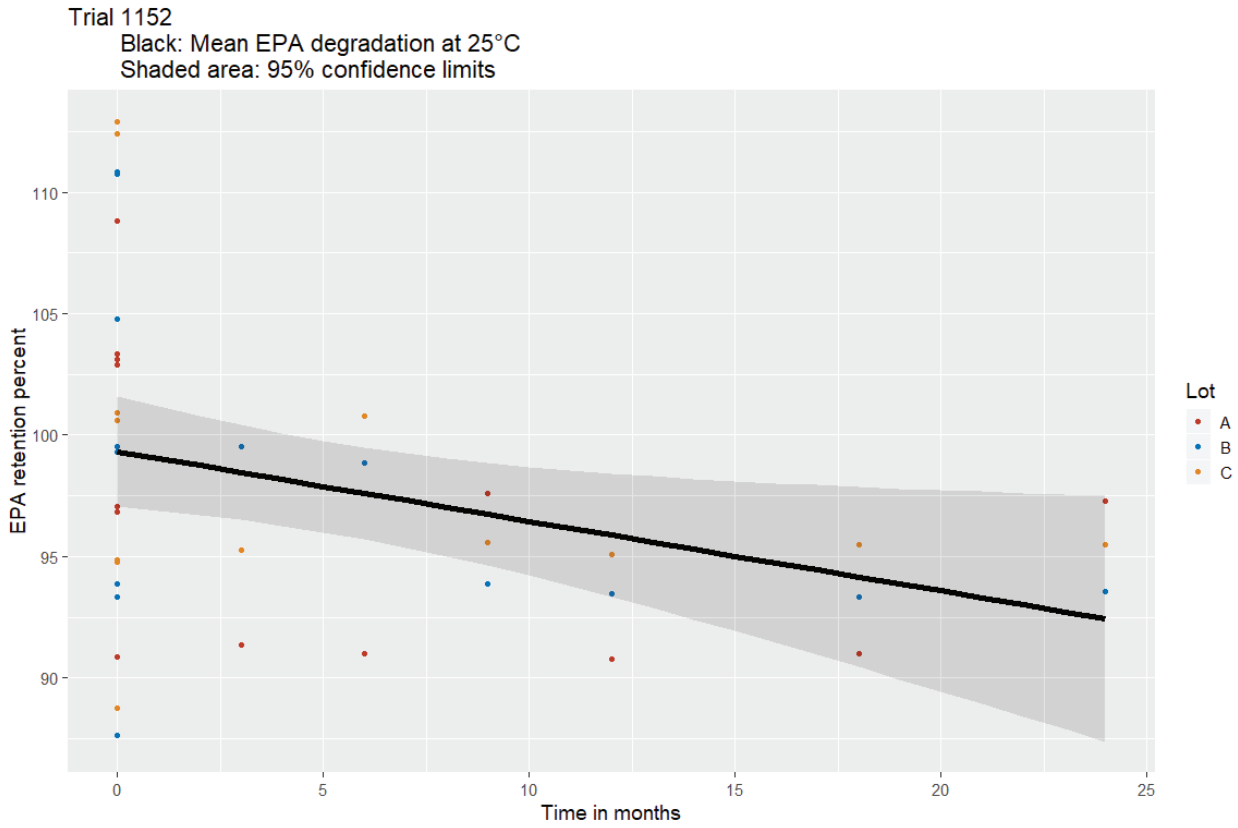

```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                 2.5 %       97.5 %
## (Intercept) 97.0389882 101.59108240
## Time        -0.5357316  -0.03778549

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

Temp	Time	EPA.estimated.mean	EPA.lower.CI	EPA.upper.CI
25	0	99.31504		
25	1	99.02828		
25	2	98.74152		
25	3	98.45476		
25	4	98.16800		
25	5	97.88124		
25	6	97.59448		
25	7	97.30773		
25	8	97.02097		
25	9	96.73421		
25	10	96.44745		
25	11	96.16069		
25	12	95.87393		

(b) (4)

(b) (4)

```
25          13              95.58717
25          14              95.30042
25          15              95.01366
25          16              94.72690
25          17              94.44014
25          18              94.15338
25          19              93.86662
25          20              93.57986
25          21              93.29311
25          22              93.00635
25          23              92.71959
25          24              92.43283

##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

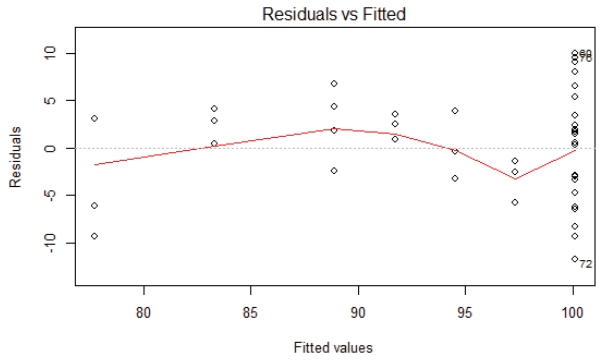


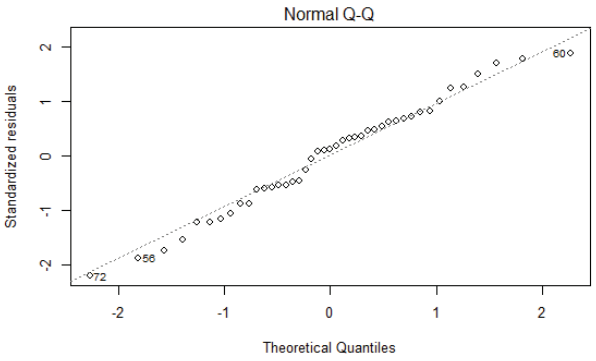
2.3 Statistical Analysis of DHA, 40°C

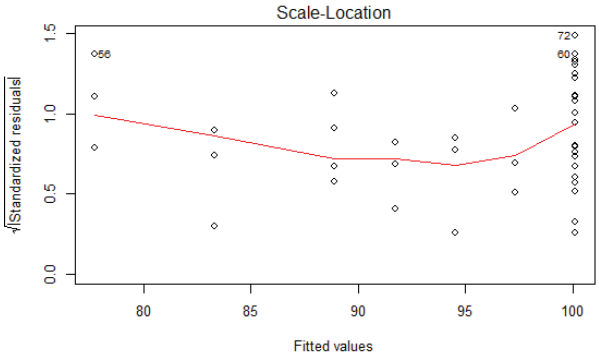
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES FOR EACH LOT AND TEST, 40°C
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
```

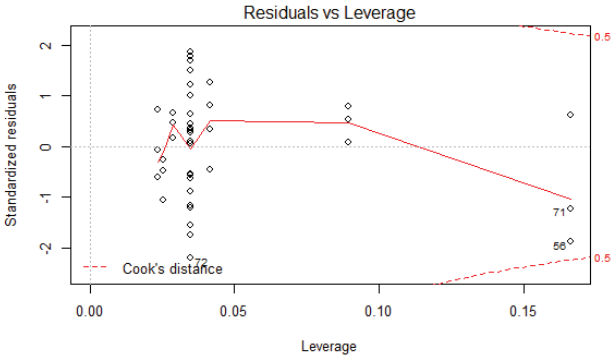
```
## Residuals:
##     Min      1Q  Median      3Q     Max
## -11.795  -3.443   0.334   3.424   9.716
##
## Coefficients:
##            Estimate Std. Error t value Pr(>|t|)
## Time       -1.07070    0.19371  -5.527 2.74e-06 ***
## LotA       99.84442    1.77084  56.383  < 2e-16 ***
## LotB      100.41794    1.76523  56.887  < 2e-16 ***
## LotC      100.16383    1.77084  56.563  < 2e-16 ***
## Time:LotB   0.05079    0.27036   0.188    0.852
## Time:LotC   0.36125    0.27395   1.319    0.195
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.478 on 37 degrees of freedom
## Multiple R-squared:  0.9972, Adjusted R-squared:  0.9967
## F-statistic:  2176 on 6 and 37 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                  Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0               0.05079    0.27036   0.188
## Time:LotC = slope.C - slope.A == 0               0.36125    0.27395   1.319
## Time:LotC - Time:LotB = slope.C - slope.B == 0   0.31046    0.27036   1.148
##                                                  Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                  0.981
## Time:LotC = slope.C - slope.A == 0                  0.394
## Time:LotC - Time:LotB = slope.C - slope.B == 0      0.491
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -12.9546  -3.4463   0.6447   3.2811  10.1921
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.9349     0.1109   -8.43 2.55e-10 ***
## LotA  99.1461     1.5721   63.07  < 2e-16 ***
## LotB  99.9419     1.5455   64.66  < 2e-16 ***
## LotC 101.3233     1.5721   64.45  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.481 on 39 degrees of freedom
## Multiple R-squared:  0.997,  Adjusted R-squared:  0.9967
## F-statistic:  3259 on 4 and 39 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                            Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0   0.7959     2.0376   0.391
## LotC - LotA = intercept.C - intercept.A == 0   2.1772     2.0718   1.051
## LotC - LotB = intercept.C - intercept.B == 0   1.3814     2.0376   0.678
```

```
##                                            Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.920
## LotC - LotA = intercept.C - intercept.A == 0    0.550
## LotC - LotB = intercept.C - intercept.B == 0    0.778
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -11.7666  -3.2836   0.5778   3.5105   9.9987
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 100.1354     1.0110  99.046  < 2e-16 ***
## Time         -0.9354     0.1097  -8.529 1.26e-10 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.423 on 41 degrees of freedom
## Multiple R-squared:  0.6396, Adjusted R-squared:  0.6308
## F-statistic: 72.75 on 1 and 41 DF,  p-value: 1.257e-10

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```









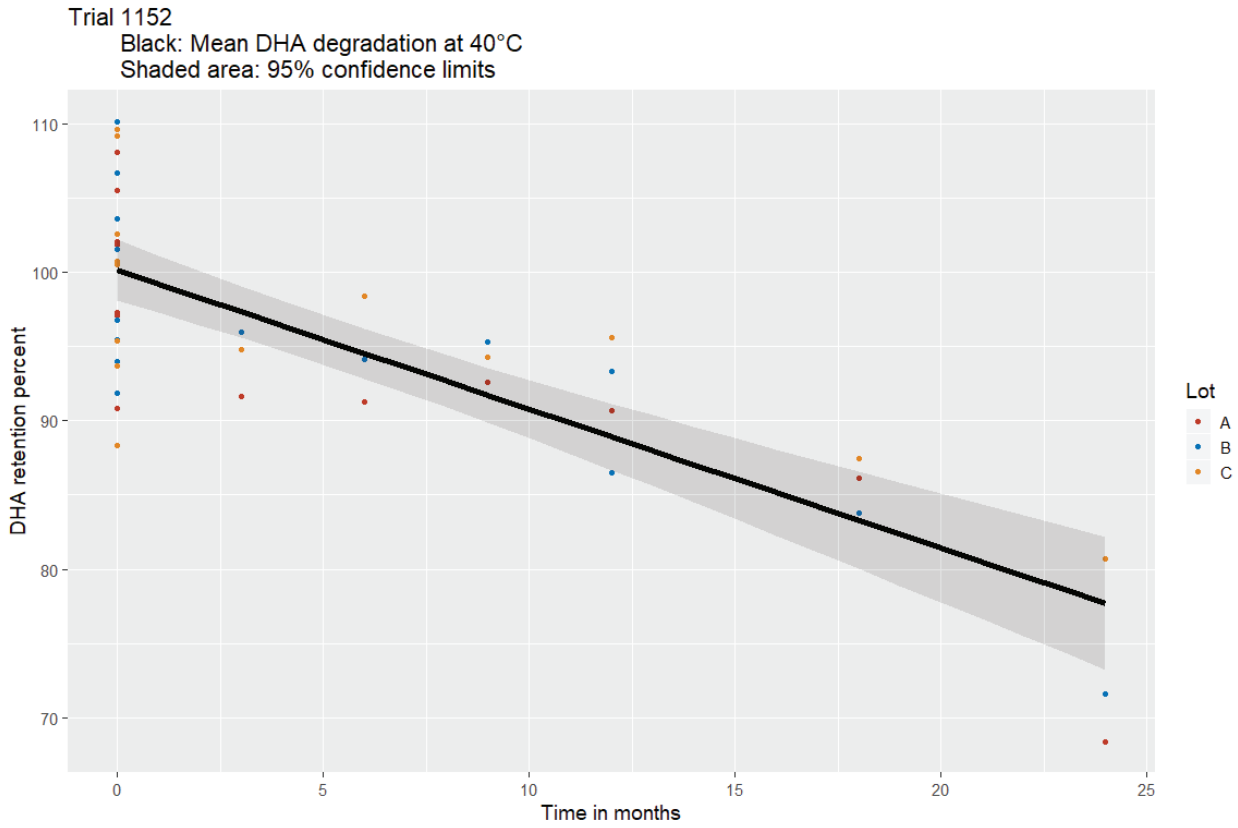

```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                2.5 %     97.5 %
## (Intercept) 98.09365 102.177148
## Time        -1.15693  -0.713952

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

Temp	Time	DHA.estimated.mean	DHA.lower.CI	DHA.upper.CI
40	0	100.13540		
40	1	99.19996		
40	2	98.26452		
40	3	97.32908		
40	4	96.39364		
40	5	95.45819		
40	6	94.52275		
40	7	93.58731		
40	8	92.65187		
40	9	91.71643		
40	10	90.78099		
40	11	89.84555		
40	12	88.91011		

(b) (4)

(b) (4)

```
40        13              87.97467
40        14              87.03923
40        15              86.10378
40        16              85.16834
40        17              84.23290
40        18              83.29746
40        19              82.36202
40        20              81.42658
40        21              80.49114
40        22              79.55570
40        23              78.62026
40        24              77.68482

##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

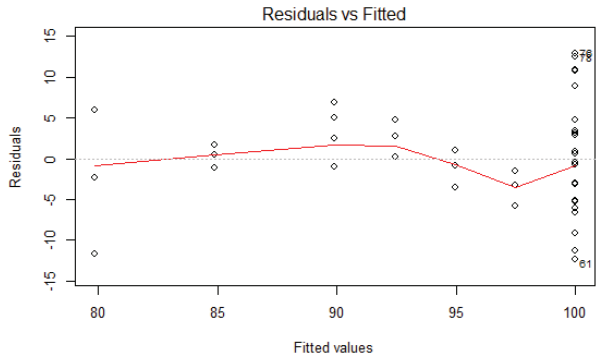


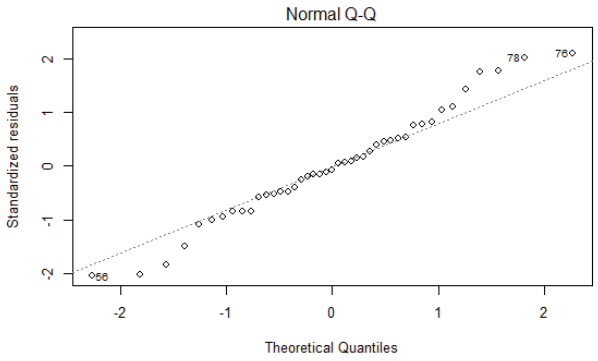
2.4 Statistical Analysis of EPA, 40˚C

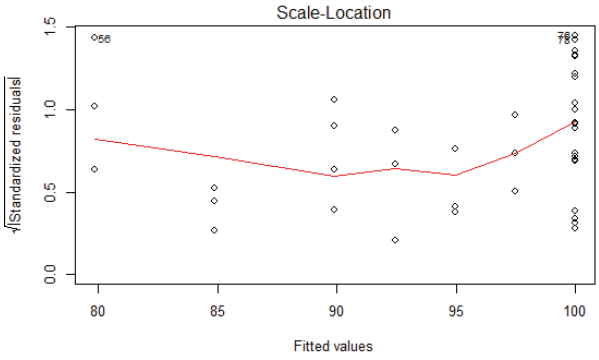
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES FOR EACH LOT AND TEST, 40°C
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
```

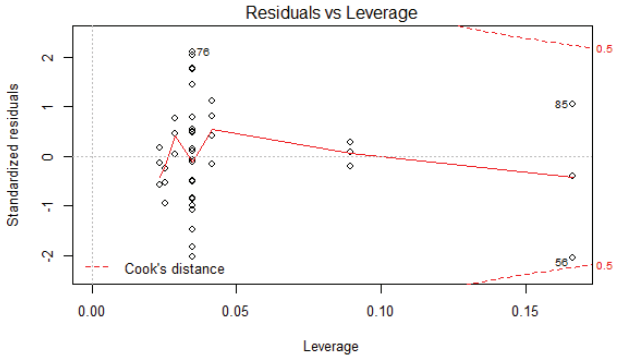
```
## Residuals:
##      Min       1Q   Median       3Q      Max
## -12.4196  -3.5570  -0.7382   3.3130  12.8642
##
## Coefficients:
##           Estimate Std. Error t value Pr(>|t|)
## Time       -1.0560     0.2228  -4.740 3.14e-05 ***
## LotA       99.9144     2.0367  49.057  < 2e-16 ***
## LotB      100.0305     2.0303  49.270  < 2e-16 ***
## LotC      100.0408     2.0367  49.119  < 2e-16 ***
## Time:LotB   0.1990     0.3110   0.640    0.526
## Time:LotC   0.4492     0.3151   1.426    0.162
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6.3 on 37 degrees of freedom
## Multiple R-squared:  0.9963, Adjusted R-squared:  0.9957
## F-statistic:  1656 on 6 and 37 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0               0.1990     0.3110   0.640
## Time:LotC = slope.C - slope.A == 0               0.4492     0.3151   1.426
## Time:LotC - Time:LotB = slope.C - slope.B == 0   0.2502     0.3110   0.805
##                                                 Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                 0.799
## Time:LotC = slope.C - slope.A == 0                 0.338
## Time:LotC - Time:LotB = slope.C - slope.B == 0     0.702
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -12.4873  -3.0350  -0.6534   4.1992  11.6635
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.8402     0.1275  -6.588 7.93e-08 ***
## LotA  98.8047     1.8079  54.651  < 2e-16 ***
## LotB  99.9366     1.7774  56.225  < 2e-16 ***
## LotC 101.2414     1.8079  55.999  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6.304 on 39 degrees of freedom
## Multiple R-squared:  0.9961, Adjusted R-squared:  0.9957
## F-statistic:  2480 on 4 and 39 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                             Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0    1.132      2.343   0.483
## LotC - LotA = intercept.C - intercept.A == 0    2.437      2.383   1.023
## LotC - LotB = intercept.C - intercept.B == 0    1.305      2.343   0.557
```

```
##                                            Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.880
## LotC - LotA = intercept.C - intercept.A == 0    0.567
## LotC - LotB = intercept.C - intercept.B == 0    0.844
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -12.3829  -3.4396  -0.4861   3.2336  12.9112
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  99.9938     1.1615   86.09  < 2e-16 ***
## Time         -0.8403     0.1260   -6.67 4.83e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 6.23 on 41 degrees of freedom
## Multiple R-squared:  0.5204, Adjusted R-squared:  0.5087
## F-statistic: 44.48 on 1 and 41 DF,  p-value: 4.833e-08

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```









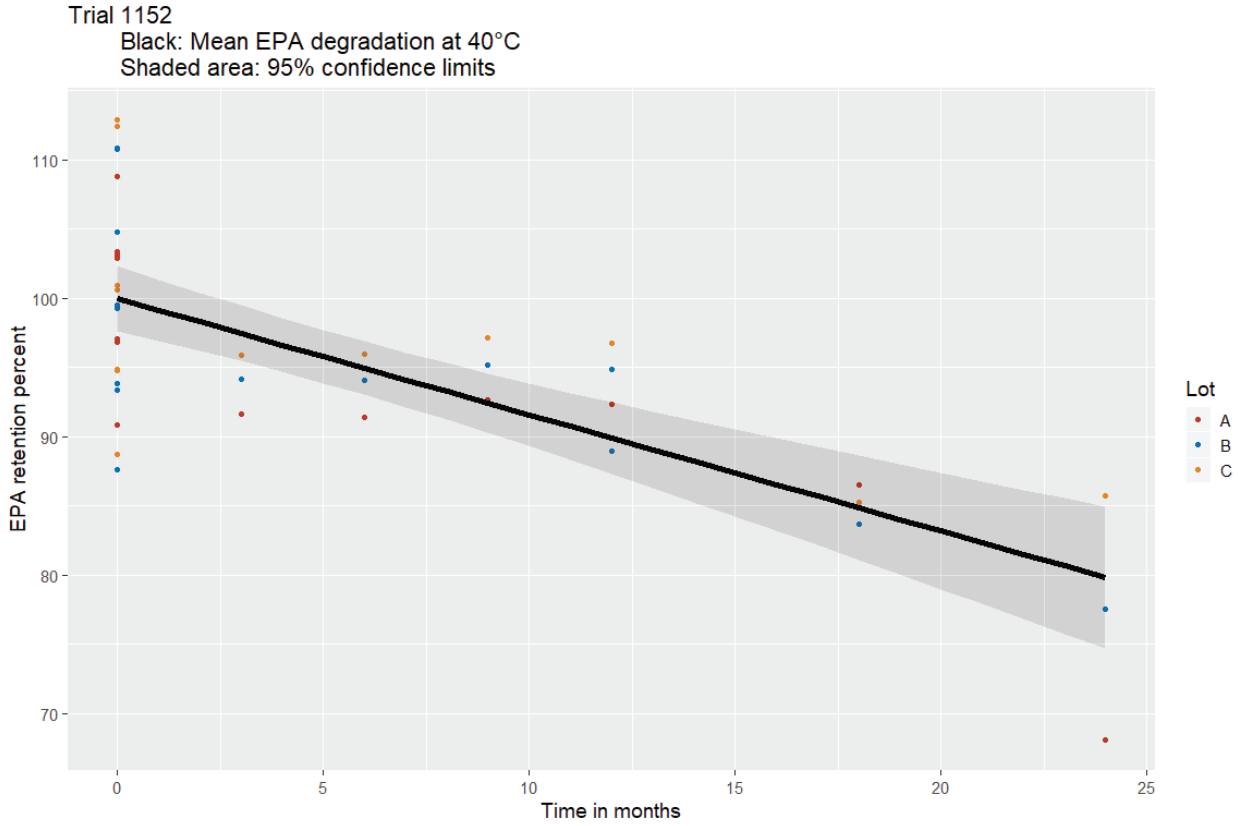

```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                 2.5 %      97.5 %
## (Intercept) 97.648155 102.3393657
## Time        -1.094795  -0.5858924

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

Temp	Time	EPA.estimated.mean	EPA.lower.CI	EPA.upper.CI
40	0	99.99376		
40	1	99.15342		
40	2	98.31307		
40	3	97.47273		
40	4	96.63238		
40	5	95.79204		
40	6	94.95170		
40	7	94.11135		
40	8	93.27101		
40	9	92.43067		
40	10	91.59032		
40	11	90.74998		
40	12	89.90963		

(b) (4)

```
40        13              89.06929
40        14              88.22895
40        15              87.38860
40        16              86.54826
40        17              85.70791
40        18              84.86757
40        19              84.02723
40        20              83.18688
40        21              82.34654
40        22              81.50620
40        23              80.66585
40        24              79.82551

##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

(b) (4)



3 Summary of results

Within all analyses, lots were poolable. Displayed are estimated mean results with 95% confidence limits of the estimate in brackets.

Endpoint	Temperature	Monthly degradation in %	Retention in % of initial value at 24M
DHA	25	-0.38 (-0.6,-0.16)	90.03 (85.58,94.47)
EPA	25	-0.29 (-0.54,-0.04)	92.43 (87.37,97.49)
DHA	40	-0.94 (-1.16,-0.71)	77.68 (73.22,82.15)
EPA	40	-0.84 (-1.09,-0.59)	79.83 (74.7,84.96)

4 Database used



1152.xlsx

5 Source code



Stat-Analysis_1152.R

6 Appendix: Reproducibility information

- This document was created with (b) (4), (b) (6)
- Script created: 27.06.2019
- Last change in script: 01.07.2019
- Date and time of analysis: 2019-07-01 11:31:20
- R version and package information:

```
## (b)version 3.5.3 (2019-03-11)
##  )atform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows >= 8 x64 (build 9200)
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=German_Switzerland.1252  LC_CTYPE=German_Switzerland.1252
## [3] LC_MONETARY=German_Switzerland.1252 LC_NUMERIC=C
## [5] LC_TIME=German_Switzerland.1252
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
##  [1] dplyr_0.8.0.1      ggsci_2.9          RColorBrewer_1.1-2
##  [4] ggplot2_3.1.0      lsmeans_2.30-0     emmeans_1.3.3
##  [7] pander_0.6.3       multcomp_1.4-10    TH.data_1.0-10
```

```
## [10] MASS_7.3-51.1      survival_2.43-3    mvtnorm_1.0-10
## [13] nlme_3.1-137       papeR_1.0-4        xtable_1.8-3
## [16] car_3.0-2          carData_3.0-2      knitr_1.22
## [19] readxl_1.3.1
##
## loaded via a namespace (and not attached):
##  [1] Rcpp_1.0.1        lattice_0.20-38   zoo_1.8-5
##  [4] gtools_3.8.1      assertthat_0.2.1  digest_0.6.18
##  [7] R6_2.4.0          cellranger_1.1.0  plyr_1.8.4
## [10] evaluate_0.13     coda_0.19-2       highr_0.8
## [13] pillar_1.3.1      rlang_0.3.2       lazyeval_0.2.2
## [16] curl_3.3          data.table_1.12.0 gdata_2.18.0
## [19] gmodels_2.18.1    Matrix_1.2-17     rmarkdown_1.12
## [22] labeling_0.3      splines_3.5.3     stringr_1.4.0
## [25] foreign_0.8-71    munsell_0.5.0     compiler_3.5.3
## [28] xfun_0.5          pkgconfig_2.0.2   htmltools_0.3.6
## [31] tidyselect_0.2.5  tibble_2.1.1      rio_0.5.16
## [34] codetools_0.2-16  crayon_1.3.4      withr_2.1.2
## [37] grid_3.5.3        gtable_0.3.0      magrittr_1.5
## [40] scales_1.0.0      zip_2.0.1         estimability_1.3
## [43] stringi_1.4.3     sandwich_2.5-0    openxlsx_4.1.0
## [46] tools_3.5.3       forcats_0.4.0     glue_1.3.1
## [49] purrr_0.3.2       hms_0.4.2         abind_1.4-5
## [52] yaml_2.2.0        colorspace_1.4-1  haven_2.1.0
```

Data table for statistical analysis

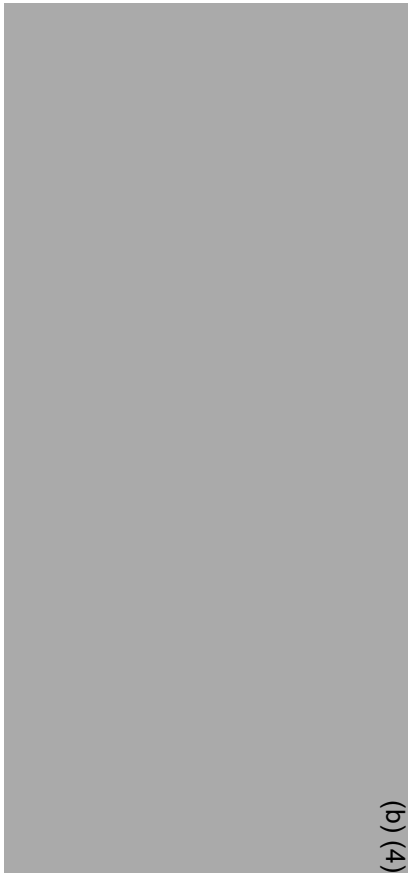
Study	Conditions	Temp	Lot	Sample ID	Pull	Time	DHA	EPA
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220567	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220568	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220569	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220570	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220571	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220572	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220573	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220574	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-08210455	Month 3	3		
1152	Ambient (25°C/60%RH)	25	A	464-2017-11200350	Month 6	6		
1152	Ambient (25°C/60%RH)	25	A	464-2018-02190201	Month 9	9		
1152	Ambient (25°C/60%RH)	25	A	464-2018-05210340	Month 12	12		
1152	Ambient (25°C/60%RH)	25	A	464-2018-11200162	Month 18	18		
1152	Ambient (25°C/60%RH)	25	A	464-2019-05210165	Month 24	24		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220575	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220576	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220577	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220578	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220579	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220580	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220581	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220582	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-08210457	Month 3	3		
1152	Ambient (25°C/60%RH)	25	B	464-2017-11200352	Month 6	6		
1152	Ambient (25°C/60%RH)	25	B	464-2018-02190203	Month 9	9		
1152	Ambient (25°C/60%RH)	25	B	464-2018-05210342	Month 12	12		
1152	Ambient (25°C/60%RH)	25	B	464-2018-11200164	Month 18	18		
1152	Ambient (25°C/60%RH)	25	B	464-2019-05210167	Month 24	24		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220583	Baseline	0		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220584	Baseline	0		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220585	Baseline	0		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220586	Baseline	0		

(b) (4)

1152	Ambient (25°C/60%RH)	25	C	464-2017-05220587	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220588	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220589	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220590	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-08210459	Month 3	3
1152	Ambient (25°C/60%RH)	25	C	464-2017-11200354	Month 6	6
1152	Ambient (25°C/60%RH)	25	C	464-2018-02190205	Month 9	9
1152	Ambient (25°C/60%RH)	25	C	464-2018-05210344	Month 12	12
1152	Ambient (25°C/60%RH)	25	C	464-2018-11200166	Month 18	18
1152	Ambient (25°C/60%RH)	25	C	464-2019-05210169	Month 24	24
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220567	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220568	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220569	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220570	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220571	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220572	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220573	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220574	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-08210456	Month 3	3
1152	Accelerated (40°C/75%RH)	40	A	464-2017-11200351	Month 6	6
1152	Accelerated (40°C/75%RH)	40	A	464-2018-02190202	Month 9	9
1152	Accelerated (40°C/75%RH)	40	A	464-2018-05210341	Month 12	12
1152	Accelerated (40°C/75%RH)	40	A	464-2018-11200163	Month 18	18
1152	Accelerated (40°C/75%RH)	40	A	464-2019-05210166	Month 24	24
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220575	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220576	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220577	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220578	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220579	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220580	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220581	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220582	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-08210458	Month 3	3

(b) (4)

1152	Accelerated (40°C/75%RH)	40	B	464-2017-11200353	Month 6	6
1152	Accelerated (40°C/75%RH)	40	B	464-2018-02190204	Month 9	9
1152	Accelerated (40°C/75%RH)	40	B	464-2018-05210343	Month 12	12
1152	Accelerated (40°C/75%RH)	40	B	464-2018-05210343	Month 12	12
1152	Accelerated (40°C/75%RH)	40	B	464-2018-11200165	Month 18	18
1152	Accelerated (40°C/75%RH)	40	B	464-2019-05210168	Month 24	24
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220583	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220584	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220585	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220586	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220587	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220588	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220589	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220590	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-08210460	Month 3	3
1152	Accelerated (40°C/75%RH)	40	C	464-2017-11200355	Month 6	6
1152	Accelerated (40°C/75%RH)	40	C	464-2018-02190206	Month 9	9
1152	Accelerated (40°C/75%RH)	40	C	464-2018-05210345	Month 12	12
1152	Accelerated (40°C/75%RH)	40	C	464-2018-11200167	Month 18	18
1152	Accelerated (40°C/75%RH)	40	C	464-2019-05210170	Month 24	24



Annex 8
Stat-Analysis 1309
Dog Kibble pre-extrusion

Visualisation and statistical analysis of stability trial data Trial 1309, Pre-extrusion application of AOCED

Dr. (b) (4), (b) (6) Senior Biostatistician, NIC-RD/HN, DSM Nutritional Products

01 Juli, 2019

Table of Contents

1 Visualisation 1

1.1 Visualisation of stability trial data in % FA Dry Matter (DM) 2

1.2 Visualisation of stability trial data in retention percent (reference: average of 8 samples per lot at baseline) 3

2 Statistical Analysis 4

2.1 Statistical Analysis using all observations 4

2.1.1 Statistical Analysis of DHA, 25°C 4

2.1.2 Statistical Analysis of EPA, 25°C 7

2.1.3 Statistical Analysis of DHA, 40°C 11

2.1.4 Statistical Analysis of EPA, 40°C 15

2.2 Statistical Analysis removing outliers 19

2.2.1 Statistical Analysis of DHA, 25°C, with outlier removal 19

2.2.2 Statistical Analysis of EPA, 25°C, with outlier removal 23

2.2.3 Statistical Analysis of DHA, 40°C, with outlier removal 27

2.2.4 Statistical Analysis of EPA, 40°C, with outlier removal 31

3 Summary of results 34

4 Database used 35

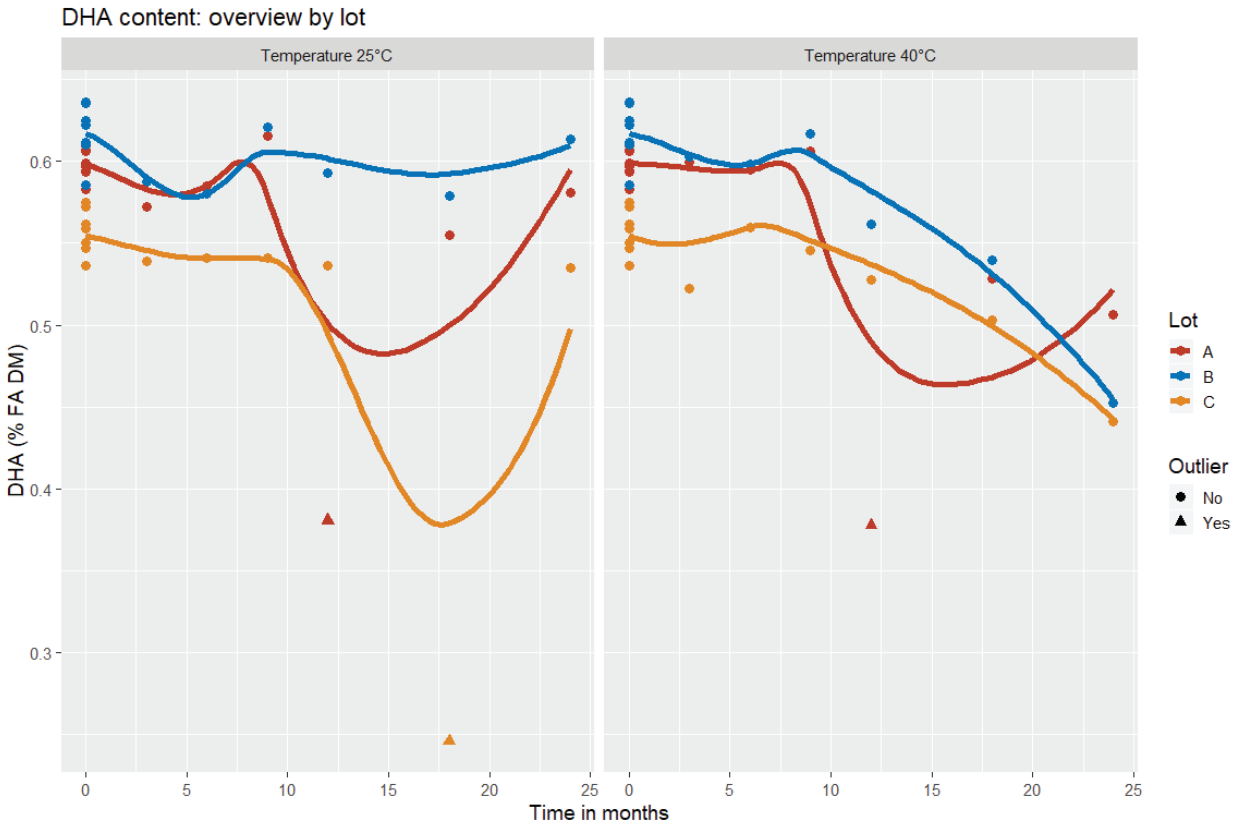
5 Source code 35

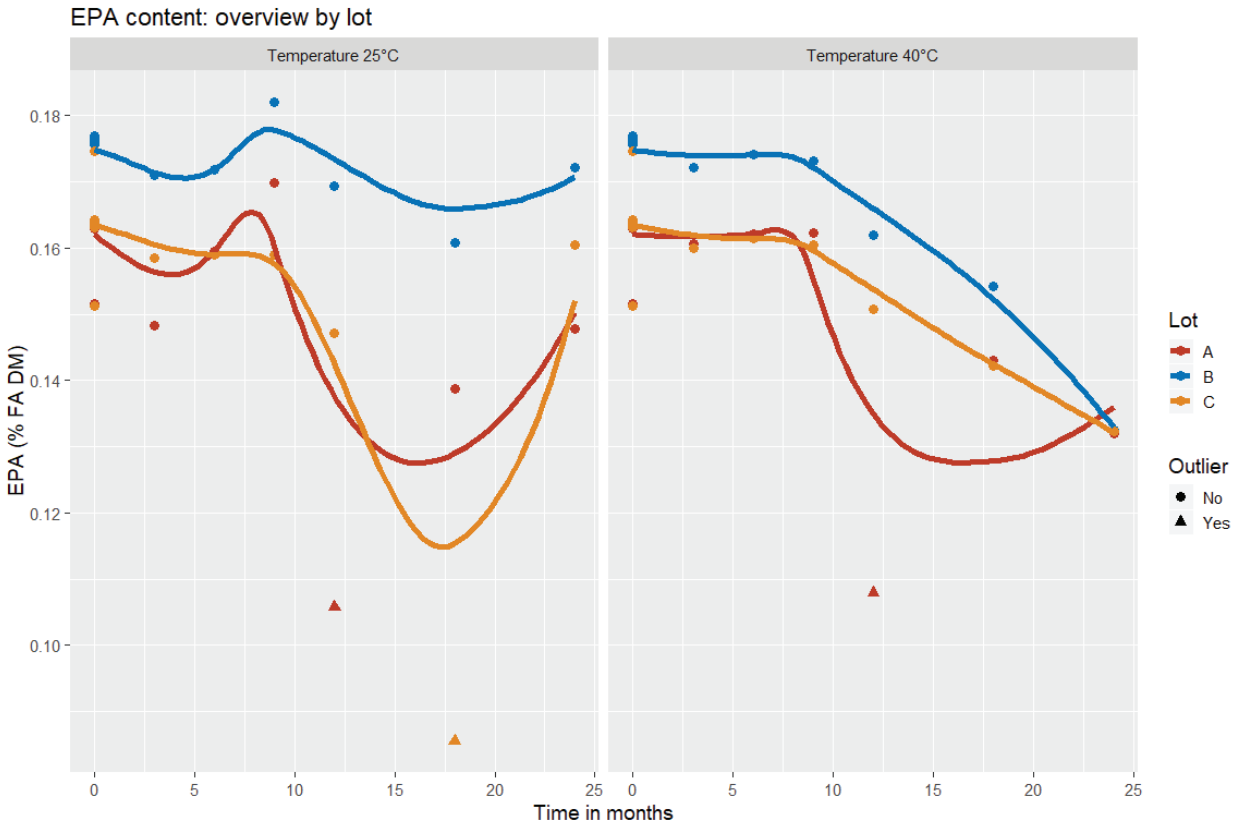
6 Appendix: Reproducibility information 35

1 Visualisation

Data are plotted by temperature and coloured by lot. A data-driven regression (loess smoother, which is a local polynomial regression fitting) is displayed to visualize the evolution of the mean values by lot and time point. Possible technical outliers are displayed as triangles.

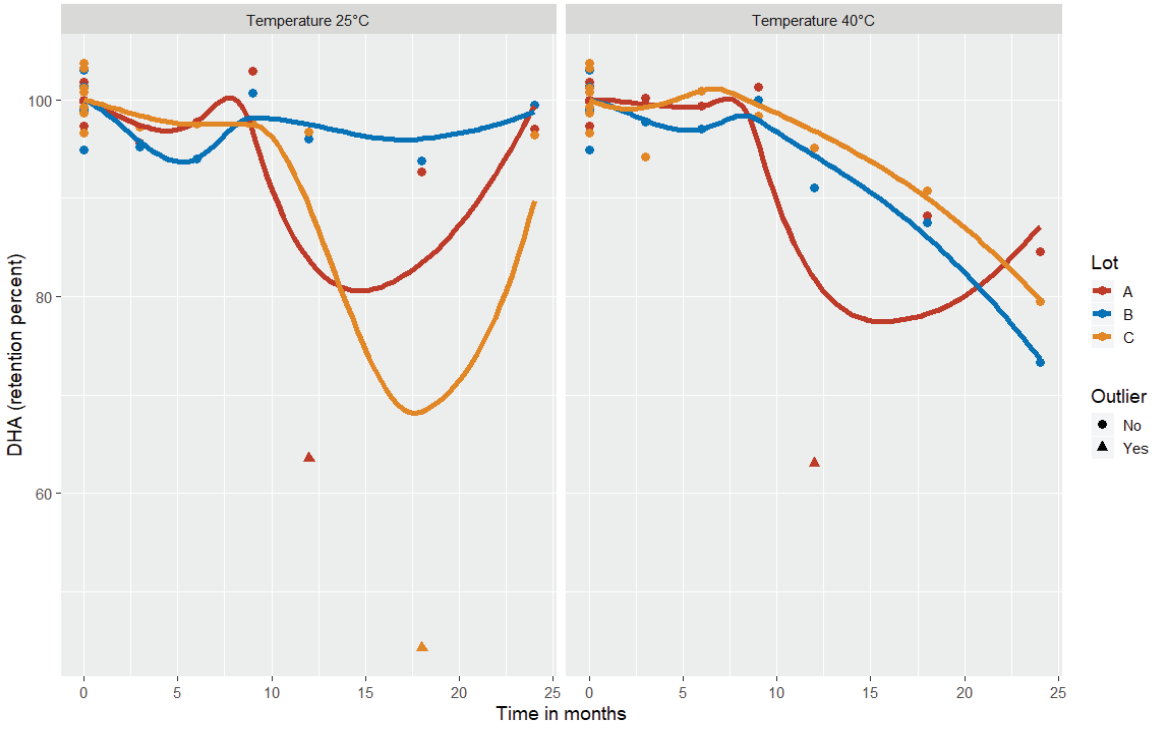
1.1 Visualisation of stability trial data in % FA Dry Matter (DM)



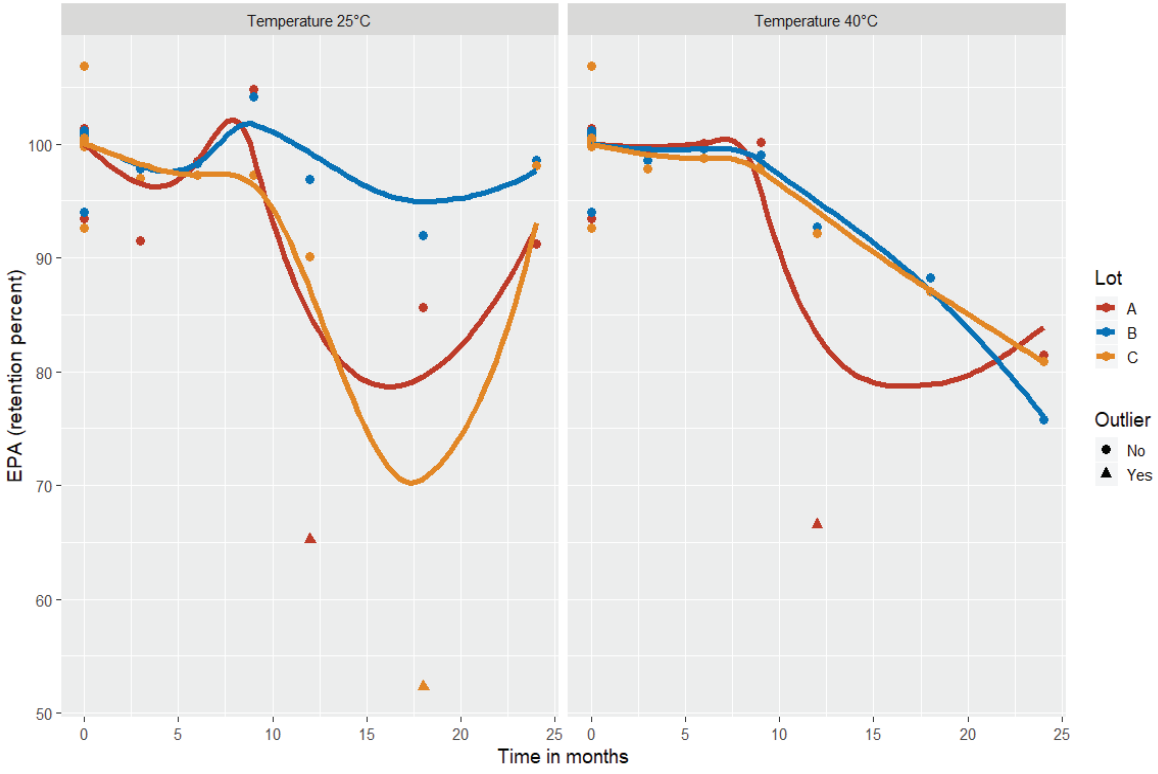


1.2 Visualisation of stability trial data in retention percent (reference: average of 8 samples per lot at baseline)

DHA retention percent: overview by lot



EPA retention percent: overview by lot



2 Statistical Analysis

Each endpoint (DHA/EPA) and temperature (25°C/40°C) combination is analysed separately.

Each statistical analysis follows a two-step regression approach. Step 1 tests the poolability of lots. At first, a separate slope and intercept is fit for each lot. The slopes are tested against each other, and if not significant, they are removed. The intercepts of the lots are then tested against each other, and if not significant, they are removed as well. Step 2 performs a pooled regression using all lots.

This analysis follows the recommendations of FDA Guidance GFI # 221 and ICCF Guidance # 01.

The statistical analysis is performed twice, once with all observations and once with the outliers removed, since they are most likely technical outliers due to possibly damaged storage bags.

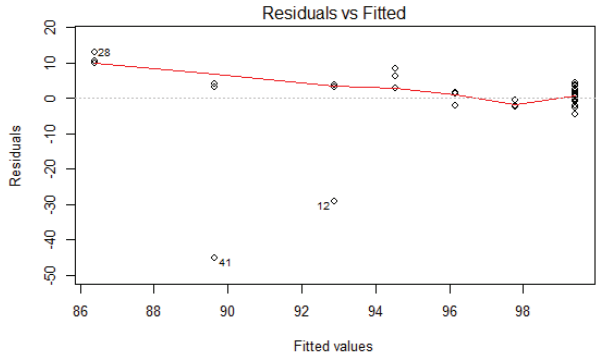
2.1 Statistical Analysis using all observations

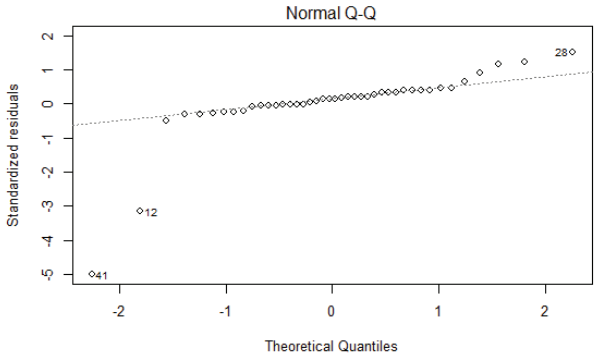
2.1.1 Statistical Analysis of DHA, 25°C

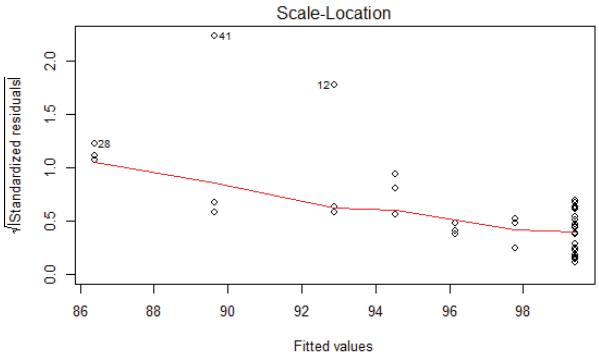
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 25°C
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -37.575  -1.520   0.967   3.002  20.576
##
## Coefficients:
##           Estimate Std. Error t value Pr(>|t|)
## Time       -0.4768     0.3336  -1.429    0.162
## LotA       98.8404     3.0500  32.407   <2e-16 ***
## LotB       99.2175     3.0500  32.531   <2e-16 ***
## LotC      100.1942     3.0500  32.851   <2e-16 ***
## Time:LotB   0.3393     0.4718   0.719    0.477
## Time:LotC  -0.5384     0.4718  -1.141    0.261
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 9.435 on 36 degrees of freedom
## Multiple R-squared:  0.9919, Adjusted R-squared:  0.9906
## F-statistic: 736.3 on 6 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0               0.3393     0.4718   0.719
## Time:LotC = slope.C - slope.A == 0              -0.5384     0.4718  -1.141
## Time:LotC - Time:LotB = slope.C - slope.B == 0  -0.8776     0.4718  -1.860
##                                                 Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                 0.754
## Time:LotC = slope.C - slope.A == 0                 0.496
## Time:LotC - Time:LotB = slope.C - slope.B == 0     0.165
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
```

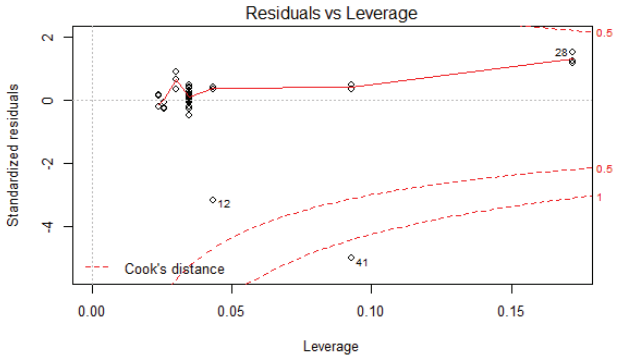
```
##
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -43.643  -1.112   1.352   3.222  11.675
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.5431     0.1964  -2.765  0.00874 **
## LotA  99.1817     2.7628  35.899  < 2e-16 ***
## LotB 101.3036     2.7628  36.667  < 2e-16 ***
## LotC  97.7668     2.7628  35.387  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 9.622 on 38 degrees of freedom
## Multiple R-squared:  0.9911, Adjusted R-squared:  0.9902
## F-statistic:  1061 on 4 and 38 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0    2.122      3.637   0.583
## LotC - LotA = intercept.C - intercept.A == 0   -1.415      3.637  -0.389
## LotC - LotB = intercept.C - intercept.B == 0   -3.537      3.637  -0.973
##                                                 Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.830
## LotC - LotA = intercept.C - intercept.A == 0    0.920
## LotC - LotB = intercept.C - intercept.B == 0    0.598
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -45.294  -0.573   1.370   3.441  13.054
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  99.4174     1.7722  56.098   <2e-16 ***
## Time         -0.5431     0.1939  -2.802   0.0078 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 9.495 on 40 degrees of freedom
## Multiple R-squared:  0.164,  Adjusted R-squared:  0.1431
## F-statistic: 7.849 on 1 and 40 DF,  p-value: 0.007798
```

```
##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```










```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                  2.5 %      97.5 %
## (Intercept) 95.8355830 102.9991657
## Time        -0.9349303  -0.1513178

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

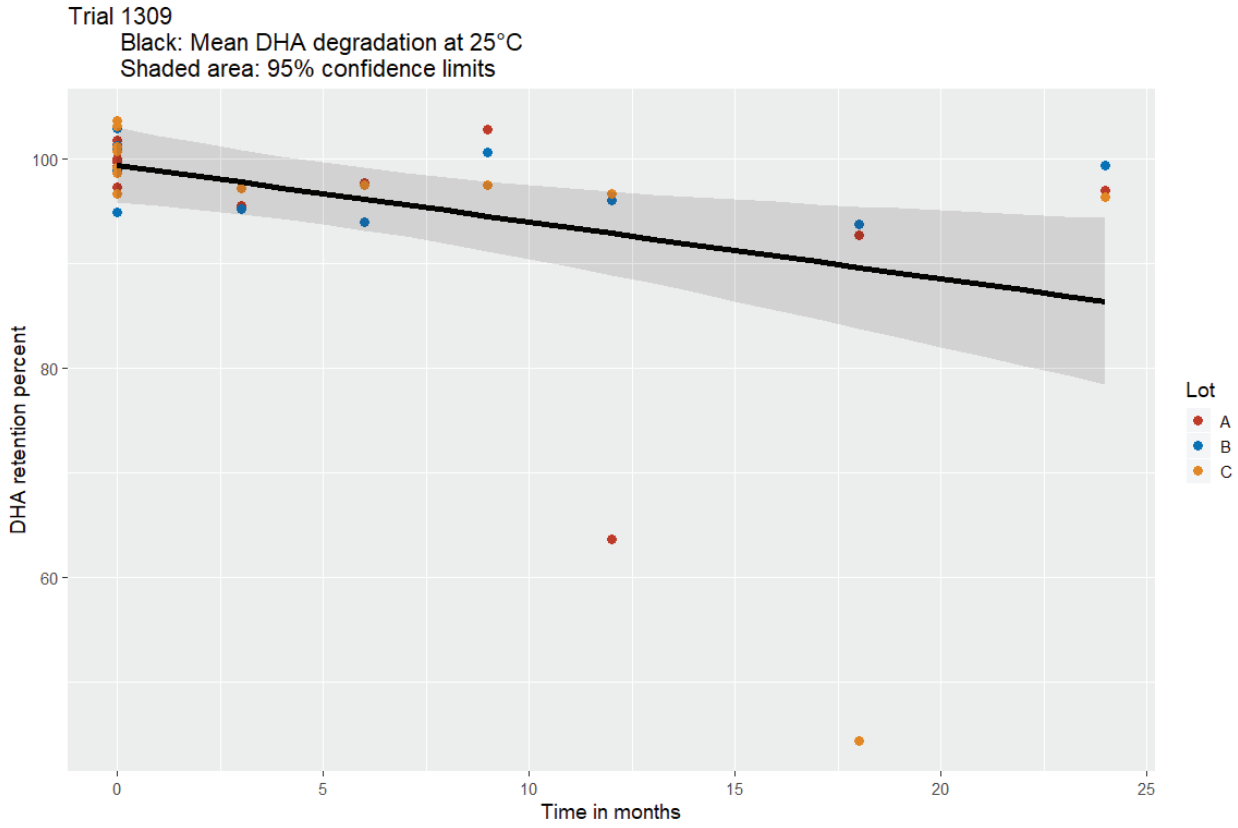
Temp	Time	DHA.estimated.mean	DHA.lower.CI	DHA.upper.CI
25	0	99.41737		
25	1	98.87425		
25	2	98.33113		
25	3	97.78800		
25	4	97.24488		
25	5	96.70175		
25	6	96.15863		
25	7	95.61551		
25	8	95.07238		

(b) (4)

```
25          9           94.52926
25         10           93.98613
25         11           93.44301
25         12           92.89989
25         13           92.35676
25         14           91.81364
25         15           91.27051
25         16           90.72739
25         17           90.18427
25         18           89.64114
25         19           89.09802
25         20           88.55489
25         21           88.01177
25         22           87.46865
25         23           86.92552
25         24           86.38240
```

(b) (4)

```
##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

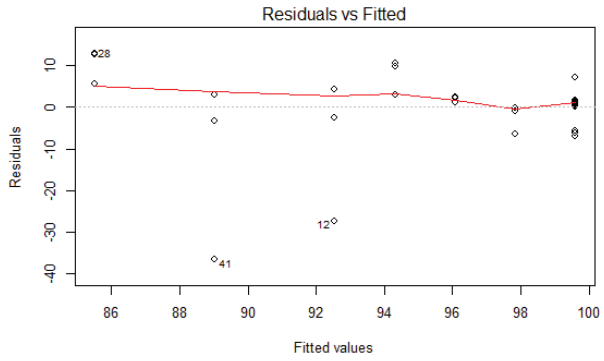


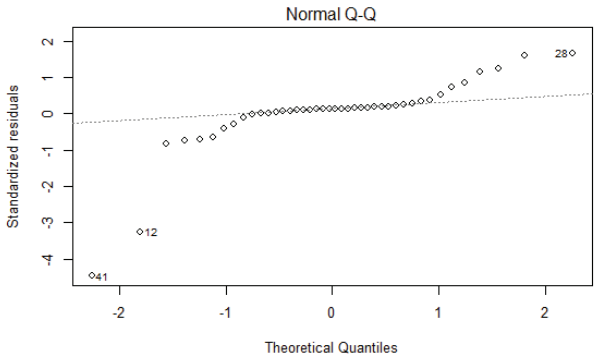
2.1.2 Statistical Analysis of EPA, 25°C

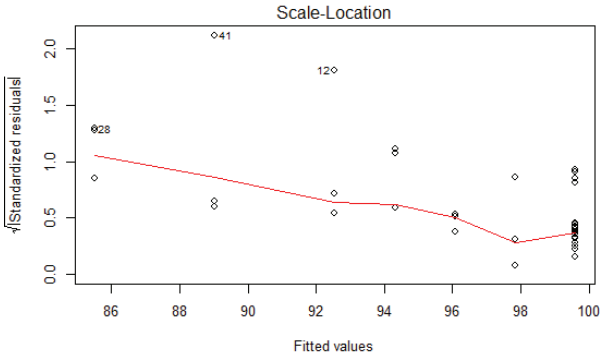
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 25°C
```

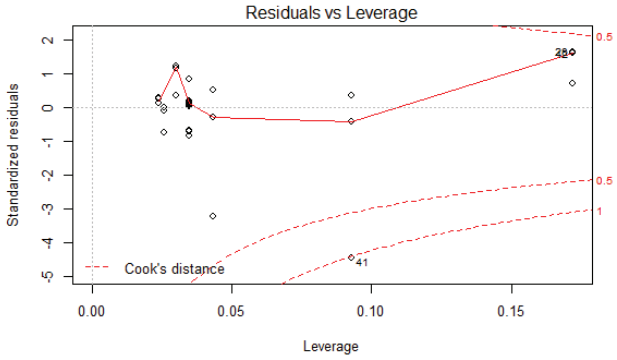
```
## ------------------------------------------------------------
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -31.1970  -0.5197   0.8551   2.1903  20.0191
##
## Coefficients:
##           Estimate Std. Error t value Pr(>|t|)
## Time       -0.6925     0.3005  -2.305   0.0271 *
## LotA       99.0477     2.7469  36.059   <2e-16 ***
## LotB       99.9690     2.7469  36.394   <2e-16 ***
## LotC       99.7973     2.7469  36.332   <2e-16 ***
## Time:LotB   0.5252     0.4249   1.236   0.2244
## Time:LotC  -0.2110     0.4249  -0.497   0.6225
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 8.497 on 36 degrees of freedom
## Multiple R-squared:  0.9934, Adjusted R-squared:  0.9923
## F-statistic: 907.1 on 6 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0               0.5252     0.4249   1.236
## Time:LotC = slope.C - slope.A == 0              -0.2110     0.4249  -0.497
## Time:LotC - Time:LotB = slope.C - slope.B == 0  -0.7362     0.4249  -1.733
##                                                Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                0.440
## Time:LotC = slope.C - slope.A == 0                0.873
## Time:LotC - Time:LotB = slope.C - slope.B == 0    0.207
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -35.257  -1.367   1.703   2.650  14.065
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.5878     0.1762  -3.336  0.00191 **
## LotA  98.5090     2.4776  39.759  < 2e-16 ***
## LotB 102.1315     2.4776  41.221  < 2e-16 ***
## LotC  98.1735     2.4776  39.624  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 8.629 on 38 degrees of freedom
## Multiple R-squared:  0.9928, Adjusted R-squared:  0.9921
## F-statistic:  1319 on 4 and 38 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
```

```
## Fit: lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0   3.6225     3.2613   1.111
## LotC - LotA = intercept.C - intercept.A == 0  -0.3356     3.2613  -0.103
## LotC - LotB = intercept.C - intercept.B == 0  -3.9581     3.2613  -1.214
##                                                 Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.513
## LotC - LotA = intercept.C - intercept.A == 0    0.994
## LotC - LotB = intercept.C - intercept.B == 0    0.453
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -36.688   0.205   1.101   2.115  13.017
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  99.6047     1.6066  61.997   <2e-16 ***
## Time         -0.5878     0.1757  -3.344   0.0018 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 8.608 on 40 degrees of freedom
## Multiple R-squared:  0.2185, Adjusted R-squared:  0.199
## F-statistic: 11.18 on 1 and 40 DF,  p-value: 0.0018

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```










```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                  2.5 %      97.5 %
## (Intercept) 96.3575732 102.8517573
## Time        -0.9429536  -0.2325655

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

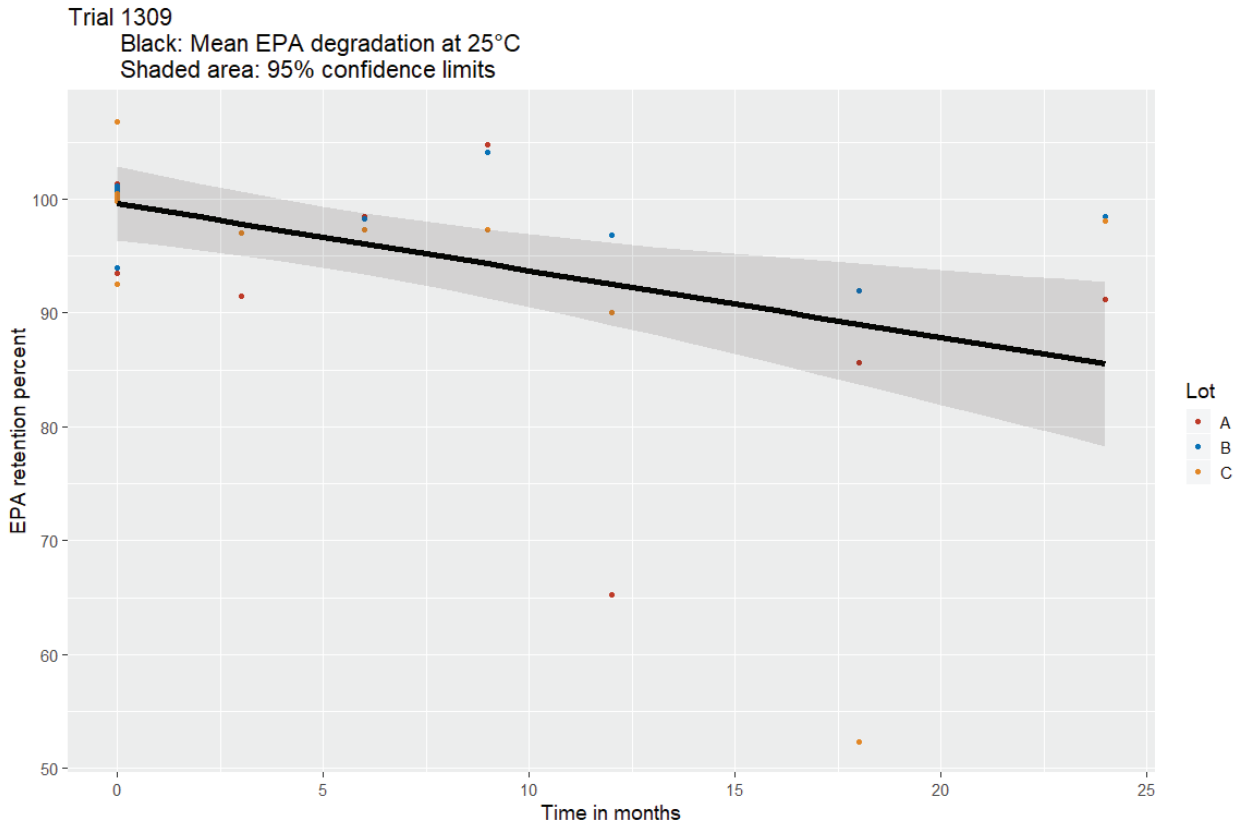
Temp	Time	EPA.estimated.mean	EPA.lower.CI	EPA.upper.CI
25	0	99.60467		
25	1	99.01691		
25	2	98.42915		
25	3	97.84139		
25	4	97.25363		
25	5	96.66587		
25	6	96.07811		
25	7	95.49035		
25	8	94.90259		
25	9	94.31483		
25	10	93.72707		
25	11	93.13931		
25	12	92.55155		

(b) (4)

(b) (4)

25	13	91.96379
25	14	91.37603
25	15	90.78827
25	16	90.20051
25	17	89.61275
25	18	89.02499
25	19	88.43723
25	20	87.84947
25	21	87.26171
25	22	86.67396
25	23	86.08620
25	24	85.49844

```
##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

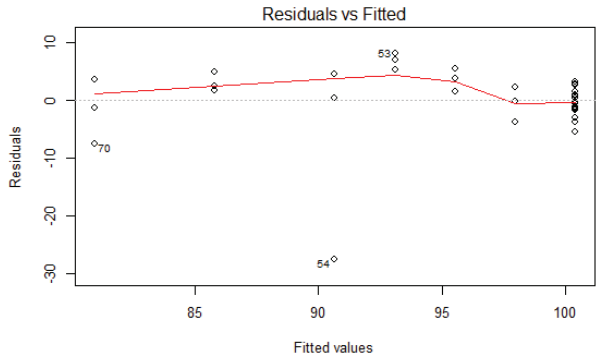


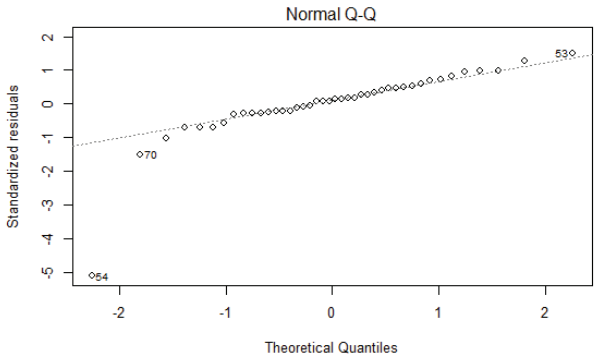
2.1.3 Statistical Analysis of DHA, 40°C

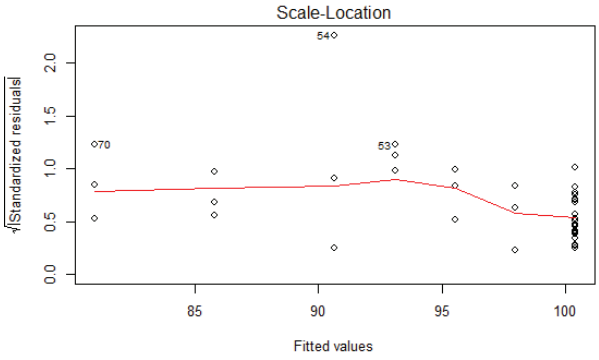
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 40°C
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
```

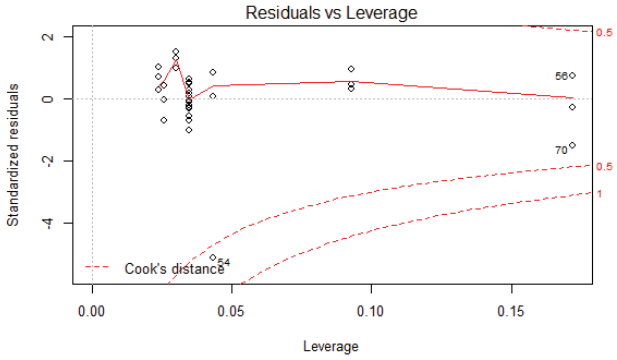
```
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -26.4577  -1.7984   0.5977   2.6909   9.1139
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## Time       -0.86607    0.20140  -4.300 0.000124 ***
## LotA       99.92081    1.84110  54.272  < 2e-16 ***
## LotB      100.82799    1.84110  54.765  < 2e-16 ***
## LotC      100.47773    1.84110  54.575  < 2e-16 ***
## Time:LotB  -0.03847    0.28482  -0.135 0.893314
## Time:LotC   0.20029    0.28482   0.703 0.486439
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.695 on 36 degrees of freedom
## Multiple R-squared:  0.997,  Adjusted R-squared:  0.9965
## F-statistic:  2007 on 6 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0             -0.03847    0.28482  -0.135
## Time:LotC = slope.C - slope.A == 0              0.20029    0.28482   0.703
## Time:LotC - Time:LotB = slope.C - slope.B == 0  0.23876    0.28482   0.838
##                                                 Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                 0.990
## Time:LotC = slope.C - slope.A == 0                 0.763
## Time:LotC - Time:LotB = slope.C - slope.B == 0     0.682
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -26.8276  -1.4401   0.4315   2.6969   8.9059
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.8121     0.1144  -7.096 1.82e-08 ***
## LotA  99.6434     1.6096  61.906  < 2e-16 ***
## LotB 100.3527     1.6096  62.347  < 2e-16 ***
## LotC 101.2304     1.6096  62.892  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.605 on 38 degrees of freedom
## Multiple R-squared:  0.997,  Adjusted R-squared:  0.9966
## F-statistic:  3107 on 4 and 38 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                           Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0   0.7093     2.1187   0.335
## LotC - LotA = intercept.C - intercept.A == 0   1.5870     2.1187   0.749
```

```
## LotC - LotB = intercept.C - intercept.B == 0   0.8776     2.1187   0.414
##                                                Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.940
## LotC - LotA = intercept.C - intercept.A == 0    0.736
## LotC - LotB = intercept.C - intercept.B == 0    0.910
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -27.5930  -1.3741   0.6039   2.6408   8.1404
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 100.4088     1.0272  97.747  < 2e-16 ***
## Time         -0.8121     0.1124  -7.227 9.06e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.504 on 40 degrees of freedom
## Multiple R-squared:  0.5663, Adjusted R-squared:  0.5555
## F-statistic: 52.24 on 1 and 40 DF,  p-value: 9.063e-09

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```










```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                 2.5 %     97.5 %
## (Intercept) 98.332737 102.484947
## Time        -1.039226  -0.585023

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

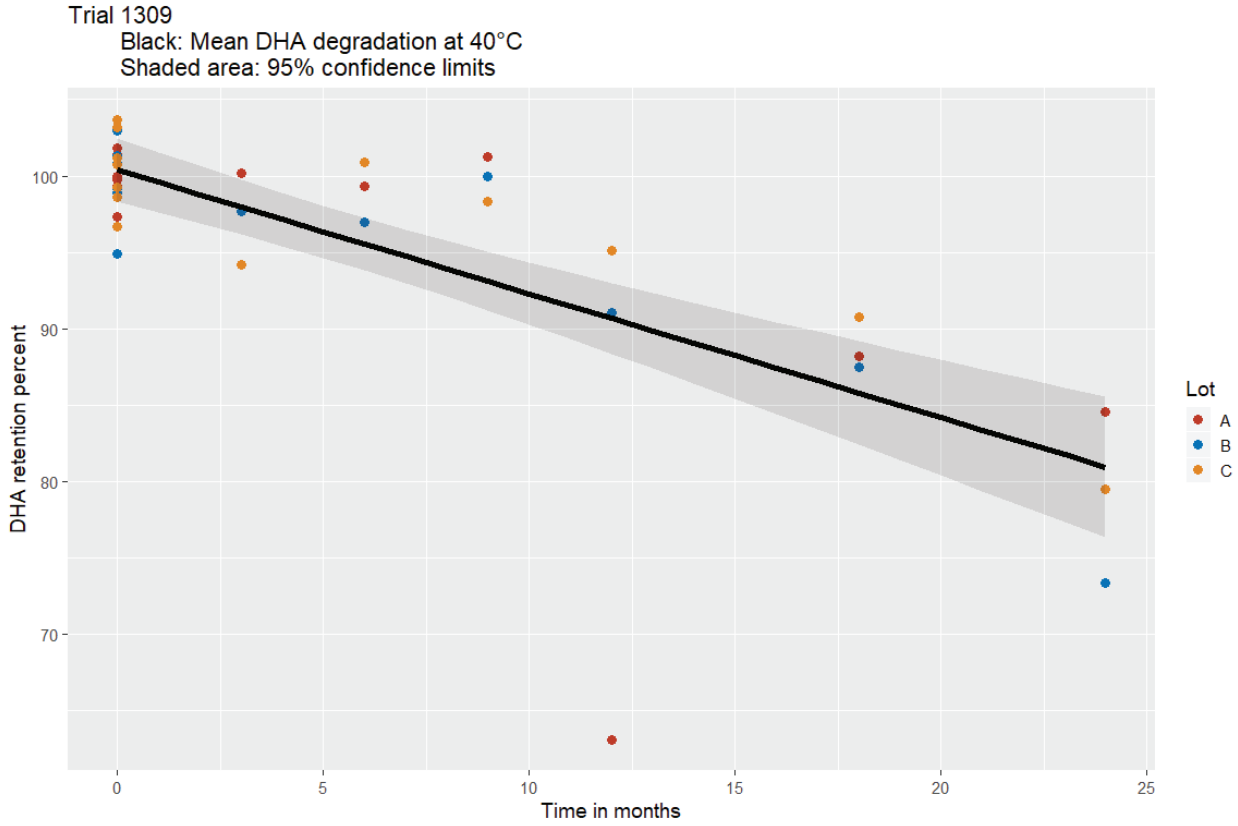
Temp	Time	DHA.estimated.mean	DHA lower CI	DHA upper CI
40	0	100.40884		
40	1	99.59672		
40	2	98.78459		
40	3	97.97247		
40	4	97.16034		
40	5	96.34822		
40	6	95.53609		
40	7	94.72397		
40	8	93.91184		
40	9	93.09972		
40	10	92.28759		
40	11	91.47547		
40	12	90.66335		

(b) (4)

(b) (4)

```
40        13              89.85122
40        14              89.03910
40        15              88.22697
40        16              87.41485
40        17              86.60272
40        18              85.79060
40        19              84.97847
40        20              84.16635
40        21              83.35422
40        22              82.54210
40        23              81.72997
40        24              80.91785
```

```
##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

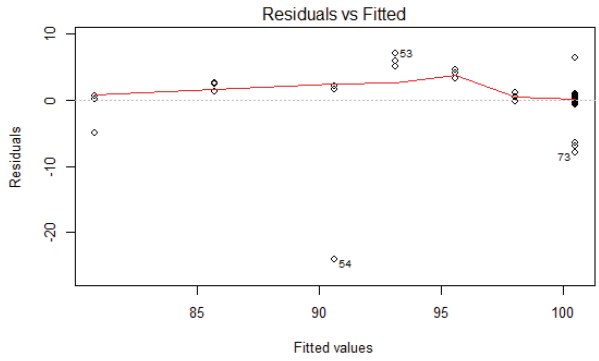


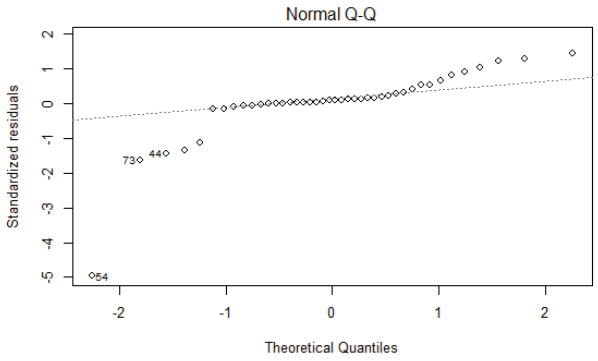
2.1.4 Statistical Analysis of EPA, 40°C

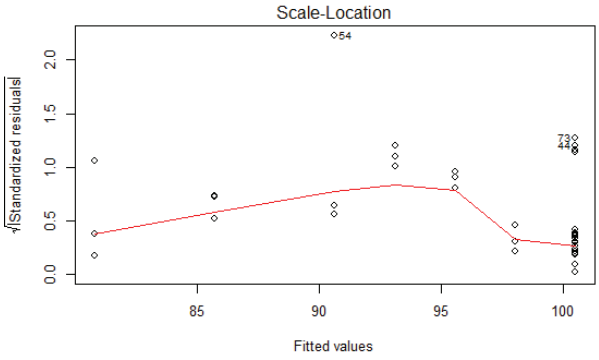
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 40°C
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
```

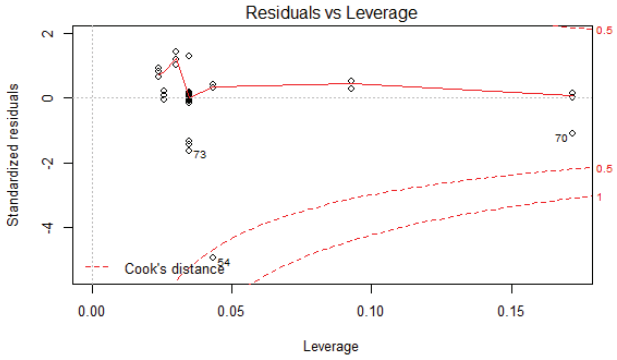
```
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -22.5989  -0.4502   0.1788   1.7131   8.2757
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## Time       -0.90982    0.18200  -4.999 1.51e-05 ***
## LotA      100.07661    1.66379  60.150  < 2e-16 ***
## LotB      100.94219    1.66379  60.670  < 2e-16 ***
## LotC      100.52877    1.66379  60.421  < 2e-16 ***
## Time:LotB   0.08451    0.25739   0.328    0.745
## Time:LotC   0.17965    0.25739   0.698    0.490
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.147 on 36 degrees of freedom
## Multiple R-squared:  0.9976, Adjusted R-squared:  0.9972
## F-statistic:  2460 on 6 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                 Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0               0.08451    0.25739   0.328
## Time:LotC = slope.C - slope.A == 0               0.17965    0.25739   0.698
## Time:LotC - Time:LotB = slope.C - slope.B == 0   0.09514    0.25739   0.370
##                                                 Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                 0.942
## Time:LotC = slope.C - slope.A == 0                 0.766
## Time:LotC - Time:LotB = slope.C - slope.B == 0     0.928
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##


##
## Call:
## lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -23.2027  -0.6588   0.5254   1.7331   7.9360
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time  -0.8218     0.1030  -7.981 1.21e-09 ***
## LotA  99.6238     1.4482  68.792  < 2e-16 ***
## LotB 100.9240     1.4482  69.690  < 2e-16 ***
## LotC 100.9998     1.4482  69.743  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 5.043 on 38 degrees of freedom
## Multiple R-squared:  0.9975, Adjusted R-squared:  0.9973
## F-statistic:  3844 on 4 and 38 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                             Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0  1.30021    1.90621   0.682
## LotC - LotA = intercept.C - intercept.A == 0  1.37607    1.90621   0.722
```

```
## LotC - LotB = intercept.C - intercept.B == 0  0.07586    1.90621   0.040
##                                                Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.775
## LotC - LotA = intercept.C - intercept.A == 0    0.752
## LotC - LotB = intercept.C - intercept.B == 0    0.999
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time, data = d)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -24.0948  -0.1856   0.4267   1.4649   7.0439
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 100.5159     0.9254 108.623  < 2e-16 ***
## Time         -0.8218     0.1012  -8.118 5.47e-10 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 4.958 on 40 degrees of freedom
## Multiple R-squared:  0.6223, Adjusted R-squared:  0.6129
## F-statistic: 65.91 on 1 and 40 DF,  p-value: 5.468e-10

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```










```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                 2.5 %      97.5 %
## (Intercept) 98.645620 102.3860900
## Time        -1.026351  -0.6171873

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

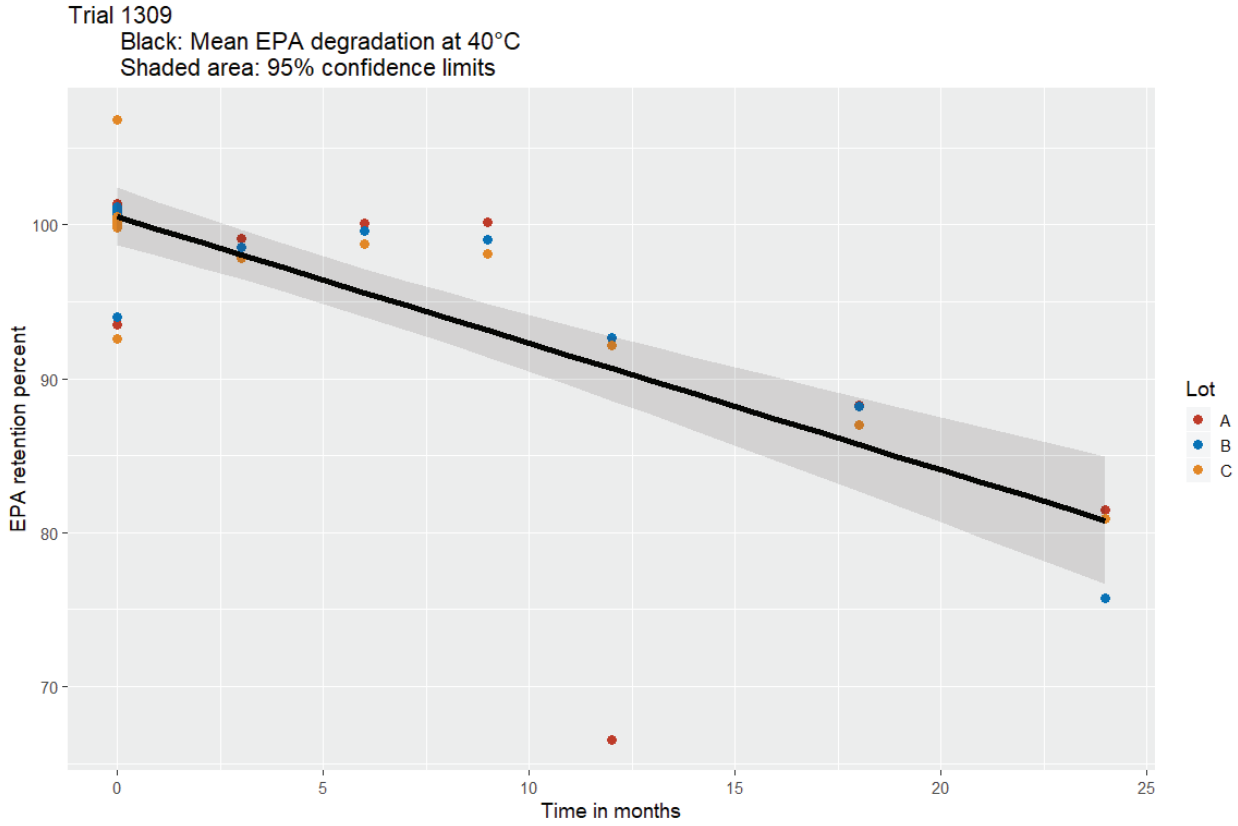
Temp	Time	EPA.estimated.mean	EPA.lower.CI	EPA.upper.CI
40	0	100.51585		
40	1	99.69409		
40	2	98.87232		
40	3	98.05055		
40	4	97.22878		
40	5	96.40701		
40	6	95.58524		
40	7	94.76347		
40	8	93.94170		
40	9	93.11993		
40	10	92.29816		
40	11	91.47639		
40	12	90.65462		

(b) (4)

```
40        13          89.83286
40        14          89.01109
40        15          88.18932
40        16          87.36755
40        17          86.54578
40        18          85.72401
40        19          84.90224
40        20          84.08047
40        21          83.25870
40        22          82.43693
40        23          81.61516
40        24          80.79339
```

(b) (4)

```
##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```



2.2 Statistical Analysis removing outliers

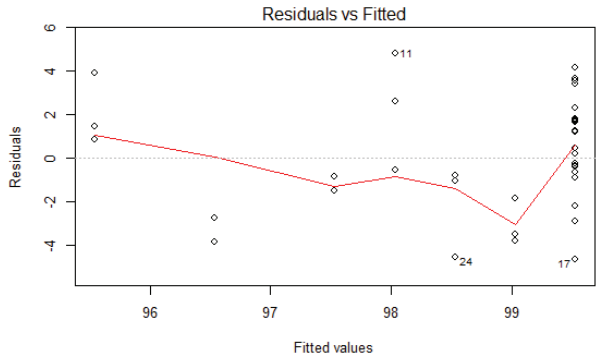
Each statistical analysis is repeated with the outliers removed, since they are most likely technical outliers due to possibly damaged storage bags.

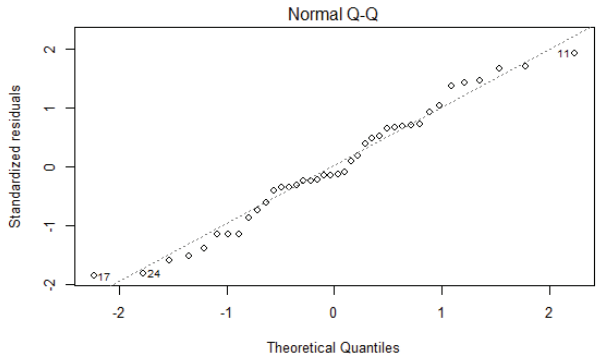
2.2.1 Statistical Analysis of DHA, 25°C, with outlier removal

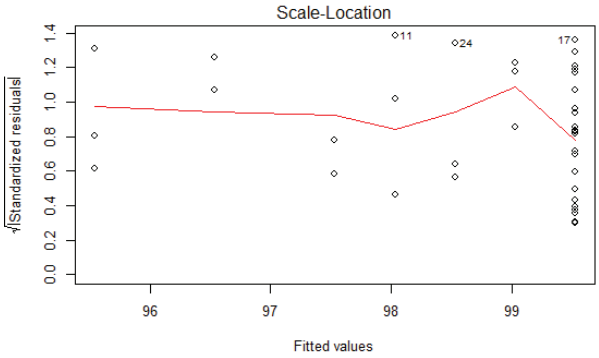
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 25°C, with outlier removal
```

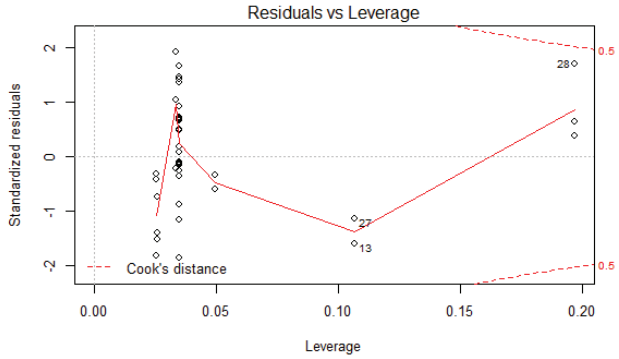
```
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -4.3916 -1.6173 -0.3049  1.6265  4.7523
##
## Coefficients:
##            Estimate Std. Error t value Pr(>|t|)
## Time      -0.185442   0.098038  -1.892   0.0671 .
## LotA      99.768965   0.870958 114.551   <2e-16 ***
## LotB      99.217531   0.867401 114.385   <2e-16 ***
## LotC      99.608386   0.868129 114.739   <2e-16 ***
## Time:LotB  0.047941   0.136435   0.351   0.7275
## Time:LotC  0.007179   0.145576   0.049   0.9610
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 2.683 on 34 degrees of freedom
## Multiple R-squared:  0.9994, Adjusted R-squared:  0.9993
## F-statistic:  9032 on 6 and 34 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                  Estimate Std. Error
## Time:LotB = slope.B - slope.A == 0               0.047941   0.136435
## Time:LotC = slope.C - slope.A == 0               0.007179   0.145576
## Time:LotC - Time:LotB = slope.C - slope.B == 0 -0.040762   0.143470
##                                                 t value Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0               0.351    0.934
## Time:LotC = slope.C - slope.A == 0               0.049    0.999
## Time:LotC - Time:LotB = slope.C - slope.B == 0  -0.284    0.957
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -4.4771 -1.4686 -0.3614  1.6609  4.6658
##
## Coefficients:
##      Estimate Std. Error t value Pr(>|t|)
## Time -0.16572    0.05609  -2.955  0.00549 **
## LotA 99.67795    0.76959 129.521  < 2e-16 ***
## LotB 99.36267    0.75561 131.501  < 2e-16 ***
## LotC 99.55629    0.76127 130.777  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 2.613 on 36 degrees of freedom
## Multiple R-squared:  0.9994, Adjusted R-squared:  0.9993
## F-statistic: 1.429e+04 on 4 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
```

```
## Fit: lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0  -0.3153     1.0069  -0.313
## LotC - LotA = intercept.C - intercept.A == 0  -0.1217     1.0253  -0.119
## LotC - LotB = intercept.C - intercept.B == 0   0.1936     1.0080   0.192
##                                               Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.947
## LotC - LotA = intercept.C - intercept.A == 0    0.992
## LotC - LotB = intercept.C - intercept.B == 0    0.980
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -4.6455 -1.5823 -0.3331  1.7217  4.8185
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 99.53103    0.47602 209.088  < 2e-16 ***
## Time        -0.16636    0.05459  -3.048  0.00418 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 2.547 on 38 degrees of freedom
## Multiple R-squared:  0.1964, Adjusted R-squared:  0.1753
## F-statistic: 9.288 on 1 and 38 DF,  p-value: 0.004182

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```









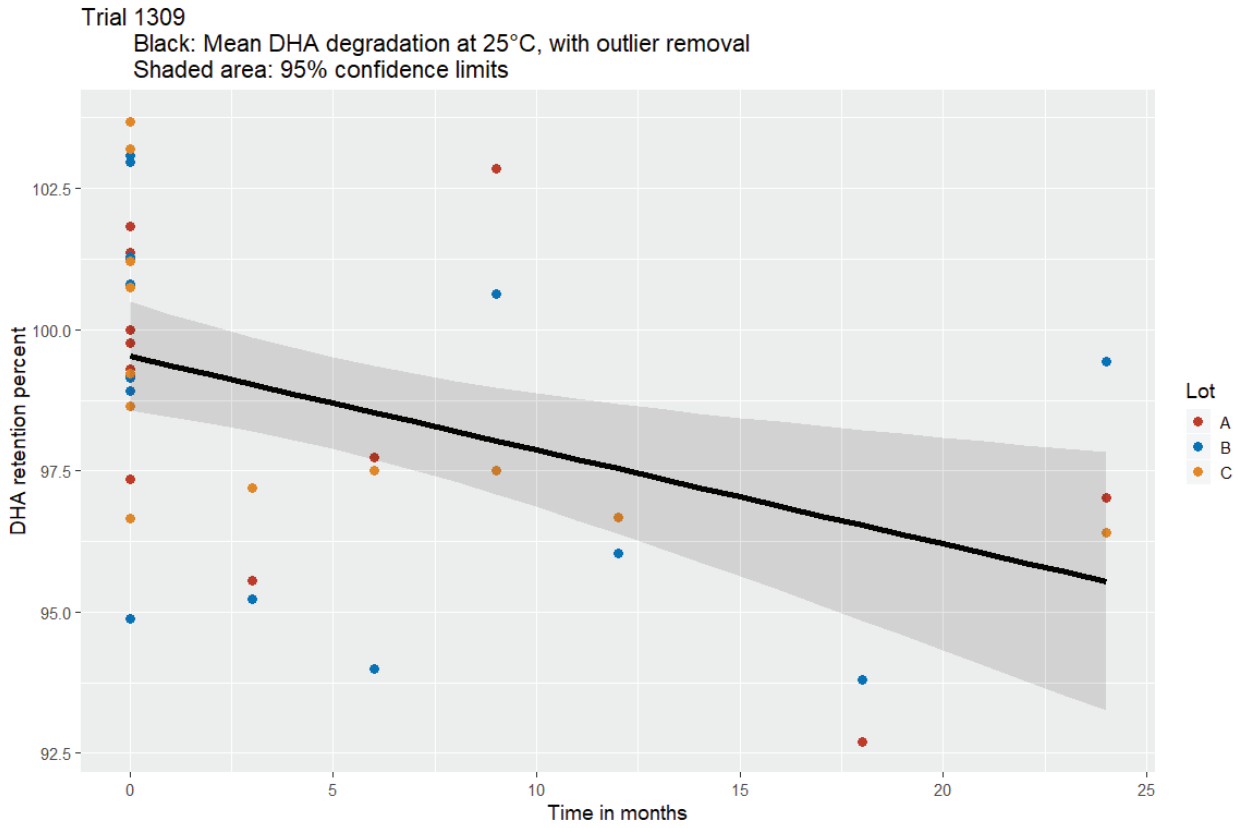

```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                  2.5 %       97.5 %
## (Intercept) 98.5673724 100.49469238
## Time        -0.2768639  -0.05585786

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

Temp	Time	DHA.estimated.mean	DHA.lower.CI	DHA.upper.CI
25	0	99.53103		
25	1	99.36467		
25	2	99.19831		
25	3	99.03195		
25	4	98.86559		
25	5	98.69923		
25	6	98.53287		
25	7	98.36651		
25	8	98.20015		
25	9	98.03378		
25	10	97.86742		
25	11	97.70106		
25	12	97.53470		

(b) (4)

```
25          13              97.36834
25          14              97.20198
25          15              97.03562
25          16              96.86926
25          17              96.70290
25          18              96.53654
25          19              96.37018
25          20              96.20381
25          21              96.03745
25          22              95.87109
25          23              95.70473
25          24              95.53837

##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

(b) (4)

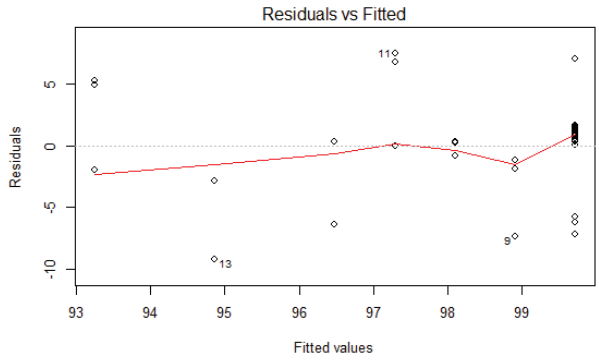


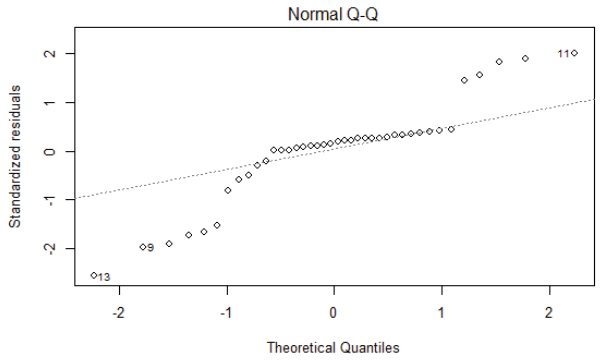
2.2.2 Statistical Analysis of EPA, 25°C, with outlier removal

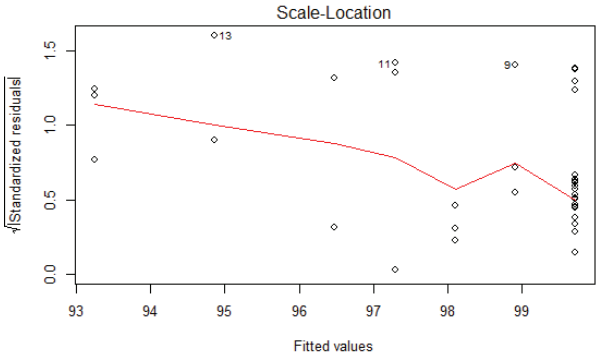
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 25°C, with outlier removal
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
```

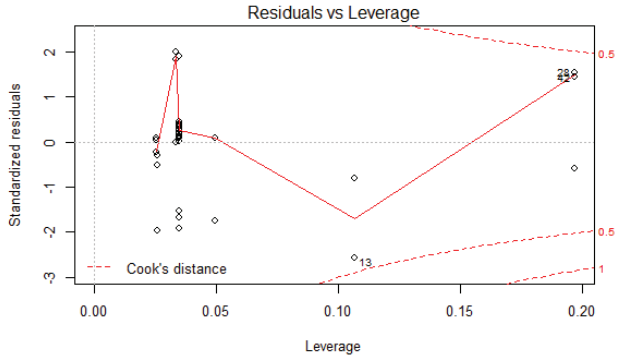
```
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -7.0209 -0.8477  0.7823  1.2226  8.9192
##
## Coefficients:
##           Estimate Std. Error t value Pr(>|t|)
## Time       -0.4410     0.1405  -3.139  0.00349 **
## LotA       99.8495     1.2479  80.013  < 2e-16 ***
## LotB       99.9690     1.2428  80.437  < 2e-16 ***
## LotC       99.3109     1.2439  79.841  < 2e-16 ***
## Time:LotB   0.2737     0.1955   1.400  0.17053
## Time:LotC   0.2323     0.2086   1.114  0.27324
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.845 on 34 degrees of freedom
## Multiple R-squared:  0.9987, Adjusted R-squared:  0.9985
## F-statistic:  4376 on 6 and 34 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                  Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0                0.27371    0.19548   1.400
## Time:LotC = slope.C - slope.A == 0                0.23229    0.20858   1.114
## Time:LotC - Time:LotB = slope.C - slope.B == 0 -0.04142    0.20557  -0.201
##                                                  Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                  0.352
## Time:LotC = slope.C - slope.A == 0                  0.512
## Time:LotC - Time:LotB = slope.C - slope.B == 0      0.978
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -8.5479 -0.8031  0.4267  1.6006  8.1853
##
## Coefficients:
##       Estimate Std. Error t value Pr(>|t|)
## Time  -0.27360    0.08276  -3.306  0.00215 **
## LotA  99.07695    1.13555  87.250  < 2e-16 ***
## LotB 100.51582    1.11492  90.155  < 2e-16 ***
## LotC  99.58052    1.12328  88.652  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.856 on 36 degrees of freedom
## Multiple R-squared:  0.9986, Adjusted R-squared:  0.9985
## F-statistic:  6526 on 4 and 36 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                             Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0   1.4389     1.4857   0.968
## LotC - LotA = intercept.C - intercept.A == 0   0.5036     1.5128   0.333
```

```
## LotC - LotB = intercept.C - intercept.B == 0  -0.9353     1.4873  -0.629
##                                                Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.601
## LotC - LotA = intercept.C - intercept.A == 0    0.941
## LotC - LotB = intercept.C - intercept.B == 0    0.805
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -9.2561 -0.8900  0.6436  1.2423  7.5047
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) 99.72994    0.71082 140.303   <2e-16 ***
## Time        -0.27053    0.08151  -3.319    0.002 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.803 on 38 degrees of freedom
## Multiple R-squared:  0.2247, Adjusted R-squared:  0.2043
## F-statistic: 11.02 on 1 and 38 DF,  p-value: 0.002

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```










```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                  2.5 %      97.5 %
## (Intercept) 98.2909681 101.1689179
## Time         -0.4355348  -0.1055198

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

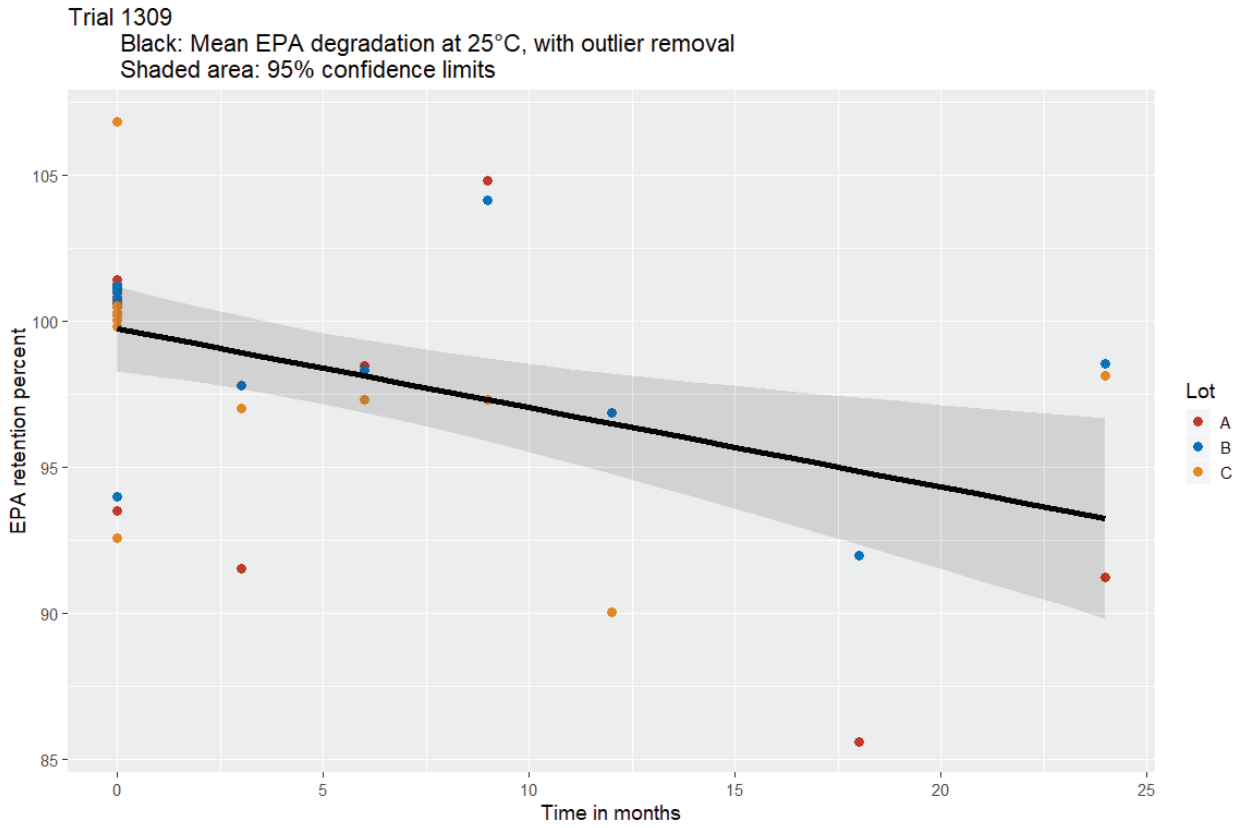
Temp	Time	EPA.estimated.mean	EPA lower CI	EPA upper CI
25	0	99.72994		
25	1	99.45942		
25	2	99.18889		
25	3	98.91836		
25	4	98.64783		
25	5	98.37731		
25	6	98.10678		
25	7	97.83625		
25	8	97.56572		
25	9	97.29520		
25	10	97.02467		
25	11	96.75414		
25	12	96.48362		

(b) (4)

(b) (4)

25	13	96.21309
25	14	95.94256
25	15	95.67203
25	16	95.40151
25	17	95.13098
25	18	94.86045
25	19	94.58992
25	20	94.31940
25	21	94.04887
25	22	93.77834
25	23	93.50781
25	24	93.23729

```
##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

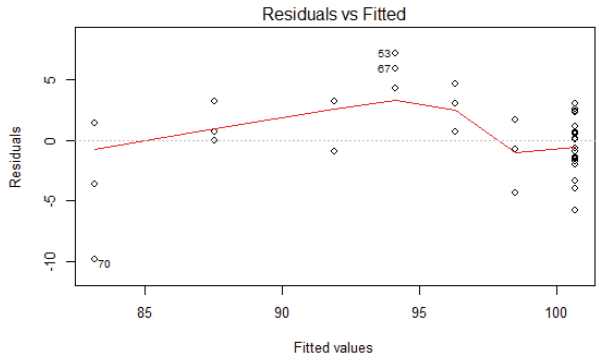


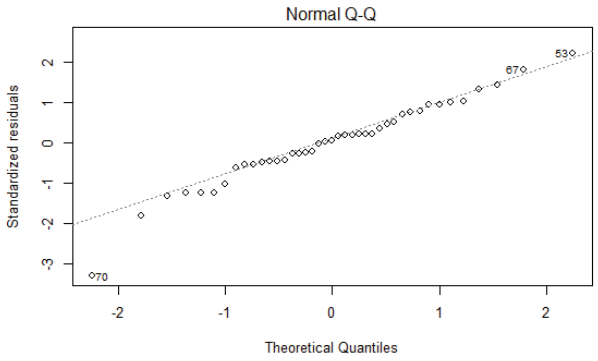
2.2.3 Statistical Analysis of DHA, 40°C, with outlier removal

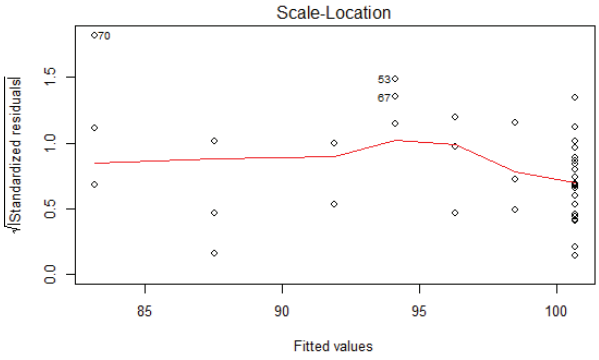
```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 40°C, with outlier removal
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
```

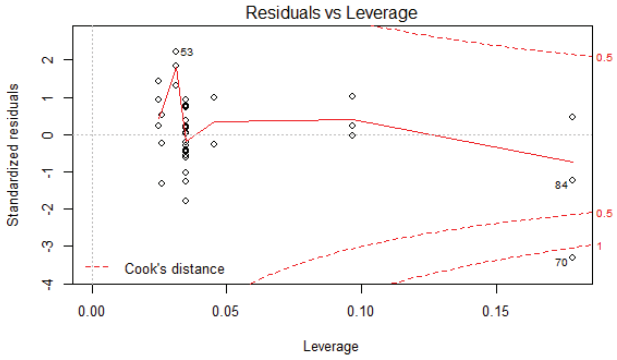
```
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -5.9424 -1.6926  0.2617  2.2040  7.2877
##
## Coefficients:
##            Estimate Std. Error t value Pr(>|t|)
## Time       -0.60524    0.11765  -5.144 1.04e-05 ***
## LotA      100.75220    1.04519  96.396  < 2e-16 ***
## LotB      100.82799    1.04092  96.864  < 2e-16 ***
## LotC      100.47773    1.04092  96.528  < 2e-16 ***
## Time:LotB  -0.29930    0.16373  -1.828   0.0761 .
## Time:LotC  -0.06054    0.16373  -0.370   0.7138
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.22 on 35 degrees of freedom
## Multiple R-squared:  0.9991, Adjusted R-squared:  0.9989
## F-statistic:  6227 on 6 and 35 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                  Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0               -0.29930    0.16373  -1.828
## Time:LotC = slope.C - slope.A == 0               -0.06054    0.16373  -0.370
## Time:LotC - Time:LotB = slope.C - slope.B == 0   0.23876    0.16103   1.483
##                                                  Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                  0.175
## Time:LotC = slope.C - slope.A == 0                  0.928
## Time:LotC - Time:LotB = slope.C - slope.B == 0      0.311
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##


##
## Call:
## lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -9.1120 -1.5783 -0.0086  2.3737  6.6059
##
## Coefficients:
##       Estimate Std. Error t value Pr(>|t|)
## Time  -0.72777    0.06803   -10.7 7.08e-13 ***
## LotA 101.31772    0.96684   104.8  < 2e-16 ***
## LotB  99.91891    0.94809   105.4  < 2e-16 ***
## LotC 100.79655    0.94809   106.3  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.297 on 37 degrees of freedom
## Multiple R-squared:  0.999,  Adjusted R-squared:  0.9989
## F-statistic:  8909 on 4 and 37 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.DHA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                              Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0  -1.3988     1.2704  -1.101
## LotC - LotA = intercept.C - intercept.A == 0  -0.5212     1.2704  -0.410
```

```
## LotC - LotB = intercept.C - intercept.B == 0   0.8776     1.2462   0.704
##                                                Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.519
## LotC - LotA = intercept.C - intercept.A == 0    0.912
## LotC - LotB = intercept.C - intercept.B == 0    0.763
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.DHA ~ Time, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -9.8188 -1.5263  0.1432  2.2870  7.1356
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) 100.67163    0.61015  165.00  < 2e-16 ***
## Time         -0.72968    0.06734  -10.84 2.51e-13 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.265 on 39 degrees of freedom
## Multiple R-squared:  0.7507, Adjusted R-squared:  0.7443
## F-statistic: 117.4 on 1 and 39 DF,  p-value: 2.51e-13

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##
```









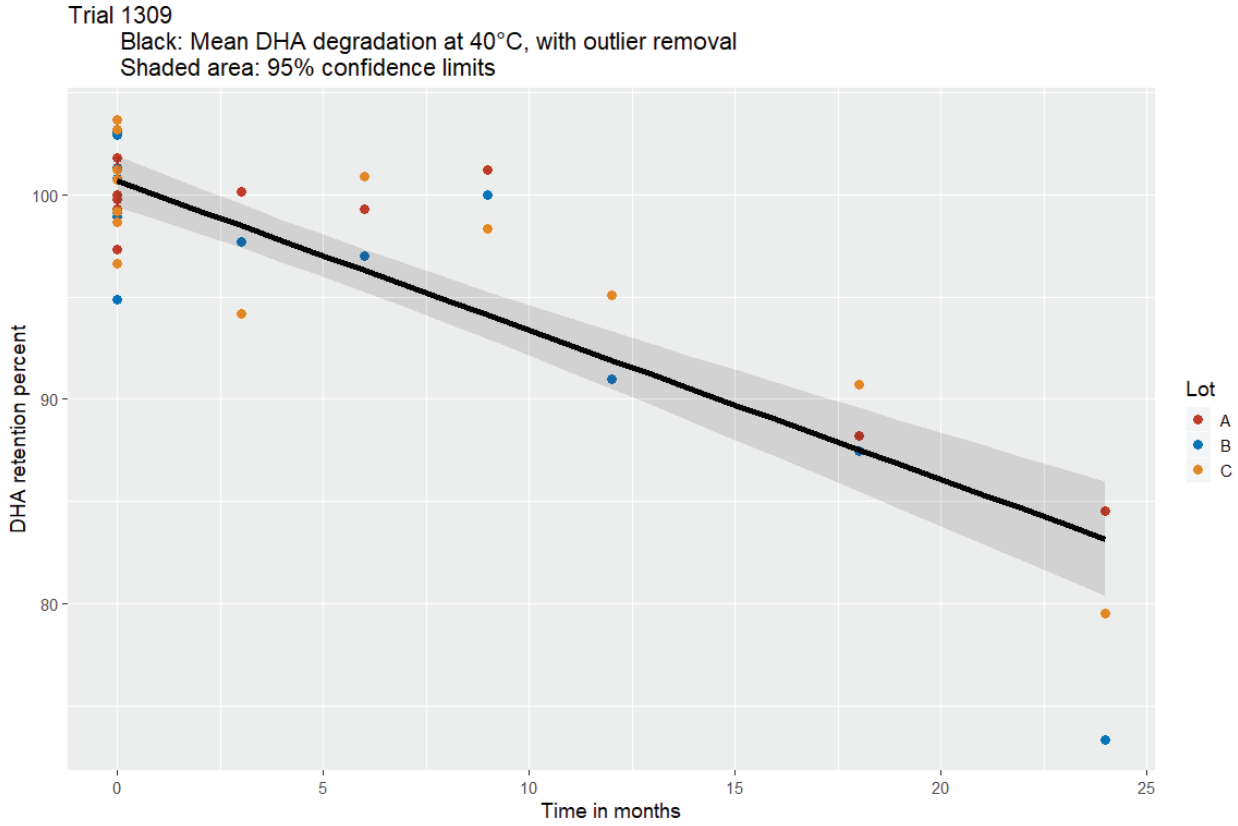

```
##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                  2.5 %      97.5 %
## (Intercept) 99.4374966 101.9057689
## Time        -0.8658871  -0.5934741

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

Temp	Time	DHA.estimated.mean	DHA.lower.CI	DHA.upper.CI
40	0	100.67163		
40	1	99.94195		
40	2	99.21227		
40	3	98.48259		
40	4	97.75291		
40	5	97.02323		
40	6	96.29355		
40	7	95.56387		
40	8	94.83419		
40	9	94.10451		
40	10	93.37483		
40	11	92.64515		
40	12	91.91547		

(b) (4)

```
40          13              91.18578
40          14              90.45610
40          15              89.72642
40          16              88.99674
40          17              88.26706
40          18              87.53738
40          19              86.80770
40          20              86.07802
40          21              85.34834
40          22              84.61866
40          23              83.88898
40          24              83.15930

##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

(b) (4)



2.2.4 Statistical Analysis of EPA, 40°C, with outlier removal

```
##
## ************************************************************
## 1. CALCULATE SEPARATE SLOPES AND INTERCEPTS
##    FOR EACH LOT AND TEST, 40°C, with outlier removal
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
```

```
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -7.9561 -0.4724 -0.0161  0.4809  6.2858
##
## Coefficients:
##            Estimate Std. Error t value Pr(>|t|)
## Time       -0.68704    0.11823  -5.811 1.37e-06 ***
## LotA      100.78674    1.05030  95.960  < 2e-16 ***
## LotB      100.94219    1.04601  96.502  < 2e-16 ***
## LotC      100.52877    1.04601  96.107  < 2e-16 ***
## Time:LotB  -0.13828    0.16453  -0.840    0.406
## Time:LotC  -0.04314    0.16453  -0.262    0.795
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.236 on 35 degrees of freedom
## Multiple R-squared:  0.9991, Adjusted R-squared:  0.9989
## F-statistic:  6164 on 6 and 35 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time * Lot - 1, data = d)
##
## Linear Hypotheses:
##                                                  Estimate Std. Error t value
## Time:LotB = slope.B - slope.A == 0               -0.13828    0.16453  -0.840
## Time:LotC = slope.C - slope.A == 0               -0.04314    0.16453  -0.262
## Time:LotC - Time:LotB = slope.C - slope.B == 0    0.09514    0.16182   0.588
##                                                  Pr(>|t|)
## Time:LotB = slope.B - slope.A == 0                  0.681
## Time:LotC = slope.C - slope.A == 0                  0.963
## Time:LotC - Time:LotB = slope.C - slope.B == 0      0.827
## (Adjusted p values reported -- single-step method)

##
##
##  # Slopes do not differ significantly, now test intercepts
##
##


##
## Call:
## lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -8.0520 -0.5115  0.1568  0.6319  6.1900
##
## Coefficients:
##       Estimate Std. Error t value Pr(>|t|)
## Time  -0.74881    0.06563  -11.41 1.12e-13 ***
## LotA 101.07186    0.93266  108.37  < 2e-16 ***
## LotB 100.54876    0.91457  109.94  < 2e-16 ***
## LotC 100.62462    0.91457  110.02  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.18 on 37 degrees of freedom
## Multiple R-squared:  0.999,  Adjusted R-squared:  0.9989
## F-statistic:  9570 on 4 and 37 DF,  p-value: < 2.2e-16

##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: lm(formula = ret.perc.EPA ~ Time + Lot - 1, data = d)
##
## Linear Hypotheses:
##                                              Estimate Std. Error t value
## LotB - LotA = intercept.B - intercept.A == 0 -0.52310    1.22549  -0.427
## LotC - LotA = intercept.C - intercept.A == 0 -0.44724    1.22549  -0.365
```

```
## LotC - LotB = intercept.C - intercept.B == 0  0.07586    1.20210   0.063
##                                                Pr(>|t|)
## LotB - LotA = intercept.B - intercept.A == 0    0.905
## LotC - LotA = intercept.C - intercept.A == 0    0.929
## LotC - LotB = intercept.C - intercept.B == 0    0.998
## (Adjusted p values reported -- single-step method)

##
##
##  # Intercepts do not differ significantly, data can be pooled
##
##

##
## ************************************************************
## 2. POOL LOTS INTO ONE REGRESSION
## ************************************************************
##

##
## Call:
## lm(formula = ret.perc.EPA ~ Time, data = d)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -8.1727 -0.5853  0.0199  0.6412  6.1665
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept) 100.74533    0.58054   173.5  < 2e-16 ***
## Time         -0.74978    0.06407   -11.7 2.49e-14 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.107 on 39 degrees of freedom
## Multiple R-squared:  0.7783, Adjusted R-squared:  0.7727
## F-statistic: 136.9 on 1 and 39 DF,  p-value: 2.49e-14

##
## ************************************************************
## 3. DIAGNOSTIC PLOTS
## ************************************************************
##



##
## ************************************************************
## 4. CONFIDENCE INTERVALS OF INTERCEPT AND SLOPE
## ************************************************************
##

##                   2.5 %      97.5 %
## (Intercept) 99.5710808 101.9195775
## Time        -0.8793742  -0.6201803

##
## ************************************************************
## 4. CONFIDENCE INTERVAL OF MEAN RETENTION 0 - 24 Months
## ************************************************************
##
```

Temp	Time	EPA.estimated.mean	EPA.lower.CI	EPA.upper.CI
40	0	100.74533		
40	1	99.99555		
40	2	99.24577		
40	3	98.49600		
40	4	97.74622		
40	5	96.99644		

(b) (4)

(b) (4)

40	6	96.24667
40	7	95.49689
40	8	94.74711
40	9	93.99733
40	10	93.24756
40	11	92.49778
40	12	91.74800
40	13	90.99823
40	14	90.24845
40	15	89.49867
40	16	88.74889
40	17	87.99912
40	18	87.24934
40	19	86.49956
40	20	85.74978
40	21	85.00001
40	22	84.25023
40	23	83.50045
40	24	82.75068

```
##
## ************************************************************
## 5. VISUALISATION OF RESULTS
## ************************************************************
##
```

3 Summary of results

Within all analyses, lots were poolable. Displayed are estimated mean results with 95% confidence limits of the estimate in brackets.

Endpoint	Temperature	Outlier removal	Monthly degradation in %	Retention in % of initial value at 24M
DHA	25	No	-0.54 (-0.93,-0.15)	86.38 (78.42,94.34)
EPA	25	No	-0.59 (-0.94,-0.23)	85.5 (78.28,92.71)
DHA	40	No	-0.81 (-1.04,-0.59)	80.92 (76.3,85.53)
EPA	40	No	-0.82 (-1.03,-0.62)	80.79 (76.64,84.95)
DHA	25	Yes	-0.17 (-0.28,-0.06)	95.54 (93.25,97.83)
EPA	25	Yes	-0.27 (-0.44,-0.11)	93.24 (89.82,96.65)
DHA	40	Yes	-0.73 (-0.87,-0.59)	83.16 (80.37,85.95)
EPA	40	Yes	-0.75 (-0.88,-0.62)	82.75 (80.1,85.4)

4 Database used



1309.xlsx

5 Source code



Stat-Analysis_1309.R

6 Appendix: Reproducibility information

- This document was created wit [redacted]
- Script created: 27.06.2019
- Last change in script: 01.07.2019
- Date and time of analysis: 2019-07-01 11:31:34
- R version and package information:

```
## [redacted] version 3.5.3 (2019-03-11)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows >= 8 x64 (build 9200)
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=German_Switzerland.1252  LC_CTYPE=German_Switzerland.1252
## [3] LC_MONETARY=German_Switzerland.1252 LC_NUMERIC=C
## [5] LC_TIME=German_Switzerland.1252
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
##  [1] dplyr_0.8.0.1      ggsci_2.9          RColorBrewer_1.1-2
##  [4] ggplot2_3.1.0      lsmeans_2.30-0     emmeans_1.3.3
##  [7] pander_0.6.3       multcomp_1.4-10    TH.data_1.0-10
## [10] MASS_7.3-51.1      survival_2.43-3    mvtnorm_1.0-10
## [13] nlme_3.1-137       papeR_1.0-4        xtable_1.8-3
## [16] car_3.0-2          carData_3.0-2      knitr_1.22
## [19] readxl_1.3.1
##
## loaded via a namespace (and not attached):
##  [1] Rcpp_1.0.1         lattice_0.20-38    zoo_1.8-5
##  [4] gtools_3.8.1       assertthat_0.2.1   digest_0.6.18
##  [7] R6_2.4.0           cellranger_1.1.0   plyr_1.8.4
## [10] evaluate_0.13      coda_0.19-2        highr_0.8
## [13] pillar_1.3.1       rlang_0.3.2        lazyeval_0.2.2
## [16] curl_3.3           data.table_1.12.0  gdata_2.18.0
## [19] gmodels_2.18.1     Matrix_1.2-17      rmarkdown_1.12
## [22] labeling_0.3       splines_3.5.3      stringr_1.4.0
## [25] foreign_0.8-71     munsell_0.5.0      compiler_3.5.3
## [28] xfun_0.5           pkgconfig_2.0.2    htmltools_0.3.6
## [31] tidyselect_0.2.5   tibble_2.1.1       rio_0.5.16
## [34] codetools_0.2-16   crayon_1.3.4       withr_2.1.2
## [37] grid_3.5.3         gtable_0.3.0       magrittr_1.5
## [40] scales_1.0.0       zip_2.0.1          estimability_1.3
## [43] stringi_1.4.3      sandwich_2.5-0     openxlsx_4.1.0
```

```
## [46] tools_3.5.3       forcats_0.4.0     glue_1.3.1
## [49] purrr_0.3.2       hms_0.4.2         abind_1.4-5
## [52] yaml_2.2.0        colorspace_1.4-1  haven_2.1.0
```

Data Table Pre-Extrusion Application

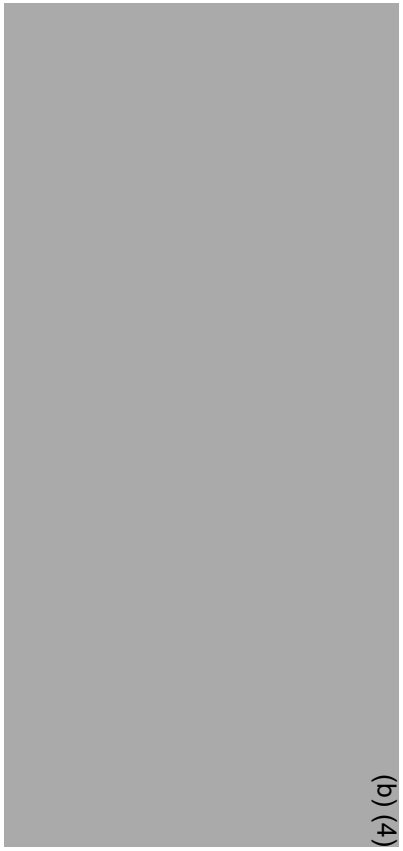
Study	Conditions	Temp	Lot	Sample ID	Pull	Time	DHA	EPA
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220567	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220568	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220569	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220570	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220571	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220572	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220573	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-05220574	Baseline	0		
1152	Ambient (25°C/60%RH)	25	A	464-2017-08210455	Month 3	3		
1152	Ambient (25°C/60%RH)	25	A	464-2017-11200350	Month 6	6		
1152	Ambient (25°C/60%RH)	25	A	464-2018-02190201	Month 9	9		
1152	Ambient (25°C/60%RH)	25	A	464-2018-05210340	Month 12	12		
1152	Ambient (25°C/60%RH)	25	A	464-2018-11200162	Month 18	18		
1152	Ambient (25°C/60%RH)	25	A	464-2019-05210165	Month 24	24		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220575	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220576	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220577	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220578	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220579	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220580	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220581	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-05220582	Baseline	0		
1152	Ambient (25°C/60%RH)	25	B	464-2017-08210457	Month 3	3		
1152	Ambient (25°C/60%RH)	25	B	464-2017-11200352	Month 6	6		
1152	Ambient (25°C/60%RH)	25	B	464-2018-02190203	Month 9	9		
1152	Ambient (25°C/60%RH)	25	B	464-2018-05210342	Month 12	12		
1152	Ambient (25°C/60%RH)	25	B	464-2018-11200164	Month 18	18		
1152	Ambient (25°C/60%RH)	25	B	464-2019-05210167	Month 24	24		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220583	Baseline	0		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220584	Baseline	0		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220585	Baseline	0		
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220586	Baseline	0		

(b) (4)

1152	Ambient (25°C/60%RH)	25	C	464-2017-05220587	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220588	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220589	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-05220590	Baseline	0
1152	Ambient (25°C/60%RH)	25	C	464-2017-08210459	Month 3	3
1152	Ambient (25°C/60%RH)	25	C	464-2017-11200354	Month 6	6
1152	Ambient (25°C/60%RH)	25	C	464-2018-02190205	Month 9	9
1152	Ambient (25°C/60%RH)	25	C	464-2018-05210344	Month 12	12
1152	Ambient (25°C/60%RH)	25	C	464-2018-11200166	Month 18	18
1152	Ambient (25°C/60%RH)	25	C	464-2019-05210169	Month 24	24
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220567	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220568	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220569	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220570	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220571	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220572	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220573	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-05220574	Baseline	0
1152	Accelerated (40°C/75%RH)	40	A	464-2017-08210456	Month 3	3
1152	Accelerated (40°C/75%RH)	40	A	464-2017-11200351	Month 6	6
1152	Accelerated (40°C/75%RH)	40	A	464-2018-02190202	Month 9	9
1152	Accelerated (40°C/75%RH)	40	A	464-2018-05210341	Month 12	12
1152	Accelerated (40°C/75%RH)	40	A	464-2018-11200163	Month 18	18
1152	Accelerated (40°C/75%RH)	40	A	464-2019-05210166	Month 24	24
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220575	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220576	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220577	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220578	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220579	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220580	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220581	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-05220582	Baseline	0
1152	Accelerated (40°C/75%RH)	40	B	464-2017-08210458	Month 3	3

(b) (4)

1152	Accelerated (40°C/75%RH)	40	B	464-2017-11200353	Month 6	6
1152	Accelerated (40°C/75%RH)	40	B	464-2018-02190204	Month 9	9
1152	Accelerated (40°C/75%RH)	40	B	464-2018-05210343	Month 12	12
1152	Accelerated (40°C/75%RH)	40	B	464-2018-05210343	Month 12	12
1152	Accelerated (40°C/75%RH)	40	B	464-2018-11200165	Month 18	18
1152	Accelerated (40°C/75%RH)	40	B	464-2019-05210168	Month 24	24
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220583	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220584	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220585	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220586	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220587	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220588	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220589	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-05220590	Baseline	0
1152	Accelerated (40°C/75%RH)	40	C	464-2017-08210460	Month 3	3
1152	Accelerated (40°C/75%RH)	40	C	464-2017-11200355	Month 6	6
1152	Accelerated (40°C/75%RH)	40	C	464-2018-02190206	Month 9	9
1152	Accelerated (40°C/75%RH)	40	C	464-2018-05210345	Month 12	12
1152	Accelerated (40°C/75%RH)	40	C	464-2018-11200167	Month 18	18
1152	Accelerated (40°C/75%RH)	40	C	464-2019-05210170	Month 24	24



Annex 9
Heavy Metals Analysis

(b) (4)

Person in charge
Client Support

(b) (4), (b) (6)

DSM NUTRITIONAL PRODUCTS/MARTEK
(b) (4), (b) (6)

Reporting Date 09/22/2016

(b) (4), (b) (6)

REPORT OF ANALYSIS

This analytical report supersedes
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Sample Code
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Test Results	Result
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Client Sample Code: (b) (4)

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
QA230 - Copper (ICP-AES) **Completion Date:** 07/13/2016 **Method:** AOCS Ca 17-01 * Copper (Cu)	(b) (4)
QA278 - Iron (ICP-AES) **Completion Date:** 07/13/2016 **Method:** AOCS Ca 17-01 * Iron (Fe)	
QA419 - Lead (ICP-AES) **Completion Date:** 07/13/2016 **Method:** AOCS Ca 17-01 * Lead (Pb)	
QD610 - Mercury (ICP-MS) **Completion Date:** 07/13/2016 **Method:** AOAC 2013.06 Mercury (Hg)	
QA01L - p-Anisidine Value **Completion Date:** 07/07/2016 **Method:** AOCS Cd 18-90 p-Anisidine Value	
QA282 - Free Fatty Acid, as Oleic **Completion Date:** 07/06/2016 **Method:** AOCS Ca 5a-40 Free fatty acids as oleic acid	
QA328 - Insoluble Impurities **Completion Date:** 07/07/2016 **Method:** AOCS Ca 3a-46 Insoluble impurities	
QA00F - Peroxide Value **Completion Date:** 07/06/2016 **Method:** AOCS Cd 8-53 Peroxide value	
QA188 - Eicosapentaenoic Acid (EPA) **Completion Date:** 07/08/2016 **Method:** AOCS Ce 1b-89 C 20:5n3 Eicosapentaenoic acid	

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REPORT OF ANALYSIS

This analytical report supersede

Test Results	Result
QA196 - Docosahexaenoic Acid (DHA) **Completion Date:** 07/08/2016 **Method:** AOCS Ce 1b-89 DHA Docosahexaenoic acid C22:6	(b) (4)
QA01N - Fatty Acid Profile (relative area %) **Completion Date:** 07/08/2016 **Method:** AOCS Ce 1b-89 C 6:0 (Caproic acid) C 8:0 (Caprylic acid) C 10:0 (Capric acid) C 12:0 (Lauric acid) C 13:0 (Tridecanoic acid) C 14:0 (Myristic acid) C 14:1 (Myristoleic acid) C 15:0 (Pentadecanoic acid) C 15:1 (Pentadecenoic acid) C 16:0 (Palmitic acid) C 16:1 (Palmitoleic acid) C 16:2 (Hexadecadienoic acid) C 16:3 (Hexadecatrienoic acid) C 16:4 (Hexadecatetraenoic acid) C 17:0 (Margaric acid) C 17:1 (Margaroleic acid) C 18:0 (Stearic acid) C 18:1n9 (Oleic acid) C 18:1n7 (Vaccenic acid) C 18:2n6 (Linoleic acid) C 20:0 (Arachidic acid) C 18:3n6 (gamma-Linolenic acid) C 20:1 (Eicosenoic acid) C 20:1n9 (Eicosenoic acid) C 18:3n3 (alpha-Linolenic acid) C 21:0 (Heneicosanoic acid) C 18:4n3 (Stearidonic acid) C 20:2n6 (Eicosadienoic acid)	

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(b) (4)

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Client Sample Code: (b) (4)

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REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

(b) (4)

[redacted]

[redacted]

Client Sample Code: 5015816001

[redacted]

REPORT OF ANALYSIS

This analytical report supersedes [redacted]

Test Results	Result
* PCB 104	[redacted]
* PCB 105	
* PCB 118	
* PCB 126	
* PCB 128	
* PCB 138	
* PCB 153	
* PCB 170	
* PCB 180	
* PCB 187	
* PCB 188	
* PCB 195	
* PCB 201	
* PCB 206	
* PCB 209	
* Total PCB	
Total of indicator non-dioxin-like PCBs (sum of PCB congeners:	[redacted]

A7158 - Dioxins and Furans: PCDD/F (17 Congeners)
Completion Date: 07/22/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

* 2,3,7,8-TetraCDD	[redacted]
* 1,2,3,7,8-PentaCDD	
* 1,2,3,4,7,8-HexaCDD	
* 1,2,3,6,7,8-HexaCDD	
* 1,2,3,7,8,9-HexaCDD	
* 1,2,3,4,6,7,8-HeptaCDD	
* OctaCDD	
* 2,3,7,8-TetraCDF	
* 1,2,3,7,8-PentaCDF	
* 2,3,4,7,8-PentaCDF	
* 1,2,3,4,7,8-HexaCDF	
* 1,2,3,6,7,8-HexaCDF	
* 1,2,3,7,8,9-HexaCDF	
* 2,3,4,6,7,8-HexaCDF	

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Client Sample Code

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REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

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Client Sample Code: (b) (4)

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result

Respectfully Submitted

(b) (4)

(b) (4)

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

ACCREDITED

(b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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(b) (4), (b) (6)

Person in charge
Client Support

DSM NUTRITIONAL PRODUCTS/MARTEK
ATTN: (b) (4), (b) (6)

(b) (4)

Reporting Date 09/22/2016

(b) (4)

REPORT OF ANALYSIS

(b) (4)

This analytical report supersedes

Sample Code (b) (4)

(b) (4)

(b) (4)

Eurofins Sample Code: (b) (4)

Client Sample Code: CRUDE OIL

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
QA230 - Copper (ICP-AES) **Completion Date:** 08/23/2016 **Method:** AOCS Ca 17-01 * Copper (Cu)	(b) (4)
QA278 - Iron (ICP-AES) **Completion Date:** 08/23/2016 **Method:** AOCS Ca 17-01 * Iron (Fe)	
QA419 - Lead (ICP-AES) **Completion Date:** 08/23/2016 **Method:** AOCS Ca 17-01 * Lead (Pb)	
QD610 - Mercury (ICP-MS) **Completion Date:** 08/22/2016 **Method:** AOAC 2013.06 Mercury (Hg)	
QA01L - p-Anisidine Value **Completion Date:** 08/15/2016 **Method:** AOCS Cd 18-90 p-Anisidine Value	
QA282 - Free Fatty Acid, as Oleic **Completion Date:** 08/15/2016 **Method:** AOCS Ca 5a-40 Free fatty acids as oleic acid	
QA328 - Insoluble Impurities **Completion Date:** 08/15/2016 **Method:** AOCS Ca 3a-46 Insoluble impurities	
QA00F - Peroxide Value **Completion Date:** 08/15/2016 **Method:** AOCS Cd 8-53 Peroxide value	
QA188 - Eicosapentaenoic Acid (EPA) **Completion Date:** 08/16/2016 **Method:** AOCS Ce 1b-89 C 20:5n3 Eicosapentaenoic acid	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
(b) (4)	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

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REPORT OF ANALYSIS

This analytical report supersede

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Test Results	Result
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	(b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
* PCB 104	(b) (4)
* PCB 105	
* PCB 118	
* PCB 126	
* PCB 128	
* PCB 138	
* PCB 153	
* PCB 170	
* PCB 180	
* PCB 187	
* PCB 188	
* PCB 195	
* PCB 201	
* PCB 206	
* PCB 209	
* Total PCB	

(b) (4)

A7158 - Dioxins and Furans: PCDD/F (17 Congeners)
Completion Date: 08/17/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

* 2,3,7,8-TetraCDD	(b) (4)
* 1,2,3,7,8-PentaCDD	
* 1,2,3,4,7,8-HexaCDD	
* 1,2,3,6,7,8-HexaCDD	
* 1,2,3,7,8,9-HexaCDD	
* 1,2,3,4,6,7,8-HeptaCDD	
* OctaCDD	
* 2,3,7,8-TetraCDF	
* 1,2,3,7,8-PentaCDF	
* 2,3,4,7,8-PentaCDF	
* 1,2,3,4,7,8-HexaCDF	
* 1,2,3,6,7,8-HexaCDF	
* 1,2,3,7,8,9-HexaCDF	
* 2,3,4,6,7,8-HexaCDF	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results

(b) (4)

* 1,2,3,4,6,7,8-HeptaCDF
* 1,2,3,4,7,8,9-HeptaCDF
* OctaCDF
* WHO(2005)-PCDD/F TEQ (lower-bound)
* WHO(2005)-PCDD/F TEQ (upper-bound)

A7347 - Dioxin-like PCBs (12 WHO-PCBs)
Completion Date: 08/17/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

(b) (4)

* PCB 77
* PCB 81
* PCB 105
* PCB 114
* PCB 118
* PCB 123
* PCB 126
* PCB 156
* PCB 157
* PCB 167
* PCB 169
* PCB 189
* WHO(2005)-PCB TEQ (lower-bound)
* WHO(2005)-PCB TEQ (upper-bound)

GF004 - WHO-PCDD/F+PCB TEQ
Completion Date: 08/17/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

(b) (4)

* WHO(2005)-PCDD/F+PCB TEQ (lower-bound)
* WHO(2005)-PCDD/F+PCB TEQ (upper-bound)

**This is not covered by our current A2LA accreditation.*

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

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REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results **Result**

Respectfully Submitted,

(b) (4)

(b) (4)

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

(b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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(b) (4), (b) (6)

Person in charge
Client Support

DSM NUTRITIONAL PRODUCTS/MARTEK
(b) (4), (b) (6)

Reporting Date 09/22/2016

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Sample Code (b) (4)

(b) (4)

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Client Sample Code (b) (4)

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
QA230 - Copper (ICP-AES) **Completion Date:** 09/14/2016 **Method:** AOCS Ca 17-01 * Copper (Cu)	(b) (4)
QA278 - Iron (ICP-AES) **Completion Date:** 09/14/2016 **Method:** AOCS Ca 17-01 * Iron (Fe)	
QA419 - Lead (ICP-AES) **Completion Date:** 09/14/2016 **Method:** AOCS Ca 17-01 * Lead (Pb)	
QD610 - Mercury (ICP-MS) **Completion Date:** 09/16/2016 **Method:** AOAC 2013.06 Mercury (Hg)	
QA01L - p-Anisidine Value **Completion Date:** 09/12/2016 **Method:** AOCS Cd 18-90 p-Anisidine Value	
QA282 - Free Fatty Acid, as Oleic **Completion Date:** 09/12/2016 **Method:** AOCS Ca 5a-40 Free fatty acids as oleic acid	
QA328 - Insoluble Impurities **Completion Date:** 09/12/2016 **Method:** AOCS Ca 3a-46 Insoluble impurities	
QA00F - Peroxide Value **Completion Date:** 09/12/2016 **Method:** AOCS Cd 8-53 Peroxide value	
QA188 - Eicosapentaenoic Acid (EPA) **Completion Date:** 09/14/2016 **Method:** AOCS Ce 1b-89 C 20:5n3 Eicosapentaenoic acid	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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Client Sample Code: VY00015465

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)

Test Results	Result
QA196 - Docosahexaenoic Acid (DHA)	
Completion Date: 09/14/2016 **Method:** AOCS Ce 1b-89	
DHA Docosahexaenoic acid C22:6	(b) (4)
QA01N - Fatty Acid Profile (relative area %)	
Completion Date: 09/14/2016 **Method:** AOCS Ce 1b-89	
C 6:0 (Caproic acid)	
C 8:0 (Caprylic acid)	
C 10:0 (Capric acid)	
C 12:0 (Lauric acid)	
C 13:0 (Tridecanoic acid)	
C 14:0 (Myristic acid)	
C 14:1 (Myristoleic acid)	
C 15:0 (Pentadecanoic acid)	
C 15:1 (Pentadecenoic acid)	
C 16:0 (Palmitic acid)	
C 16:1 (Palmitoleic acid)	
C 16:2 (Hexadecadienoic acid)	
C 16:3 (Hexadecatrienoic acid)	
C 16:4 (Hexadecatetraenoic acid)	
C 17:0 (Margaric acid)	
C 17:1 (Margaroleic acid)	
C 18:0 (Stearic acid)	
C 18:1n9 (Oleic acid)	
C 18:1n7 (Vaccenic acid)	
C 18:2n6 (Linoleic acid)	
C 20:0 (Arachidic acid)	
C 18:3n6 (gamma-Linolenic acid)	
C 20:1 (Eicosenoic acid)	
C 20:1n9 (Eicosenoic acid)	
C 18:3n3 (alpha-Linolenic acid)	
C 21:0 (Heneicosanoic acid)	
C 18:4n3 (Stearidonic acid)	
C 20:2n6 (Eicosadienoic acid)	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

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[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

This analytical report supersedes [redacted]

Test Results

	Result
C 22:0 (Behenic acid)	[redacted] (b) (4)
C 22:1n9 (Erucic acid)	
C 22:1n11 (Cetoleic acid)	
C 20:3n6 (homo-gamma-Linolenic acid)	
C 20:3n3 (Eicosatrienoic acid)	
C 20:4n5 (Eicosatetraenoic)	
C 20:4n6 (Arachidonic acid)	
C 23:0 (Tricosanoic acid)	
C 22:2n6 (Docosadienoic acid)	
C 20:4n3 (Eicosatetraenoic acid)	
C 22:4n3 (Eicosatetraenoic acid)	
C 24:0 (Lignoceric acid)	
C 20:5n3 (Eicosapentaenoic acid)	
C 24:1 (Nervonic acid)	
C 21:5n3 (Heneicosapentaenoic acid)	
C 22:4n6 (Docosatetraenoic acid)	
C 22:5n6 (Docosapentaenoic acid)	
C 22:5n3 (Docosapentaenoic acid)	
C 22:6n3 (Docosahexaenoic acid)	
Unknown Components	

QA052 - Polychlorinated Biphenyls (Oils & Fats)
Completion Date: 09/14/2016 **Method:** ASU L00.00-34

* PCB 1	
* PCB 8	
* PCB 18	
* PCB 28	
* PCB 29	
* PCB 44	
* PCB 50	
* PCB 52	
* PCB 66	
* PCB 77	
* PCB 87	
* PCB 101	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes

Test Results

* PCB 104
* PCB 105
* PCB 118
* PCB 126
* PCB 128
* PCB 138
* PCB 153
* PCB 170
* PCB 180
* PCB 187
* PCB 188
* PCB 195
* PCB 201
* PCB 206
* PCB 209
* *Total PCB*

Total of indicator non-dioxin-like PCBs (sum of PCB congeners:

(b) (4)

A7158 - Dioxins and Furans: PCDD/F (17 Congeners)
Completion Date: 09/15/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

* 2,3,7,8-TetraCDD
* 1,2,3,7,8-PentaCDD
* 1,2,3,4,7,8-HexaCDD
* 1,2,3,6,7,8-HexaCDD
* 1,2,3,7,8,9-HexaCDD
* 1,2,3,4,6,7,8-HeptaCDD
* OctaCDD
* 2,3,7,8-TetraCDF
* 1,2,3,7,8-PentaCDF
* 2,3,4,7,8-PentaCDF
* 1,2,3,4,7,8-HexaCDF
* 1,2,3,6,7,8-HexaCDF
* 1,2,3,7,8,9-HexaCDF
* 2,3,4,6,7,8-HexaCDF

(b) (4)

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(b) (4)

[redacted]

[redacted]

[redacted]

REPORT OF ANALYSIS

This analytical report supersedes [redacted]

Test Results

Result

* 1,2,3,4,6,7,8-HeptaCDF [redacted]
* 1,2,3,4,7,8,9-HeptaCDF
* OctaCDF
* WHO(2005)-PCDD/F TEQ (lower-bound)
* WHO(2005)-PCDD/F TEQ (upper-bound)

A7347 - Dioxin-like PCBs (12 WHO-PCBs)
Completion Date: 09/15/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

* PCB 77 [redacted]
* PCB 81
* PCB 105
* PCB 114
* PCB 118
* PCB 123
* PCB 126
* PCB 156
* PCB 157
* PCB 167
* PCB 169
* PCB 189
* WHO(2005)-PCB TEQ (lower-bound)
* WHO(2005)-PCB TEQ (upper-bound)

GF004 - WHO-PCDD/F+PCB TEQ
Completion Date: 09/15/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

* WHO(2005)-PCDD/F+PCB TEQ (lower-bound) [redacted]
* WHO(2005)-PCDD/F+PCB TEQ (upper-bound)

**This is not covered by our current A2LA accreditation.*

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted]

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4) t

Test Results

Respectfully Submitted,

(b) (4)

(b) (4)

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

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(b) (4)

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(b) (4)

(b) (4)

Person in charge
Client Support
(b) (4), (b) (6)

DSM NUTRITIONAL PRODUCTS/MARTEK
(b) (4), (b) (6)

Reporting Date 09/22/2016
(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes (b) (4)
Sample Code (b) (4)

Sample Description CRUDE OIL
Client Sample Code (b) (4)
Sample Reference

Reception Date 09/09/2016
Reception Temperature -41 (Celsius)
Sample Condition Acceptable
Purchase Order 4701594417

Test Results

Result

QA377 - Moisture (Air Oven 135C 2 hrs)
Completion Date: 09/12/2016 **Method:** AOAC 930.15
* Moisture (b) (4)

QA271 - Crude Fat (Acid Hydrolysis)
Completion Date: 09/14/2016 **Method:** AOAC 954.02
* Crude Fat

QA270 - Total Fat (as FAME)
Completion Date: 09/16/2016 **Method:** AOAC 996.06
* FAME total (%fat)

QA133 - Arsenic (ICP-MS)
Completion Date: 09/16/2016 **Method:** AOAC 2013.06
Arsenic (As)

QA205 - Cadmium (ICP-MS)
Completion Date: 09/16/2016 **Method:** AOAC 2013.06
Cadmium (Cd)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

This analytical report supersedes [redacted] (b) (4)

Test Results	Result
QA230 - Copper (ICP-AES) **Completion Date:** 09/14/2016 **Method:** AOCS Ca 17-01 * Copper (Cu)	[redacted] (b) (4)
QA278 - Iron (ICP-AES) **Completion Date:** 09/14/2016 **Method:** AOCS Ca 17-01 * Iron (Fe)	
QA419 - Lead (ICP-AES) **Completion Date:** 09/14/2016 **Method:** AOCS Ca 17-01 * Lead (Pb)	
QD610 - Mercury (ICP-MS) **Completion Date:** 09/16/2016 **Method:** AOAC 2013.06 Mercury (Hg)	
QA01L - p-Anisidine Value **Completion Date:** 09/12/2016 **Method:** AOCS Cd 18-90 p-Anisidine Value	
QA282 - Free Fatty Acid, as Oleic **Completion Date:** 09/12/2016 **Method:** AOCS Ca 5a-40 Free fatty acids as oleic acid	
QA328 - Insoluble Impurities **Completion Date:** 09/12/2016 **Method:** AOCS Ca 3a-46 Insoluble impurities	
QA00F - Peroxide Value **Completion Date:** 09/12/2016 **Method:** AOCS Cd 8-53 Peroxide value	
QA188 - Eicosapentaenoic Acid (EPA) **Completion Date:** 09/16/2016 **Method:** AOCS Ce 1b-89 C 20:5n3 Eicosapentaenoic acid	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

This analytical report supersede(b) (4)

Test Results	Result
(b) (4)	

(b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

This analytical report supersede[redacted] (b) (4)

Test Results	Result
C 22:0 (Behenic acid)	[redacted] (b) (4)
C 22:1n9 (Erucic acid)	
C 22:1n11 (Cetoleic acid)	
C 20:3n6 (homo-gamma-Linolenic acid)	
C 20:3n3 (Eicosatrienoic acid)	
C 20:4n5 (Eicosatetraenoic)	
C 20:4n6 (Arachidonic acid)	
C 23:0 (Tricosanoic acid)	
C 22:2n6 (Docosadienoic acid)	
C 20:4n3 (Eicosatetraenoic acid)	
C 22:4n3 (Eicosatetraenoic acid)	
C 24:0 (Lignoceric acid)	
C 20:5n3 (Eicosapentaenoic acid)	
C 24:1 (Nervonic acid)	
C 21:5n3 (Heneicosapentaenoic acid)	
C 22:4n6 (Docosatetraenoic acid)	
C 22:5n6 (Docosapentaenoic acid)	
C 22:5n3 (Docosapentaenoic acid)	
C 22:6n3 (Docosahexaenoic acid)	
Unknown Components	

QA052 - Polychlorinated Biphenyls (Oils & Fats)
Completion Date: 09/14/2016 **Method:** ASU L00.00-34

* PCB 1	
* PCB 8	
* PCB 18	
* PCB 28	
* PCB 29	
* PCB 44	
* PCB 50	
* PCB 52	
* PCB 66	
* PCB 77	
* PCB 87	
* PCB 101	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

(b) (4)

(b) (4)

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(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes

Test Results	Result
* PCB 104	(b) (4)
* PCB 105	
* PCB 118	
* PCB 126	
* PCB 128	
* PCB 138	
* PCB 153	
* PCB 170	
* PCB 180	
* PCB 187	
* PCB 188	
* PCB 195	
* PCB 201	
* PCB 206	
* PCB 209	
* Total PCB	

Total of indicator non-dioxin-like PCBs (sum of PCB congeners: 101, 138, 153, 180, 28 and 52) < 10 ppb

A7158 - Dioxins and Furans: PCDD/F (17 Congeners)
Completion Date: 09/21/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

* 2,3,7,8-TetraCDD	(b) (4)
* 1,2,3,7,8-PentaCDD	
* 1,2,3,4,7,8-HexaCDD	
* 1,2,3,6,7,8-HexaCDD	
* 1,2,3,7,8,9-HexaCDD	
* 1,2,3,4,6,7,8-HeptaCDD	
* OctaCDD	
* 2,3,7,8-TetraCDF	
* 1,2,3,7,8-PentaCDF	
* 2,3,4,7,8-PentaCDF	
* 1,2,3,4,7,8-HexaCDF	
* 1,2,3,6,7,8-HexaCDF	
* 1,2,3,7,8,9-HexaCDF	
* 2,3,4,6,7,8-HexaCDF	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes A (b) (4)

Test Results

Result

(b) (4)

* 1,2,3,4,6,7,8-HeptaCDF
* 1,2,3,4,7,8,9-HeptaCDF
* OctaCDF
* WHO(2005)-PCDD/F TEQ (lower-bound)
* WHO(2005)-PCDD/F TEQ (upper-bound)

A7347 - Dioxin-like PCBs (12 WHO-PCBs)
Completion Date: 09/21/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

(b) (4)

* PCB 77
* PCB 81
* PCB 105
* PCB 114
* PCB 118
* PCB 123
* PCB 126
* PCB 156
* PCB 157
* PCB 167
* PCB 169
* PCB 189
* WHO(2005)-PCB TEQ (lower-bound)
* WHO(2005)-PCB TEQ (upper-bound)

GF004 - WHO-PCDD/F+PCB TEQ
Completion Date: 09/21/2016 **Method:** EC Reg 589/2014 (food) and EC Reg 709/2014 (feed)

(b) (4)

* WHO(2005)-PCDD/F+PCB TEQ (lower-bound)
* WHO(2005)-PCDD/F+PCB TEQ (upper-bound)

**This is not covered by our current A2LA accreditation.*

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

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Eurofins Sample Code:

(b) (4)

REPORT OF ANALYSIS

This analytical report supersedes A (b) (4)

Test Results **Result**

Respectfully Submitted,

(b) (4)

(b) (4)

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Uncertainty can be obtained upon request.

(b) (4)

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(b) (4)

Annex 10
Pesticide Analysis

(b) (4)

(b) (4), (b) (6)

Person in charge
Client Support

DSM Nutritional Products (Martek)
(b) (4), (b) (6)

Reporting Date 08/10/2017

(b) (4)

REPORT OF ANALYSIS

Sample Code (b) (4)

Sample Description (b) (4)
Client Sample Code
Sample Reference

Reception Date 07/21/2017
Reception Temperature -33.0 (Celsius)
Sample Condition Acceptable
Purchase Order 4701471730

Test Results

Result

QA383 - Moisture & Volatiles (Air Oven 130C)
Completion Date: 08/10/2017 **Method:** AOCS Ca 2c-25
* Moisture & Volatiles

QD298 - Protein - Kjeltec
Completion Date: 08/02/2017 **Method:** AOAC 2001.11
* Protein- Kjeltec

QA274 - Crude Fat / Oil (Pet ether extr - SBM)
Completion Date: 07/27/2017 **Method:** AOCS Ba 3-38
Oil (Fat)

QA13A - Ash
Completion Date: 07/26/2017 **Method:** AOAC 923.03 / 32.1.05 16th Ed.
* Ash

QD230 - Fiber, Total Dietary
Completion Date: 08/02/2017 **Method:** AOAC 991.43
* Total Dietary Fiber

(b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results	Result
QA106 - Aluminum (ICP-AES)	
Completion Date: 07/31/2017 **Method:** J.AOAC 92, 1484-1518 (2009)	[redacted] (b) (4)
* Aluminum (Al)	
QA00P - Calcium NLEA	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Calcium (Ca)	
QA00G - Chromium (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 986.15	
Chromium (Cr)	
QA417 - Lead (ICP-MS)	
Completion Date: 07/31/2017 **Method:** AOAC 2013.06	
Lead (Pb)	
QA003 - Manganese (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Manganese (Mn)	
QA00D - Phosphorus (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Phosphorus (P)	
QA004 - Potassium (ICP-AES)	[redacted] (b) (4)
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Potassium (K)	
QA00Q - Sodium NLEA	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Sodium (Na)	
QQ182 - Total Vitamin A	
Completion Date: 08/02/2017 **Method:** AOAC 974.29 Mod.	
* Retinol	
* ß-carotene	
* Total Vitamin A	

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[redacted] (b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

QQ188 - Vitamin E-Tocopherol Profile (AOAC, Most Matrices)
Completion Date: 08/02/2017 **Method:** AOAC 971.30 with HPLC quantification mod.

* Alpha-Tocopherol
* Beta-Tocopherol
* Delta-Tocopherol
* Gamma-Tocopherol
* Total Vitamin E (Tocopherols)

QA202 - Calories from Fat
Completion Date: 08/10/2017 **Method:**

* Calories from fat

QA204 - Carbohydrate
Completion Date: 08/10/2017 **Method:**

* Carbohydrates (calculated)

QA052 - Polychlorinated Biphenyls (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Sum Non-Dioxin-Like PCBs (28+52+101+138+153+180)
* PCB 1
* PCB 8
* PCB 18
* PCB 28
* PCB 29
* PCB 44
* PCB 50
* PCB 52
* PCB 66
* PCB 77
* PCB 87
* PCB 101
* PCB 104
* PCB 105
* PCB 118
* PCB 126

(b) (4)

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(b) (4)

364

(b) (4)

(b) (4)

(b) (4)







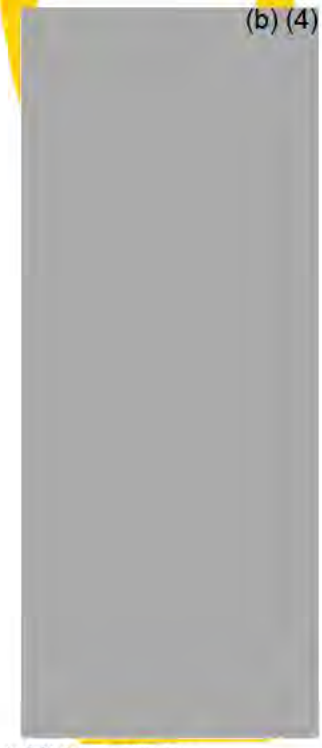
REPORT OF ANALYSIS



Test Results	Result
* PCB 128	(b) (4)
* PCB 138	
* PCB 153	
* PCB 170	
* PCB 180	
* PCB 187	
* PCB 188	
* PCB 195	
* PCB 201	
* PCB 206	
* PCB 209	
* Total PCB	

QA02B - Pesticides - Organochlorine (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

(b) (4)



* a, ß, d-BHC (Benzene hexachloride)
* Alachlor
* Aldrin
* Benfluralin
* Bifenox
* Boscalid
* Bromacil
* Captafol
* Captan
* Chlordane (total)
* Chlorfenapyr
* Chlorobenzilate
* Chlorothalonil
* Cyanazine
* Dacthal (Chlorthal)
* DDD
* DDE
* DDT
* Dichlobenil
* Dichlone
* Dicloran

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.



(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
* Dicofol, p,p-	(b) (4)
* Dieldrin	
* Endosulfan, alpha-	
* Endosulfan, beta-	
* Endosulfan-sulfate	
* Endrin	
* Ethalfluralin	
* Fenhexamid	
* Folpet	
* HCB (Hexachlorbenzene)	
* Heptachlor	
* Heptachlor epoxide	
* Indoxacarb	
* Iprodione	
* Lindane (gamma-HCH)	
* Linuron	
* Methoxychlor	
* Metribuzin	
* Mirex	
* Myclobutanil	
* Oxadiazon	
* Oxyfluorfen	
* Pendimethalin	
* Pentachloroaniline	
* Pentachloronitrobenzene (PCNB)	
* Perthane	
* Procymidone	
* Profluralin	
* Pronamide	
* Propanil	
* Pyraflufen-ethyl	
* Pyrethrins	
* Tetradifon	
* Tridimephon	
* Trifloxystrobin	
* Triflumizole	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results

Result

(b) (4)

* Trifluralin
* Vegadex
* Vinclozolin

QA02C - Pesticides - Pyrethroids (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Bifenthrin
* Cyfluthrin
* Cyhalothrin lambda-
* Cypermethrin
* Deltamethrin
* Esfenvalerate
* Fenpropathrin
* Fluvalinate
* Permethrin
* Tralomethrin

QA02D - Pesticides - Organophosphorus (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Azinphos-methyl
* Carbophenothion
* Chlorfenvinphos
* Chlorpyrifos (-ethyl)
* Chlorpyrifos-methyl
* Coumaphos
* Diazinon
* Dibrom (Naled)
* Dicrotophos
* Dimethoate
* Disulfoton
* EPN
* Ethion
* Ethoprop
* Fenamiphos
* Fenitrothion
* Fenthion

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

367

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

Result

(b) (4)

* Fonofos
* Isofenphos
* Malathion
* Methyl Parathion
* Mevinphos
* Omethoate
* Parathion
* Phorate
* Phosalone
* Phosmet
* Phosphamidon
* Pirimiphos-methyl
* Profenofos
* Propetamphos
* Ronnel
* Sulprofos
* Tetrachlorvinphos
* Thionazin

QA22A - Pesticides (LC-MSMS)
Completion Date: 07/26/2017 **Method:** Internal LC-MS/MS

* Aldicarb
* Buprofezin
* Carbaryl
* Carfentrazone-ethyl
* Chlorantraniliprole
* Clethodim
* Cyproconazole
* Diuron
* Flusilazole
* Indaziflam
* Methidathion
* Methomyl
* Oryzalin
* Pendimethalin
* Penthiopyrad

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's [illegible] accreditation.

(b) (4)

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(b) (4)

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REPORT OF ANALYSIS

Test Results	Result
* Propargite	(b) (4)
* Pyriproxyfen	
* Simazine	
* Spinosad	

UMMFL - Aerobic Plate Count - AOAC 966.23
Completion Date: 07/27/2017 **Method:** AOAC 966.23
* Aerobic Plate Count

QD034 - Calories by Bomb Calorimeter
Completion Date: 08/02/2017 **Method:** Parr Instruments
* Calories By Bomb Calorimeter

UM73J - Coliforms - AOAC 991.14
Completion Date: 07/27/2017 **Method:** AOAC 991.14
* Total Coliforms

UM73J - Escherichia coli - AOAC 991.14
Completion Date: 07/27/2017 **Method:** AOAC 991.14
* E. coli

UM4BV - Moulds - BAM Chapter 18
Completion Date: 07/27/2017 **Method:** FDA BAM Chapter 18
* Mold

UM4BV - Yeast - BAM Chapter 18
Completion Date: 07/27/2017 **Method:** FDA BAM Chapter 18
* Yeast

UMAEK - Salmonella - AOAC 2003.09
Completion Date: 07/27/2017 **Method:** AOAC 2003.09
* Salmonella

UMJR7 - Staphylococcus aureus - AOAC 2003.07
Completion Date: 07/27/2017 **Method:** AOAC 2003.07
* Staphylococcus aureus

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

TK198 - Total Fluorine by Ion Chromatography
Completion Date: 08/10/2017 **Method:** EPA 9056 1994 (SW-846)
* Fluorine (F)

**This is not covered by our current A2LA accreditation.*

Result

(b) (4)

Respectfully Submitted,

(b) (4)

(b) (4)

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

ACCREDITED

(b) (4)

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(b) (4)

370

(b) (4)

Person in charge
Client Support

(b) (4), (b) (6)

DSM Nutritional Products (Martek)
(b) (4), (b) (6)

Reporting Date 08/10/2017

(b) (4)

REPORT OF ANALYSIS

Sample Code (b) (4)

(b) (4)

Sample Description
Client Sample Cod
Sample Referenc

Reception Date 07/21/2017
Reception Temperature -33.0 (Celsius)
Sample Condition Acceptable
Purchase Order 4701471730

Test Results	Result
QA383 - Moisture & Volatiles (Air Oven 130C) **Completion Date:** 08/10/2017 **Method:** AOCS Ca 2c-25 * Moisture & Volatiles	(b) (4)
QD298 - Protein - Kjeltec **Completion Date:** 08/03/2017 **Method:** AOAC 2001.11 * Protein- Kjeltec	
QA274 - Crude Fat / Oil (Pet ether extr - SBM) **Completion Date:** 07/27/2017 **Method:** AOCS Ba 3-38 Oil (Fat)	
QA13A - Ash **Completion Date:** 07/26/2017 **Method:** AOAC 923.03 / 32.1.05 16th Ed. * Ash	
QD230 - Fiber, Total Dietary **Completion Date:** 08/03/2017 **Method:** AOAC 991.43 * Total Dietary Fiber	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results	Result
QA106 - Aluminum (ICP-AES)	
Completion Date: 07/31/2017 **Method:** J.AOAC 92, 1484-1518 (2009)	[redacted] (b) (4)
* Aluminum (Al)	
QA00P - Calcium NLEA	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Calcium (Ca)	
QA00G - Chromium (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 986.15	
Chromium (Cr)	
QA417 - Lead (ICP-MS)	
Completion Date: 07/31/2017 **Method:** AOAC 2013.06	
Lead (Pb)	
QA003 - Manganese (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Manganese (Mn)	
QA00D - Phosphorus (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Phosphorus (P)	
QA004 - Potassium (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Potassium (K)	
QA00Q - Sodium NLEA	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Sodium (Na)	
QQ182 - Total Vitamin A	
Completion Date: 08/03/2017 **Method:** AOAC 974.29 Mod.	
* Retinol	
* ß-carotene	
* Total Vitamin A	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results **Result**

QQ188 - Vitamin E-Tocopherol Profile (AOAC, Most Matrices)
Completion Date: 08/03/2017 **Method:** AOAC 971.30 with HPLC quantification mod.
* Alpha-Tocopherol
* Beta-Tocopherol
* Delta-Tocopherol
* Gamma-Tocopherol
* Total Vitamin E (Tocopherols)

[redacted] (b) (4)

QA202 - Calories from Fat
Completion Date: 08/10/2017 **Method:**
* Calories from fat

QA204 - Carbohydrate
Completion Date: 08/10/2017 **Method:**
* Carbohydrates (calculated)

QA052 - Polychlorinated Biphenyls (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34
* Sum Non-Dioxin-Like PCBs (28+52+101+138+153+180)
* PCB 1
* PCB 8
* PCB 18
* PCB 28
* PCB 29
* PCB 44
* PCB 50
* PCB 52
* PCB 66
* PCB 77
* PCB 87
* PCB 101
* PCB 104
* PCB 105
* PCB 118
* PCB 126

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
* PCB 128	(b) (4)
* PCB 138	
* PCB 153	
* PCB 170	
* PCB 180	
* PCB 187	
* PCB 188	
* PCB 195	
* PCB 201	
* PCB 206	
* PCB 209	
* Total PCB	

QA02B - Pesticides - Organochlorine (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* a, ß, d-BHC (Benzene hexachloride)	
* Alachlor	
* Aldrin	
* Benfluralin	
* Bifenox	
* Boscalid	
* Bromacil	
* Captafol	
* Captan	
* Chlordane (total)	
* Chlorfenapyr	
* Chlorobenzilate	
* Chlorothalonil	
* Cyanazine	
* Dacthal (Chlorthal)	
* DDD	
* DDE	
* DDT	
* Dichlobenil	
* Dichlone	
* Dicloran	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

	Result
* Dicofol, p,p-	(b) (4)
* Dieldrin	
* Endosulfan, alpha-	
* Endosulfan, beta-	
* Endosulfan-sulfate	
* Endrin	
* Ethalfluralin	
* Fenhexamid	
* Folpet	
* HCB (Hexachlorbenzene)	
* Heptachlor	
* Heptachlor epoxide	
* Indoxacarb	
* Iprodione	
* Lindane (gamma-HCH)	
* Linuron	
* Methoxychlor	
* Metribuzin	
* Mirex	
* Myclobutanil	
* Oxadiazon	
* Oxyfluorfen	
* Pendimethalin	
* Pentachloroaniline	
* Pentachloronitrobenzene (PCNB)	
* Perthane	
* Procymidone	
* Profluralin	
* Pronamide	
* Propanil	
* Pyraflufen-ethyl	
* Pyrethrins	
* Tetradifon	
* Tridimephon	
* Trifloxystrobin	
* Triflumizole	

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(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

Result

(b) (4)

* Trifluralin
* Vegadex
* Vinclozolin

QA02C - Pesticides - Pyrethroids (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Bifenthrin
* Cyfluthrin
* Cyhalothrin lambda-
* Cypermethrin
* Deltamethrin
* Esfenvalerate
* Fenpropathrin
* Fluvalinate
* Permethrin
* Tralomethrin

QA02D - Pesticides - Organophosphorus (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

(b) (4)

* Azinphos-methyl
* Carbophenothion
* Chlorfenvinphos
* Chlorpyrifos (-ethyl)
* Chlorpyrifos-methyl
* Coumaphos
* Diazinon
* Dibrom (Naled)
* Dicrotophos
* Dimethoate
* Disulfoton
* EPN
* Ethion
* Ethoprop
* Fenamiphos
* Fenitrothion
* Fenthion

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(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
* Fonofos	(b) (4)
* Isofenphos	
* Malathion	
* Methyl Parathion	
* Mevinphos	
* Omethoate	
* Parathion	
* Phorate	
* Phosalone	
* Phosmet	
* Phosphamidon	
* Pirimiphos-methyl	
* Profenofos	
* Propetamphos	
* Ronnel	
* Sulprofos	
* Tetrachlorvinphos	
* Thionazin	

QA22A - Pesticides (LC-MSMS)
Completion Date: 07/26/2017 **Method:** Internal LC-MS/MS

* Aldicarb	
* Buprofezin	
* Carbaryl	
* Carfentrazone-ethyl	
* Chlorantraniliprole	
* Clethodim	
* Cyproconazole	
* Diuron	
* Flusilazole	
* Indaziflam	
* Methidathion	
* Methomyl	
* Oryzalin	
* Pendimethalin	
* Penthiopyrad	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results

* Propargite
* Pyriproxyfen
* Simazine
* Spinosad

UMMFL - Aerobic Plate Count - AOAC 966.23
Completion Date: 07/27/2017 **Method:** AOAC 966.23
* Aerobic Plate Count

QD034 - Calories by Bomb Calorimeter
Completion Date: 08/03/2017 **Method:** Parr Instruments
* Calories By Bomb Calorimeter

UM73J - Coliforms - AOAC 991.14
Completion Date: 07/27/2017 **Method:** AOAC 991.14
* Total Coliforms

UM73J - Escherichia coli - AOAC 991.14
Completion Date: 07/27/2017 **Method:** AOAC 991.14
* E. coli

UM4BV - Moulds - BAM Chapter 18
Completion Date: 07/27/2017 **Method:** FDA BAM Chapter 18
* Mold

UM4BV - Yeast - BAM Chapter 18
Completion Date: 07/27/2017 **Method:** FDA BAM Chapter 18
* Yeast

UMAEK - Salmonella - AOAC 2003.09
Completion Date: 07/27/2017 **Method:** AOAC 2003.09
* Salmonella

UMJR7 - Staphylococcus aureus - AOAC 2003.07
Completion Date: 07/27/2017 **Method:** AOAC 2003.07
* Staphylococcus aureus

Result

[redacted] (b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
TK198 - Total Fluorine by Ion Chromatography **Completion Date:** 08/10/2017 **Method:** EPA 9056 1994 (SW-846)	(b) (4)
* Fluorine (F)	

**This is not covered by our current A2LA accreditation.*

Respectfully Submitted

(b) (4)

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Uncertainty can be obtained upon request.

ACCREDITED

(b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

(b) (4)

Person in charge (b) (4), (b) (6)
Client Support

DSM Nutritional Products (Martek)
(b) (4), (b) (6)

Reporting Date 08/15/2017

(b) (4)

REPORT OF ANALYSIS

Sample Code (b) (4)

Sample Description (b) (4)
Client Sample Code
Sample Reference

Reception Date 07/21/2017
Reception Temperature -33.0 (Celsius)
Sample Condition Acceptable
Purchase Order 4701471730

Test Results	Result
QA383 - Moisture & Volatiles (Air Oven 130C) **Completion Date:** 08/10/2017 **Method:** AOCS Ca 2c-25 * Moisture & Volatiles	(b) (4)
QD298 - Protein - Kjeltec **Completion Date:** 08/02/2017 **Method:** AOAC 2001.11 * Protein- Kjeltec	
QA274 - Crude Fat / Oil (Pet ether extr - SBM) **Completion Date:** 07/27/2017 **Method:** AOCS Ba 3-38 Oil (Fat)	
QA13A - Ash **Completion Date:** 07/26/2017 **Method:** AOAC 923.03 / 32.1.05 16th Ed. * Ash	
QD230 - Fiber, Total Dietary **Completion Date:** 08/02/2017 **Method:** AOAC 991.43 * Total Dietary Fiber	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

Client Sample Code: VY00015465

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results	Result
QA106 - Aluminum (ICP-AES)	
Completion Date: 07/31/2017 **Method:** J.AOAC 92, 1484-1518 (2009)	[redacted] (b) (4)
* Aluminum (Al)	
QA00P - Calcium NLEA	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Calcium (Ca)	
QA00G - Chromium (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 986.15	
Chromium (Cr)	
QA417 - Lead (ICP-MS)	
Completion Date: 07/31/2017 **Method:** AOAC 2013.06	
Lead (Pb)	
QA003 - Manganese (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Manganese (Mn)	
QA00D - Phosphorus (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Phosphorus (P)	
QA004 - Potassium (ICP-AES)	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Potassium (K)	
QA00Q - Sodium NLEA	
Completion Date: 07/31/2017 **Method:** AOAC 2011.14	
* Sodium (Na)	
QQ182 - Total Vitamin A	
Completion Date: 08/02/2017 **Method:** AOAC 974.29 Mod.	
* Retinol	
* ß-carotene	
* Total Vitamin A	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results **Result**

QQ188 - Vitamin E-Tocopherol Profile (AOAC, Most Matrices)
Completion Date: 08/02/2017 **Method:** AOAC 971.30 with HPLC quantification mod.

* Alpha-Tocopherol
* Beta-Tocopherol
* Delta-Tocopherol
* Gamma-Tocopherol
* Total Vitamin E (Tocopherols)

[redacted] (b) (4)

QA202 - Calories from Fat
Completion Date: 08/10/2017 **Method:**

* Calories from fat

QA204 - Carbohydrate
Completion Date: 08/10/2017 **Method:**

* Carbohydrates (calculated)

QA052 - Polychlorinated Biphenyls (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Sum Non-Dioxin-Like PCBs (28+52+101+138+153+180)
* PCB 1
* PCB 8
* PCB 18
* PCB 28
* PCB 29
* PCB 44
* PCB 50
* PCB 52
* PCB 66
* PCB 77
* PCB 87
* PCB 101
* PCB 104
* PCB 105
* PCB 118
* PCB 126

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[redacted] (b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
* PCB 128	(b) (4)
* PCB 138	
* PCB 153	
* PCB 170	
* PCB 180	
* PCB 187	
* PCB 188	
* PCB 195	
* PCB 201	
* PCB 206	
* PCB 209	
* Total PCB	

QA02B - Pesticides - Organochlorine (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* a, ß, d-BHC (Benzene hexachloride)	
* Alachlor	
* Aldrin	
* Benfluralin	
* Bifenox	
* Boscalid	
* Bromacil	
* Captafol	
* Captan	
* Chlordane (total)	
* Chlorfenapyr	
* Chlorobenzilate	
* Chlorothalonil	
* Cyanazine	
* Dacthal (Chlorthal)	
* DDD	
* DDE	
* DDT	
* Dichlobenil	
* Dichlone	
* Dicloran	

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(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

	Result
* Dicofol, p,p-	(b) (4)
* Dieldrin	
* Endosulfan, alpha-	
* Endosulfan, beta-	
* Endosulfan-sulfate	
* Endrin	
* Ethalfluralin	
* Fenhexamid	
* Folpet	
* HCB (Hexachlorbenzene)	
* Heptachlor	
* Heptachlor epoxide	
* Indoxacarb	
* Iprodione	
* Lindane (gamma-HCH)	
* Linuron	
* Methoxychlor	
* Metribuzin	
* Mirex	
* Myclobutanil	
* Oxadiazon	
* Oxyfluorfen	
* Pendimethalin	
* Pentachloroaniline	
* Pentachloronitrobenzene (PCNB)	
* Perthane	
* Procymidone	
* Profluralin	
* Pronamide	
* Propanil	
* Pyraflufen-ethyl	
* Pyrethrins	
* Tetradifon	
* Tridimephon	
* Trifloxystrobin	
* Triflumizole	

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(b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results

Result

[redacted] (b) (4)

* Trifluralin
* Vegadex
* Vinclozolin

QA02C - Pesticides - Pyrethroids (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Bifenthrin
* Cyfluthrin
* Cyhalothrin lambda-
* Cypermethrin
* Deltamethrin
* Esfenvalerate
* Fenpropathrin
* Fluvalinate
* Permethrin
* Tralomethrin

QA02D - Pesticides - Organophosphorus (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Azinphos-methyl
* Carbophenothion
* Chlorfenvinphos
* Chlorpyrifos (-ethyl)
* Chlorpyrifos-methyl
* Coumaphos
* Diazinon
* Dibrom (Naled)
* Dicrotophos
* Dimethoate
* Disulfoton
* EPN
* Ethion
* Ethoprop
* Fenamiphos
* Fenitrothion
* Fenthion

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

[redacted] (b) (4)

REPORT OF ANALYSIS

Test Results

* Fonofos
* Isofenphos
* Malathion
* Methyl Parathion
* Mevinphos
* Omethoate
* Parathion
* Phorate
* Phosalone
* Phosmet
* Phosphamidon
* Pirimiphos-methyl
* Profenofos
* Propetamphos
* Ronnel
* Sulprofos
* Tetrachlorvinphos
* Thionazin

QA22A - Pesticides (LC-MSMS)
Completion Date: 07/26/2017 **Method:** Internal LC-MS/MS

* Aldicarb
* Buprofezin
* Carbaryl
* Carfentrazone-ethyl
* Chlorantraniliprole
* Clethodim
* Cyproconazole
* Diuron
* Flusilazole
* Indaziflam
* Methidathion
* Methomyl
* Oryzalin
* Pendimethalin
* Penthiopyrad

Result

[redacted] (b) (4)

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[redacted] (b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

Result

(b) (4)

* Propargite
* Pyriproxyfen
* Simazine
* Spinosad

UMMFL - Aerobic Plate Count - AOAC 966.23
Completion Date: 08/15/2017 **Method:** AOAC 966.23
* Aerobic Plate Count

QD034 - Calories by Bomb Calorimeter
Completion Date: 08/02/2017 **Method:** Parr Instruments
* Calories By Bomb Calorimeter

UM73J - Coliforms - AOAC 991.14
Completion Date: 08/15/2017 **Method:** AOAC 991.14
* Total Coliforms

UM73J - Escherichia coli - AOAC 991.14
Completion Date: 08/15/2017 **Method:** AOAC 991.14
* E. coli

UM4BV - Moulds - BAM Chapter 18
Completion Date: 08/15/2017 **Method:** FDA BAM Chapter 18
* Mold

UM4BV - Yeast - BAM Chapter 18
Completion Date: 08/15/2017 **Method:** FDA BAM Chapter 18
* Yeast

UMAEK - Salmonella - AOAC 2003.09
Completion Date: 08/15/2017 **Method:** AOAC 2003.09
* Salmonella

UMJR7 - Staphylococcus aureus - AOAC 2003.07
Completion Date: 08/15/2017 **Method:** AOAC 2003.07
* Staphylococcus aureus

(b) (4)

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

Result

TK198 - Total Fluorine by Ion Chromatography
Completion Date: 08/10/2017 **Method:** EPA 9056 1994 (SW-846)
* Fluorine (F)

(b) (4)

**This is not covered by our current A2LA accreditation.*

Respectfully Submitted,

(b) (4)

(b) (4)

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Uncertainty can be obtained upon request.

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(b) (4)

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(b) (4)

(b) (4)

Person in charge
Client Support

(b) (4), (b) (6)

DSM Nutritional Products (Martek)

(b) (4), (b) (6)

Reporting Date 08/10/2017

(b) (4)

REPORT OF ANALYSIS

Sample Code (b) (4)

Sample Description (b) (4)
Client Sample Code
Sample Reference

Reception Date 07/21/2017
Reception Temperature -33.0 (Celsius)
Sample Condition Acceptable
Purchase Order 4701471730

Test Results

Result

QA383 - Moisture & Volatiles (Air Oven 130C)
Completion Date: 08/10/2017 **Method:** AOCS Ca 2c-25
* Moisture & Volatiles

QD298 - Protein - Kjeltec
Completion Date: 08/03/2017 **Method:** AOAC 2001.11
* Protein- Kjeltec

QA274 - Crude Fat / Oil (Pet ether extr - SBM)
Completion Date: 07/27/2017 **Method:** AOCS Ba 3-38
Oil (Fat)

QA13A - Ash
Completion Date: 07/26/2017 **Method:** AOAC 923.03 / 32.1.05 16th Ed.
* Ash

QD230 - Fiber, Total Dietary
Completion Date: 08/03/2017 **Method:** AOAC 991.43
* Total Dietary Fiber

(b) (4)

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(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
QA106 - Aluminum (ICP-AES) **Completion Date:** 07/31/2017 **Method:** J.AOAC 92, 1484-1518 (2009) * Aluminum (Al)	(b) (4)
QA00P - Calcium NLEA **Completion Date:** 07/31/2017 **Method:** AOAC 2011.14 * Calcium (Ca)	
QA00G - Chromium (ICP-AES) **Completion Date:** 07/31/2017 **Method:** AOAC 986.15 Chromium (Cr)	
QA417 - Lead (ICP-MS) **Completion Date:** 07/31/2017 **Method:** AOAC 2013.06 Lead (Pb)	
QA003 - Manganese (ICP-AES) **Completion Date:** 07/31/2017 **Method:** AOAC 2011.14 * Manganese (Mn)	
QA00D - Phosphorus (ICP-AES) **Completion Date:** 07/31/2017 **Method:** AOAC 2011.14 * Phosphorus (P)	
QA004 - Potassium (ICP-AES) **Completion Date:** 07/31/2017 **Method:** AOAC 2011.14 * Potassium (K)	
QA00Q - Sodium NLEA **Completion Date:** 07/31/2017 **Method:** AOAC 2011.14 * Sodium (Na)	
QQ182 - Total Vitamin A **Completion Date:** 08/03/2017 **Method:** AOAC 974.29 Mod. * Retinol * ß-carotene * Total Vitamin A	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result

QQ188 - Vitamin E-Tocopherol Profile (AOAC, Most Matrices)
Completion Date: 08/03/2017 **Method:** AOAC 971.30 with HPLC quantification mod.

(b) (4)

* Alpha-Tocopherol
* Beta-Tocopherol
* Delta-Tocopherol
* Gamma-Tocopherol
* Total Vitamin E (Tocopherols)

QA202 - Calories from Fat
Completion Date: 08/10/2017 **Method:**
* Calories from fat

QA204 - Carbohydrate
Completion Date: 08/10/2017 **Method:**
* Carbohydrates (calculated)

QA052 - Polychlorinated Biphenyls (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34
* Sum Non-Dioxin-Like PCBs (28+52+101+138+153+180)
* PCB 1
* PCB 8
* PCB 18
* PCB 28
* PCB 29
* PCB 44
* PCB 50
* PCB 52
* PCB 66
* PCB 77
* PCB 87
* PCB 101
* PCB 104
* PCB 105
* PCB 118
* PCB 126

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

(b) (4)

[redacted]

[redacted]

[redacted]

REPORT OF ANALYSIS

Test Results	Result
* PCB 128	[redacted]
* PCB 138	
* PCB 153	
* PCB 170	
* PCB 180	
* PCB 187	
* PCB 188	
* PCB 195	
* PCB 201	
* PCB 206	
* PCB 209	
* Total PCB	

QA02B - Pesticides - Organochlorine (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* a, ß, d-BHC (Benzene hexachloride)	
* Alachlor	
* Aldrin	
* Benfluralin	
* Bifenox	
* Boscalid	
* Bromacil	
* Captafol	
* Captan	
* Chlordane (total)	
* Chlorfenapyr	
* Chlorobenzilate	
* Chlorothalonil	
* Cyanazine	
* Dacthal (Chlorthal)	
* DDD	
* DDE	
* DDT	
* Dichlobenil	
* Dichlone	
* Dicloran	

Any opinions/interpretations expressed on the Report of Analysis are outside the scope of this lab's A2LA accreditation.

[redacted]

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
* Dicofol, p,p-	(b) (4)
* Dieldrin	
* Endosulfan, alpha-	
* Endosulfan, beta-	
* Endosulfan-sulfate	
* Endrin	
* Ethalfluralin	
* Fenhexamid	
* Folpet	
* HCB (Hexachlorbenzene)	
* Heptachlor	
* Heptachlor epoxide	
* Indoxacarb	
* Iprodione	
* Lindane (gamma-HCH)	
* Linuron	
* Methoxychlor	
* Metribuzin	
* Mirex	
* Myclobutanil	
* Oxadiazon	
* Oxyfluorfen	
* Pendimethalin	
* Pentachloroaniline	
* Pentachloronitrobenzene (PCNB)	
* Perthane	
* Procymidone	
* Profluralin	
* Pronamide	
* Propanil	
* Pyraflufen-ethyl	
* Pyrethrins	
* Tetradifon	
* Tridimephon	
* Trifloxystrobin	
* Triflumizole	

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(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

(b) (4)

Test Results

* Trifluralin
* Vegadex
* Vinclozolin

QA02C - Pesticides - Pyrethroids (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Bifenthrin
* Cyfluthrin
* Cyhalothrin lambda-
* Cypermethrin
* Deltamethrin
* Esfenvalerate
* Fenpropathrin
* Fluvalinate
* Permethrin
* Tralomethrin

QA02D - Pesticides - Organophosphorus (Oils & Fats)
Completion Date: 07/27/2017 **Method:** ASU L00.00-34

* Azinphos-methyl
* Carbophenothion
* Chlorfenvinphos
* Chlorpyrifos (-ethyl)
* Chlorpyrifos-methyl
* Coumaphos
* Diazinon
* Dibrom (Naled)
* Dicrotophos
* Dimethoate
* Disulfoton
* EPN
* Ethion
* Ethoprop
* Fenamiphos
* Fenitrothion
* Fenthion

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(b) (4)

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(b) (4)

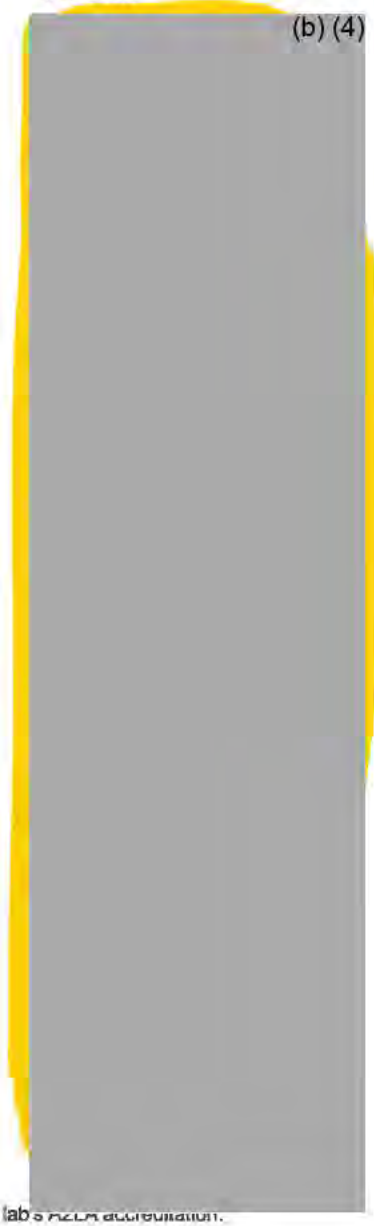
(b) (4)







REPORT OF ANALYSIS



Test Results	Result
* Fonofos	(b) (4)
* Isofenphos	
* Malathion	
* Methyl Parathion	
* Mevinphos	
* Omethoate	
* Parathion	
* Phorate	
* Phosalone	
* Phosmet	
* Phosphamidon	
* Pirimiphos-methyl	
* Profenofos	
* Propetamphos	
* Ronnel	
* Sulprofos	
* Tetrachlorvinphos	
* Thionazin	

QA22A - Pesticides (LC-MSMS)
Completion Date: 07/26/2017 **Method:** Internal LC-MS/MS

* Aldicarb
* Buprofezin
* Carbaryl
* Carfentrazone-ethyl
* Chlorantraniliprole
* Clethodim
* Cyproconazole
* Diuron
* Flusilazole
* Indaziflam
* Methidathion
* Methomyl
* Oryzalin
* Pendimethalin
* Penthiopyrad

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(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results	Result
* Propargite	(b) (4)
* Pyriproxyfen	
* Simazine	
* Spinosad	

UMMFL - Aerobic Plate Count - AOAC 966.23
Completion Date: 07/27/2017 **Method:** AOAC 966.23
* Aerobic Plate Count

QD034 - Calories by Bomb Calorimeter
Completion Date: 08/03/2017 **Method:** Parr Instruments
* Calories By Bomb Calorimeter

UM73J - Coliforms - AOAC 991.14
Completion Date: 07/27/2017 **Method:** AOAC 991.14
* Total Coliforms

UM73J - Escherichia coli - AOAC 991.14
Completion Date: 07/27/2017 **Method:** AOAC 991.14
* E. coli

UM4BV - Moulds - BAM Chapter 18
Completion Date: 07/27/2017 **Method:** FDA BAM Chapter 18
* Mold

UM4BV - Yeast - BAM Chapter 18
Completion Date: 07/27/2017 **Method:** FDA BAM Chapter 18
* Yeast

UMAEK - Salmonella - AOAC 2003.09
Completion Date: 07/27/2017 **Method:** AOAC 2003.09
* Salmonella

UMJR7 - Staphylococcus aureus - AOAC 2003.07
Completion Date: 07/27/2017 **Method:** AOAC 2003.07
* Staphylococcus aureus

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(b) (4)

(b) (4)

(b) (4)

(b) (4)

REPORT OF ANALYSIS

Test Results

Result

TK198 - Total Fluorine by Ion Chromatography
Completion Date: 08/10/2017 **Method:** EPA 9056 1994 (SW-846)
* Fluorine (F)

(b) (4)

**This is not covered by our current A2LA accreditation.*

Respectfully Submitted,

(b) (4)

Results shown in this report relate solely to the item submitted for analysis.
Uncertainty can be obtained upon request.

(b) (4)

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(b) (4)

Annex 11
Dog GLG Final Report



CONFIDENTIAL

FINAL REPORT

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies





Sponsor:
DSM Nutritional Products AG
6480 Dobbin Road
Columbia, MD
USA 21045

Issue Date: October 12, 2018

This document is confidential and should not be disseminated to entities or individuals, without the written approval of the Sponsor.

GENERAL INFORMATION

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Study Monitor and Sponsor's Representative (b) (4), (b) (6) PhD, DABT
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DSM Nutritional Products

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Principal Investigators (Test Sites – Sponsor Designate)

Diet analysis (primary samples) (b) (4), (b) (6)

Diet analysis (retention samples) (b) (4), (b) (6)

Bioanalysis

Statistical Analysis of Bioanalysis Data

Interpretation of Bioanalysis Data and of Diet Analysis Data

(b) (4), (b) (6)



(b) (4)

COMPLIANCE STATEMENT

This study was conducted according to the Standard Operating Procedures of (b) (4) (b) (4) This study did not comply with Good Laboratory Practice regulations.

(b) (4)

October 12, 2018
Date

The study described in this report was peer reviewed and approved by the undersigned:

(b) (4)

October 12, 2018
Date

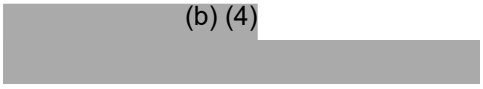
CONTRIBUTORS:



Team Leaders:



Pharmacy:



Veterinary Services:



Pathology:



Statistics and Report Production:



TABLE OF CONTENTS

GENERAL INFORMATION 2
COMPLIANCE STATEMENT 4
TABLE OF CONTENTS 6
INDEX TO SUMMARY TABLES 10
INDEX TO APPENDICES 12
INDEX TO FIGURES 15
1 SUMMARY 19
2 OBJECTIVE 21
3 EXPERIMENTAL DESIGN 21
3.1 Study Schedule 21
3.2 Test Methods and/or Guidelines 22
3.3 Justification for Dose Levels 22
3.4 Reason for Choice of Route of Administration 22
3.5 Reason for Choice of Test System 22
3.6 Justification for Numbers of Animals Selected 22
4 STUDY DEVIATIONS 22
5 TEST ITEM INFORMATION 23
5.1 Preparation of Dietary Admixtures 24
5.2 Stability of Test Item 25
5.3 Analysis of Diets 25
5.4 Archive Sampling and Disposition of Diets 25
5.5 Administration of Diets 26
6 TEST SYSTEM 27
6.1 Health Status 27
6.2 Animal Assignment and Blinding Procedure 27
6.3 Animal Replacement 28
6.4 Identification 29
6.5 Housing 29

6.6 Room Environment 30
6.7 Diet/Water 31
6.8 Acclimation/Socialization 31
7 IN-LIFE OBSERVATIONS 32
7.1 Mortality 32
7.2 Clinical Observations 32
7.3 Medical treatments 33
7.4 Body Weights 33
7.5 Food Consumption 34
7.6 Parturition Observations 35
7.7 Litter Size 35
7.8 External Sex Determination Puppies (F_1 Generation) 36
7.9 Standardization of Litter (Culling) 36
7.10 Weaning 36
7.11 Clinical Pathology 36
7.12 Buccal Mucosal Bleeding Time 38
7.13 Bioanalysis 38
7.14 Remaining Sample Disposal Policy Statement 39
8 TERMINAL PROCEDURES 39
8.1 Histopathology 39
9 DATA HANDLING AND REPORTING 40
9.1 Data Capture 40
9.2 Data Analysis 40
9.3 Archives 45
9.4 Multisite 45
9.5 Standard Operating Procedures 46
10 RESULTS 47
10.1 Analysis of Diets 47
10.1.1 Peroxide Value (PV) Determination 48
10.2 RESULTS F_0 Generation 48

10.2.1 Mortality F_0 Generation 48
10.3 Clinical Observations – F_0 Generation – Gestation and Lactation Periods 49
10.4 Body Temperature – F_0 Generation – Gestation and Lactation Periods 49
10.5 Heart Rate – F_0 Generation – Gestation and Lactation Periods 49
10.6 Respiratory Rate – F_0 Generation – Gestation and Lactation Periods 50
10.7 Body Weight – F_0 – Gestation and Lactation Periods 50
10.8 Food Consumption – F_0 Generation – Gestation and Lactation Periods 50
10.9 Achieved AOCED Intake – F_0 Generation – Gestation and Lactation Periods 50
10.10 Clinical Pathology – F_0 Generation – Gestation and Lactation Periods 51
10.10.1 Hematology – F_0 Generation..... 51
10.10.2 Clinical Chemistry – F_0 Generation 51
10.11 Maternal Performance – F_0 Generation 51
10.12 Bioanalysis – F_0 Generation – Gestation and Lactation Periods 51
10.13 RESULTS – F_1 Generation – Lactation Period (PPD0 to 56) 53
10.13.1 Puppy Viability 53
10.14 Clinical Observations – F_1 Generation – Lactation Period (PPD0 to 56)..... 54
10.15 Body Weight – F_1 Generation – Lactation Period (PPD0 to 56) 54
10.16 Head Circumference – F_1 Generation – Lactation Period (PPD0 to 56) 55
10.17 Height – F_1 Generation – Lactation Period (PPD0 to 56)..... 55
10.18 RESULTS F_1 – Growth Phase..... 55
10.18.1 Mortality F_1 Generation – Growth Phase (PPD56 to PPD238) 55
10.19 Clinical Observations – F_1 Generation – Growth Phase (PPD56 to PPD238)..... 55
10.20 Body Temperature – F_1 Generation – Growth Phase (PPD56 to PPD238) 56
10.21 Heart Rate – F_1 Generation – Growth Phase (PPD56 to PPD238) 56
10.22 Respiratory Rate – F_1 Generation – Growth Phase (PPD56 to PPD238) 56
10.23 Body Weight – F_1 Generation – Growth Phase (PPD56 to PPD238)..... 56
10.24 Head Circumference – F_1 Generation – Growth Phase (PPD56 to PPD238) 57
10.25 Height – F_1 Generation – Growth Phase (PPD56 to PPD238) 57
10.26 Food Consumption – F_1 Generation – Growth Phase (PPD56 to PPD238)..... 57
10.27 Achieved AOCED Intake – F_1 Generation – Growth Phase (PPD56 to PPD238) 58

10.28 Clinical Pathology – F_1 Generation – Growth Phase (PPD56 to PPD238) 58
10.28.1 Hematology and Coagulation – F_1 Generation 58
10.28.2 Clinical Chemistry – F_1 Generation 59
10.28.3 Buccal Mucosal Bleeding Time – F_1 Generation 59
10.28.4 Urinalysis – F_1 Generation 60
10.29 Bioanalysis – F_1 Generation – Growth Phase (PPD56 to PPD238) 60
11 CONCLUSION 62
12 REFERENCES 63
13 DEVIATIONS 64

INDEX TO SUMMARY TABLES

F_0 Generation

Table No. 1	Summary of Clinical Observations – Pre-Treatment and Gestation	180
Table No. 2	Summary of Clinical Observations – Lactation	188
Table No. 3	Body Temperature Summary – Pre-Treatment and Gestation	194
Table No. 4	Body Temperature Summary – Lactation	197
Table No. 5	Heart Rate Summary – Pre-Treatment and Gestation	199
Table No. 6	Heart Rate Summary – Lactation	202
Table No. 7	Respiratory Rate Summary – Pre-Treatment and Gestation	204
Table No. 8	Respiratory Rate Summary – Lactation	207
Table No. 9	Body Weight Summary – Pre-Treatment and Gestation	209
Table No. 10	Body Weight Summary – Lactation	212
Table No. 11	Body Weight Change Summary – Pre-Treatment and Gestation	214
Table No. 12	Body Weight Change Summary – Lactation	217
Table No. 13	Food Consumption Summary – Pre-Treatment and Gestation	219
Table No. 14	Food Consumption Summary – Lactation	233
Table No. 15	Hematology Summary – Pre-Treatment	242
Table No. 16	Hematology Summary – Lactation	245
Table No. 17	Clinical Chemistry Summary – Pre-Treatment	248
Table No. 18	Clinical Chemistry Summary – Lactation	251
Table No. 19	Maternal	254

F_1 Puppies – Pre-Weaning

Table No. 20	Summary of Clinical Observations – Puppies	256
Table No. 21	Group Litter Mean Body Weight – Puppies	258
Table No. 22	Group Litter Mean Body Weight Change – Puppies	267
Table No. 23	Group Mean Body Weight – Puppies	276
Table No. 24	Group Litter Body Weight Change – Puppies	280
Table No. 25	Group Litter Mean Head Circumference – Puppies	284

Table No. 26 Group Litter Mean Head Circumference Change – Puppies 290
Table No. 27 Group Mean Head Circumference – Puppies 298
Table No. 28 Group Mean Head Circumference Change – Puppies 300
Table No. 29 Group Litter Mean Height – Puppies 302
Table No. 30 Group Litter Mean Height Change – Puppies 308
Table No. 31 Group Mean Height – Puppies 314
Table No. 32 Group Mean Height Change – Puppies 316

F_1 Puppies – Post-Weaning

Table No. 33 Summary of Clinical Observations 319
Table No. 34 Body Weight Summary 330
Table No. 35 Body Weight Change Summary 339
Table No. 36 Head Circumference Summary 351
Table No. 37 Head Circumference Change Summary 360
Table No. 38 Height Summary 369
Table No. 39 Height Change Summary 378
Table No. 40 Food Consumption Summary 387
Table No. 41 Body Temperature Summary 397
Table No. 42 Heart Rate Summary 403
Table No. 43 Respiratory Rate Summary 407
Table No. 44 Hematology Summary 411
Table No. 45 Clinical Chemistry Summary 456
Table No. 46 Coagulation Summary 501
Table No. 47 Buccal Mucosal Bleeding Time Summary 510
Table No. 48 Urinalysis Summary 511
Table No. 49 Achieved AOCED Intake Summary (F_0 and F_1 Generations) 520

INDEX TO APPENDICES

Appendix No. 1	Certificates of Analysis	536
Appendix No. 2	Analytical Chemistry Report	557
Appendix No. 3	Experimental Design	603
Appendix No. 4	Medical Treatments	605
F_0 Generation		
Appendix No. 5	Clinical Observations – Pre-Treatment and Gestation	608
Appendix No. 6	Clinical Observations with Site by Animal – Lactation	672
Appendix No. 7	Body Temperature – Pre-Treatment and Gestation	697
Appendix No. 8	Body Temperature – Lactation	701
Appendix No. 9	Heart Rate – Pre-Treatment and Gestation	704
Appendix No. 10	Heart Rate – Lactation	707
Appendix No. 11	Respiratory Rate – Pre-Treatment and Gestation	710
Appendix No. 12	Respiratory Rate – Lactation	713
Appendix No. 13	Body Weight – Pre-Treatment and Gestation	716
Appendix No. 14	Body Weight – Lactation	719
Appendix No. 15	Body Weight Change – Pre-Treatment and Gestation	722
Appendix No. 16	Body Weight Change – Lactation	726
Appendix No. 17	Food Consumption – Pre-Treatment and Gestation	729
Appendix No. 18	Food Consumption – Lactation	741
Appendix No. 19	Clinical Pathology Abbreviations, Methods and Units	752
Appendix No. 20	Hematology – Pre-Treatment	759
Appendix No. 21	Hematology – Lactation (Weaning)	767
Appendix No. 22	Clinical Chemistry – Pre-Treatment	775
Appendix No. 23	Clinical Chemistry – Lactation (Weaning)	783
Appendix No. 24	Maternal	790

F_1 Puppies – Pre-Weaning

Appendix No. 25	Litter Size	794
Appendix No. 26	Clinical Observations with Site by Animal – Puppies	803
Appendix No. 27	Body Weight by Litter – Puppies	817
Appendix No. 28	Litter Mean Body Weight – Puppies	834
Appendix No. 29	Body Weight Change by Litter – Puppies	847
Appendix No. 30	Litter Mean Body Weight Change – Puppies	860
Appendix No. 31	Body Weight – Puppies	873
Appendix No. 32	Body Weight Change – Puppies	890
Appendix No. 33	Head Circumference by Litter – Puppies	907
Appendix No. 34	Litter Mean Head Circumference – Puppies	916
Appendix No. 35	Head Circumference Change by Litter – Puppies	925
Appendix No. 36	Litter Mean Head Circumference Change – Puppies	938
Appendix No. 37	Head Circumference – Puppies	951
Appendix No. 38	Head Circumference Change– Puppies	956
Appendix No. 39	Height by Litter – Puppies	961
Appendix No. 40	Litter Mean Height – Puppies	970
Appendix No. 41	Height Change by Litter – Puppies	979
Appendix No. 42	Litter Mean Height Change – Puppies	988
Appendix No. 43	Height – Puppies	997
Appendix No. 44	Height Change – Puppies	1002

F_1 Puppies – Post-Weaning

Appendix No. 45	Clinical Observations with Site by Animal	1008
Appendix No. 46	Body Weight	1197
Appendix No. 47	Body Weight Change	1204
Appendix No. 48	Food Consumption	1213
Appendix No. 49	Head Circumference	1271
Appendix No. 50	Head Circumference Change	1287
Appendix No. 51	Height	1297
Appendix No. 52	Height Change	1313
Appendix No. 53	Body Temperature	1323
Appendix No. 54	Heart Rate	1326
Appendix No. 55	Respiratory Rate	1329
Appendix No. 56	Hematology	1332
Appendix No. 57	Clinical Chemistry	1353
Appendix No. 58	Coagulation	1366
Appendix No. 59	Buccal Mucosal Bleeding Time	1369
Appendix No. 60	Urinalysis	1372
Appendix No. 61	Clinical Pathology Report	1381
Appendix No. 62	Bioanalytical Report	1387
Appendix No. 63	Achieved AOCED Intake (F_0 and F_1 Generations)	1425
Appendix No. 64	Statistical Report	1441
Appendix No. 65	Study Plan, Study Plan Amendments	1473
Appendix No. 66	Facility Diagram, Orientation, Ventilation, Lighting	1551

INDEX TO FIGURES

F_0 Generation

Figure No. 1	Body Temperature – Gestation	67
Figure No. 2	Body Temperature Summary – Gestation	68
Figure No. 3	Heart Rate – Gestation	69
Figure No. 4	Heart Rate Summary – Gestation	70
Figure No. 5	Respiratory Rate – Gestation	71
Figure No. 6	Respiratory Rate Summary – Gestation	72
Figure No. 7	Body Weight – Gestation	73
Figure No. 8	Body Weight Summary – Gestation	74
Figure No. 9	Food Consumption – Gestation	75
Figure No. 10	Food Consumption Summary – Gestation	76
Figure No. 11	Body Temperature – Lactation	77
Figure No. 12	Body Temperature Summary – Lactation	78
Figure No. 13	Heart Rate – Lactation	79
Figure No. 14	Heart Rate Summary – Lactation	80
Figure No. 15	Respiratory Rate – Lactation	81
Figure No. 16	Respiratory Rate – Lactation	82
Figure No. 17	Body Weight – Lactation	83
Figure No. 18	Body Weight Summary – Lactation	84
Figure No. 19	Food Consumption – Lactation	85
Figure No. 20	Food Consumption Summary – Lactation	86
Figure No. 21	Achieved AOCED Intake – Lactation PPD 0 to 35	87
Figure No. 22	Achieved AOCED Intake Summary – Lactation PPD0-35	88

F_0 and F_1 Generations – Lactation

Figure No. 23	Achieved AOCED Intake – Lactation PPD 35 to 55	90
Figure No. 24	Achieved AOCED Intake Summary – Lactation PPD 35-55	91

F_1 Puppies – Pre-Weaning

Figure No. 25	Body Weight - Males	93
Figure No. 26	Body Weight - Females	94
Figure No. 27	Body Weight - Combined	95
Figure No. 28	Body Weight Summary - Males	96
Figure No. 29	Body Weight Summary - Females	97
Figure No. 30	Body Weight Summary - Combined	98
Figure No. 31	Body Weight Change - Males	99
Figure No. 32	Body Weight Change - Females	100
Figure No. 33	Body Weight Change - Combined	101
Figure No. 34	Body Weight Change Summary - Males	102
Figure No. 35	Body Weight Change Summary - Females	103
Figure No. 36	Body Weight Change Summary - Combined	104
Figure No. 37	Head Circumference - Males	105
Figure No. 38	Head Circumference - Females	106
Figure No. 39	Head Circumference - Combined	107
Figure No. 40	Head Circumference Summary - Males	108
Figure No. 41	Head Circumference Summary - Females	109
Figure No. 42	Head Circumference Summary - Combined	110
Figure No. 43	Head Circumference Change - Males	111
Figure No. 44	Head Circumference Change - Females	112
Figure No. 45	Head Circumference Change - Combined	113
Figure No. 46	Head Circumference Change Summary - Males	114
Figure No. 47	Head Circumference Change Summary - Females	115
Figure No. 48	Head Circumference Change Summary - Combined	116
Figure No. 49	Height - Males	117
Figure No. 50	Height - Females	118
Figure No. 51	Height - Combined	119
Figure No. 52	Height Summary - Males	120

Figure No. 53 Height Summary - Females 121
Figure No. 54 Height Summary - Combined 122
Figure No. 55 Height Change - Males 123
Figure No. 56 Height Change - Females 124
Figure No. 57 Height Change - Combined 125
Figure No. 58 Height Change Summary - Males 126
Figure No. 59 Height Change Summary - Females 127
Figure No. 60 Height Change Summary - Combined 128

F_1 Puppies – Post-Weaning

Figure No. 61 Body Weight - Males 130
Figure No. 62 Body Weight - Females 131
Figure No. 63 Body Weight Summary - Males 132
Figure No. 64 Body Weight Summary - Females 133
Figure No. 65 Body Weight Change - Males 134
Figure No. 66 Body Weight Change - Females 135
Figure No. 67 Body Weight Change Summary - Males 136
Figure No. 68 Body Weight Change Summary - Females 137
Figure No. 69 Food Consumption Weeks 1 and 2 - Combined 138
Figure No. 70 Food Consumption Summary Weeks 1 and 2 - Combined ... 139
Figure No. 71 Food Consumption Weeks 3 to 26 - Males 140
Figure No. 72 Food Consumption Weeks 3 and 26 - Females 141
Figure No. 73 Food Consumption Summary Weeks 3 to 26 - Males 142
Figure No. 74 Food Consumption Summary Weeks 3 to 26 - Females 143
Figure No. 75 Head Circumference - Males 144
Figure No. 76 Head Circumference - Females 145
Figure No. 77 Head Circumference Summary - Males 146
Figure No. 78 Head Circumference Summary - Females 147
Figure No. 79 Head Circumference Change - Males 148
Figure No. 80 Head Circumference Change - Females 149

Figure No. 81	Head Circumference Change Summary - Males	150
Figure No. 82	Head Circumference Change Summary - Females	151
Figure No. 83	Height - Males	152
Figure No. 84	Height - Females	153
Figure No. 85	Height Summary - Males	154
Figure No. 86	Height Summary - Females	155
Figure No. 87	Height Change - Males	156
Figure No. 88	Height Change - Females	157
Figure No. 89	Height Change Summary - Males	158
Figure No. 90	Height Change Summary - Females	159
Figure No. 91	Body Temperature - Males	160
Figure No. 92	Body Temperature - Females	161
Figure No. 93	Body Temperature Summary - Males	162
Figure No. 94	Body Temperature Summary - Females	163
Figure No. 95	Heart Rate - Males	164
Figure No. 96	Heart Rate - Females	165
Figure No. 97	Heart Rate Summary - Males	166
Figure No. 98	Heart Rate Summary - Females	167
Figure No. 99	Respiratory Rate - Males	168
Figure No. 100	Respiratory Rate - Females	169
Figure No. 101	Respiratory Rate Summary - Males	170
Figure No. 102	Respiratory Rate Summary - Females	171
Figure No. 103	Achieved AOCED Intake Weeks 1 and 2	172
Figure No. 104	Achieved AOCED Intake Summary Weeks 1 and 2	173
Figure No. 105	Achieved AOCED Intake Weeks 3 to 26 - Males	174
Figure No. 106	Achieved AOCED Intake Weeks 3 to 26 - Females	175
Figure No. 107	Achieved AOCED Intake Summary Weeks 3 to 26 - Males	176
Figure No. 108	Achieved AOCED Intake Summary Week 3-26 - Females	177
Figure No. 109	Buccal Mucosal Bleeding Time Summary – Combined	178

1 SUMMARY

The objective of this study was to evaluate safety and bioavailability of Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old).

The test and reference items were administered as a diet as shown below:

Text Table 1: Study Design

Treatment Group	Dosage Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F_0 Generation (dams)@	F_1 Generation (puppies) [a]	
					F	M(Spare)	F(Spare)
1. Control diet*	0	0	0.11%	0.12%	5	4(1)	4(1)
2. AOCED - CDS003	½X	0.75%	0.41%**	0.44%	5	4(1)	4(1)
3. AOCED - CDS004	1X	1.5%	0.77% **	0.83%	5	4(1)	4(1)
4. AOCED - CDS005	2X	3.0%	1.55%**	1.69%	5	4(1)	4(1)

* Group 1 animals received the control diet, which was formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA level (0.11%) was achieved by using the chicken by-product meal as one of the ingredients.

** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content was the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA) and from the chicken by-product meal (0.11%). Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.

*** Calculated based on dry matter basis (adjusted for moisture content).

[a] Two puppies per litter (1 male and 1 female), randomly selected, the spare was randomly selected from any litter within each group.

@ Six (6) females per group were mated, as an attempt to have at least 5 females per group confirmed pregnant at GD29 to 35. Only confirmed pregnant females (up to a maximum of 5/group, randomly selected, as needed) were shipped to (b) (4)

M: male; F: female

AOCED diets coded CDS003, CDS004 and CDS005 were used on this study, with dosing initiated at (b) (4) as soon as mating was confirmed, i.e., starting July 14, 2017. The control group received the reference diet coded CDS002. Animals were 1.5 to 2.9 years old and weighed 9.3 to 11.6 kg at the start of treatment (GD0), and were transferred to (b) (4) on August 22, 2017 where gestation continued, with each dam receiving the same test or control diet as provided whilst at (b) (4), based on group assignment.

During the gestation and lactation phases, assessments on dams included mortality checks, clinical observations, body temperature, heart rate, respiratory rate, body weights, food consumption, parturition observations, and determination of litter size with external sex

determination of puppies, standardization of litter, and weaning. During the lactation and growth phases, assessments on puppies included mortality checks, clinical observations (litter check until post-partum day 56), height, head circumference, body temperature, heart rate, respiratory rate, body weights, food consumption. Blood samples were collected for hematology and clinical chemistry from dams once pretreatment and at weaning, and from puppies at weaning and every two months thereafter. Similarly, blood samples and urine samples were collected for coagulation and urinalysis from puppies at Weeks 13 and 34 of age. Buccal mucosal bleeding time was measured on puppies at Week 34, prior to release. Blood samples for bioanalysis were collected from dams once pretreatment, after 4 to 5 weeks of gestation, and at weaning; while on puppies, samples for bioanalysis were obtained at weaning and during Weeks 13 and 34.

Dams and puppies not selected for the growth phase were released from the study and transferred to (b) (4) animal colony at weaning. Similarly, two weeks after weaning of the youngest litter, once abilit to thrive of selected puppies was confirmed, all spare puppies were transferred to (b) (4) animal colony. Finally, at study completion, all puppies were transferred to (b) (4) animal colony as they reached 34 weeks of age.

Administration of Algal Oil containing EPA and DHA (AOCED) to gestational and lactating females, and to their offspring, had no impact on any of the evaluated parameters at any dose during this study. Differences were considered to be within the normal biological variability and noted in controls.

Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet was bioavailable to the F_0 and F_1 generation as seen by the increases in plasma levels of these fatty acids. In the F_0 generation, DHA and EPA levels were significantly higher than control levels and pretreatment levels in the 1X and 2X dose groups at each timepoint; however, in the ½X dose group, DHA levels also substantially increased compared to the control and baseline while EPA increases did not reach statistical significance compared to the control. In the F_1 generation, DHA and EPA levels were significantly higher than control levels at each timepoint at ½X to 2X. EPA increases were dose-dependent at each timepoint while those of DHA, although generally dose-dependent, did not reach statistical significance at every timepoint. This could be related to substantially higher amounts of DHA in AOCED compare to EPA leading to earlier saturation of DHA in plasma. Since arachidonic acid (ARA) is known to compete with DHA and EPA for inclusion in membrane phospholipids, therefore, ARA levels were analyzed as well in the study. ARA levels indeed decreased in the F_0 generation but not in the F_1 generation. This may be due to the presence ARA in the diets, sufficient to maintain and even increase ARA levels after weaning of puppies. At earlier stages of the development, during lactation, their dams provided ARA via milk could have depleted their own ARA deposits.

In conclusion, the results of this study showed that Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old) was well-tolerated at ½X, 1X, and 2X the recommended dose.

2 OBJECTIVE

The objective of this study was to evaluate safety and bioavailability of Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old).

3 EXPERIMENTAL DESIGN

The test and reference items were administered as a diet as shown below:

Text Table 2: Study Design

Treatment Group	Dosage Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F_0 Generation (dams)@	F_1 Generation (puppies) [a]	
					F	M(Spare)	F(Spare)
1. Control diet*	0	0	0.11%	0.12%	5	4(1)	4(1)
2. AOCED - CDS003	½ X	0.75%	0.41%**	0.44%	5	4(1)	4(1)
3. AOCED - CDS004	1X	1.5%	0.77% **	0.83%	5	4(1)	4(1)
4. AOCED - CDS005	2X	3.0%	1.55%**	1.69%	5	4(1)	4(1)

* Group 1 animals received the control diet (CDS002), which was formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA level (0.11%) was achieved by using the chicken by-product meal as one of the ingredients.

** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content was the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA) and from the chicken by-product meal (0.11%). Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.

*** Calculated based on dry matter basis (adjusted for moisture content).

[a] Two puppies per litter (1 male and 1 female), randomly selected, the spare was randomly selected from any litter within each group.

@ Six (6) females per group were mated, as an attempt to have at least 5 females per group confirmed pregnant at GD 29 to 35. Onl confirmed re nant females (a maximum of 5/group, randomly selected, as needed) were shipped to (b) (4).

M: male; F: female

3.1 Study Schedule

The study initiation date (date of signature of the study plan) was July 5, 2017, and the experimental start date (first mating at (b) (4) was July 14, 2017. Animals were randomly assigned to the study, and dosing initiated, as soon as mating was confirmed (starting July 14, 2017). The last observation was performed on May 22, 2018. The experimental completion date was August 21, 2018 (date of last diet sample analysis).

3.2 Test Methods and/or Guidelines

This study was designed with reference to the following test methods and/or guidelines:

- CVM Guidance for Industry 56: Protocol Development Guideline for Clinical Effectiveness and Target Animal Safety Trials
- CVM Guidance 221: Recommendations for Preparation and submission of Animal Food additive petitions
- VICH GL43 (CVM GFI #185): Guidance for Industry. Target Animal Safety for Veterinary Pharmaceutical Products
- AAFCO Dog Food Gestation/Lactation and Growth Feeding Protocols

3.3 Justification for Dose Levels

Dose levels were selected by the Sponsor based on available marketing data. The recommended dose level (1X) was defined as the dose which provides the actual maximum dose of EPA and DHA currently available on the market worldwide. The survey of labels of dog food products was conducted by the DSM marketing team in December 2016. The high dose as a 2x multiple of the use dose was agreed upon with the CVM staff at the pre-submission conference in June 2016. The half dose was selected to provide information on dose-response relations of test item-related findings, if any.

3.4 Reason for Choice of Route of Administration

The dietary route is the intended route of administration of the test item in dogs.

3.5 Reason for Choice of Test System

The dog (*Canis familiaris)* was selected by the Sponsor to satisfy the regulatory requirements for safety testing in the selected species. The dog was selected for use in this study by the Sponsor since the dog is the target animal for the investigated feed ingredient.

3.6 Justification for Numbers of Animals Selected

The number of animals used on the study was considered the minimum required to achieve the study objectives, based on regulatory requirements, statistical power and/or availability of historical data and were within IACUC and CVM approved guidelines.

4 STUDY DEVIATIONS

Occasional minor deviations to the procedures listed below mandated by the Study Plan were noted and are presented in the appropriate section or table of deviations as considered appropriate.

5 TEST ITEM INFORMATION

Test Item Action Feed ingredient and a source of omega-3 fatty acids (EPA and DHA)

Characterization of Test Item, Test Item Diets and Control Diet

Test Item*

Identity:	Algal Oil containing EPA and DHA
Alternative Name:	AOCED
Description / Physical Appearance:	Not provided
Batch/Lot No.:	(b) (4)
Expiry Date / Retest Date:	Not provided
Correction Factor:	None
Purity:	Not provided
Storage Conditions:	Room temperature
Supplier/Manufacturer:	Not provided

** The test item was provided already formulated into food pellets.*

High Dose Diet

Identity:	CDS005 2X
Alternative Name (coding):	CD610
Description / Physical Appearance:	Brown food pellets
Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	3.0%
Actual DHA+EPA content in diet (as it is):	1.55%
DHA+EPA content (on a dry matter basis):	1.69%
Best before:	October 14, 2018
Storage Conditions:	Room temperature
Handling Precautions:	Standard laboratory precautions
Supplier/Manufacturer:	DSM Nutritional Products AG

Mid Dose Diet

Identity:	CDS004 1X
Alternative Name (coding):	CD049
Description / Physical Appearance:	Brown food pellets
Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	1.5%
Actual DHA+EPA content in diet (as it is):	0.77%
DHA+EPA content (on a dry matter basis):	0.83%
Best before:	October 14, 2018
Storage Conditions:	Room temperature
Handling Precautions:	Standard laboratory precautions
Supplier/Manufacturer:	DSM Nutritional Products AG

Low Dose Diet

Identity:	CDS003 0.5X
Alternative Name (coding):	CD165
Description / Physical Appearance:	Brown food pellets
Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	0.75%
Actual DHA+EPA content in diet (as it is):	0.41%
DHA+EPA content (on a dry matter basis):	0.44%
Best before:	October 14, 2018
Storage Conditions:	Room temperature
Handling Precautions:	Standard laboratory precautions
Supplier/Manufacturer:	DSM Nutritional Products AG

Control Diet

Identity:	CDS002 0X
Alternative Name (coding):	CD907
Description / Physical Appearance:	Brown food pellets
Batch/Lot No.*:	Not applicable
Actual DHA+EPA content in diet (as it is):	0.11%
Best before:	October 14, 2018
Storage Conditions:	Room temperature
Handling Precautions:	Standard laboratory precautions
Supplier/Manufacturer:	DSM Nutritional Products AG

**The diets were produced once for the entire study duration; therefore, lot numbers were not assigned.*

Documentation characterizing AOCED, the test diets and the reference diet (control) was supplied by the Sponsor (Appendix No. 1).

Upon receipt at (b) (4), diets were stored in a temperature controlled room (humidity not controlled/monitored), separated from any other diets.

Upon receipt at (b) (4) diets were stored in a room where other diets were stored. The room was only controlled for temperature, but both the temperature and humidity were monitored daily.

5.1 Preparation of Dietary Admixtures

Extruded dry diets (one each for control, low, mid, and high concentrations of AOCED) were provided by the Sponsor as ready-to-use.

The control diet fulfilled the 2016 AAFCO Dog Food Nutrient Profiles, which included recommendations for inclusion of EPA+DHA for puppies.

5.2 Stability of Test Item

Documentation of AOCED stability over the period of the study was provided by the Sponsor (Appendix No. 2).

5.3 Analysis of Diets

Representative samples (approximately 500 g, in duplicate) of each manufactured batch of each formulation were taken from one bag used on Day 1 at (b) (4), from the first day of dosing a (b) (4) (day of animal arrival), at two months intervals throughout the study, and at the end of treatment.

The samples were kept at room temperature.

One set of the duplicate samples was shipped at room temperature to the Sponsor-designated laboratory, for analysis:

(b) (4)
Analytics Laboratory
(b) (4)

The samples collected at (b) (4) transited through (b) (4) rior to shipment to the analytical laboratory. The second set of samples collected at (b) (4), which was not required for analysis, was shipped to (b) (4) (b) (4) here it was kept pending shipment.

The analysis was performed by the analytical laboratory to verify the DHA and EPA contents (b) (4) and PV values (CDR FoodLabFat Analyzer for Measuring Peroxide Value – equivalent to AOCS Cd 8-53 reapproved 1997) in all diets. The acceptance criterion for the formulation was ±15% of nominal.

The second set of samples was requested by the analytical laboratory and was shipped for analysis. Any analytical samples not employed in the primary analysis or required following completion of the primary analysis were discarded after finalization of the Analysis Report.

5.4 Archive Sampling and Disposition of Diets

An adequate sample (minimum of 1 g) of each lot of each diet was collected when diets were received at (b) (4) and stored in the archives of (b) (4) under the same storage conditions used during the study.

After completion of the study, any sealed bags of diet remaining at (b) (4) were destroyed (incinerated). Similarly, any individual amount of food remaining daily (at (b) (4)) were retained for incineration at intervals throughout the study.

Any diets remaining at (b) (4) at shipment of animals were discarded.

5.5 Administration of Diets

As the Sponsor provided the diets already coded, each animal's actual treatment designation was unknown to staff performing dosing or data collection.

As animals were housed in different rooms (at (b) (4), due to the space restrictions), treatment was done in a separate designated room. Treatment of the animals was by each housing room (applicable to (b) (4) only), by ascending animal number (see section 6.2 *Animal Assignment and Blinding Procedure* for details).

At (b) (4) animals were housed in separate pens from animals not assigned to the study, starting 3 to 14 days prior to Day 1, to receive the reference/control diet.

F_0 (at (b) (4)): During the acclimation/pre-treatment period, the females received (b) (4) standard diet for breeders up until 3 to 14 days prior to Day 1 when they received the reference/control diet (approximately 400 g of food per day). Daily oral dietary administration to dams (approximately 600 g of food per day) started on the day of the first successful mating and continued until shipment to the Test Facility.

Females were mated 2 or 3 times (only once for (b) (4), with one day of rest between each mating. Successful mating was described as observation of the tie. Males used for mating were proven breeders of at least 12 months of age and confirmed healthy (health record of both sires and dams were provided to the Study Director – only the health record of dams were reported, health records of sires are retained on file).

F_0 (at (b) (4)): Daily oral dietary administration to dams continued immediately after arrival and throughout gestation and lactation (approximately 15 weeks in total). Dams received approximately 600 g of food per day from arrival to parturition, and 900 g per day from parturition until weaning. As per SOP, as soon as the parturition process started, no additional food was provided to the dam, as the cage door was not to be opened unless problems with the ongoing parturition were observed; therefore, no food consumption data was acquired on these occasions.

F_1 (at (b) (4)): Starting at 5 weeks of age and until weaning, puppies were provided with a feeding pan. During that period, the daily food intake was calculated for the dam plus its litter (i.e.: dam's bowl, plus feeding pan) since the dam also had access to the feeding pan (approximately 300 g, taken from the 900 g measured for the dam).

As of weaning, puppies selected for the study continued on their mothers' respective diets (approximately 400 g per day/dog for a 6-8 hour daily feeding period) for the additional 6 months until 34 weeks of age. Puppies remained pair-housed for feeding during the first two weeks post-weaning to confirm ability to properly thrive, and were then individually housed for feeding for the remainder of the study (including for some individuals, while waiting for the youngest litter to complete the first two weeks post-weaning). Similarly, puppies not selected to continue on the study continued on their mothers' respective diets until released from the study (approximately 2 weeks after weaning).

The remaining puppies were released to the (b) (4) dog colony once ability to thrive of all randomly selected puppies was confirmed.

6 TEST SYSTEM

Twenty-four (24) female beagle dogs were assigned to the study, at (b) (4) (b) (4) starting on July 14, 2017. Six (6) females per group were mated, as an attempt to have at least 5 females per group confirmed pregnant prior to shipment. Five (5 dams er rou , confirmed 4- to 5-week pregnant (GD 29 to 35), were shipped to (b) (4) on August 22, 2017.

At the onset of dosing (start of mating, random assignment and administration of test diets), the age of the animals ranged from 1.5 to 2.9 years. The body weights ranged from 9.3 to 11.6 kg. Bitches were in at least their second heat period when they were mated.

6.1 Health Status

Animals were vaccinated and dewormed at (b) (4) (standard program) prior to dosing start, and free of infectious diseases which could complicate the interpretation of the study results.

Following arrival, all animals were subject to a health assessment (including weight measurement). The evaluation was performed in accordance with the standard operating procedures by technical staff. The results of the evaluations (including body weight) were reviewed by the Clinical Veterinarian to confirm that animals were healthy and were not affected by transportation.

Puppies were vaccinated, dewormed and examined at (b) (4) as per SOP and data retained on file.

6.2 Animal Assignment and Blinding Procedure

The animal assignment was performed at (b) (4). The order of the animal number assignment was randomly determined. In order to preserve the blinding, the table describing the assignment of animals based on timing of mating confirmation was maintained in a separate document, with access restricted to unblinded personnel only.

(b) (4) tested animals for pregnancy 29 to 35 days after mating. When all 6 dams within a group were confirmed pregnant, one dam was randomly selected using a dice to be released from the study, so that a maximum of 5 pregnant dams per group was shipped to (b) (4). Although all females in the low dose (Group 2) were pregnant, low dose dam (b) (4) exhibited a propensit to s ill food and therefore was excluded from the study. The dams were shipped to (b) (4), in one shipment.

One puppy/sex/litter was randomly retained for the F_1 assessments (See section 7.10 *Weaning* for details). As at least 4 litters/group were obtained, it was not required to select additional puppies/sex/litter.

During the in-life portion of the study, each animal's treatment designation was unknown to the blinded staff. The animal cage cards only displayed the study number, animal sex, the blinded animal identification number (i.e., mating number) and the animal tattoo number.

Blinding in the study was applied to the identity of the test item or reference item (control) assigned to each experimental dose group (i.e., Group 1 through Group 4). As the animal arrival numbers (e.g., 1, 2, etc.) were maintained in Provantis for the in-life portion of the study, there were no indicators of animal assignment to treatment rou s in Provantis until the study was unblinded. The Provantis system was employed at (b) (4), whereas at (b) (4), data were captured manually.

Personnel involved in the in-life data collection were blinded to the experimental groups. However, the Study Director, the Principal Investigator (at (b) (4)), the Clinical Pathologist, the pharmacy staff and the departmental team leaders were not blinded. These unblinded personnel did not participate in direct evaluation of the animals or data collection. This exception to the blinding requirement was necessary in order to permit adequate monitoring and quality checks during the course of the study. For ethical reasons, the veterinary staff were not blinded, since access to an animal's identification and treatment type were required in order to assess the correct interventions that were needed and to properly ensure animal welfare.

6.3 Animal Replacement

Any dam considered unsuitable for use on study was excluded prior to assignment (day of first mating). There was no replacement of dams after initiation of treatment.

Any dam confirmed not pregnant on GD 28 was not shipped to (b) (4).

Any F_1 generation puppy considered unsuitable for use on study was excluded at selection on PPD 56. There was no replacement of puppies after the first two weeks of weaning, once the ability to thrive of the youngest litter was confirmed.

6.4 Identification

Each dam arrived from the supplier individually identified by means of a tattoo and was implanted with a microchip. Each dam was assigned an animal number as described in the following table. The first number corresponds to the respective dose group while the second number identifies the sex of the animal (numbers 5 to 9 used for females). The third and fourth number identifies the animal's rank per gender within each group.

Text Table 3: Dams Assignment

Group	Dosage Level (X of targeted dose)	Animal Numbers - F_0 Generation
		Dams
1	0	(b) (4)
2	½ X	
3	1X	
4	2X	

** Dam with no live puppies remaining after completion of the whelping process; released from the study.*

The puppies (F_1) were identified with paper collar on PPD 0, then with a microchip from PPD 1. For the second generation, the utilization of animal number with 3 numbers was used. Animal identification was interpreted using example below (b) (4)

i.e.: First generation (F_0) = (b) (4) for dam

Second generation (F_1) = (b) (4), etc. for male puppies

an (b) (4), tc. for female puppies

Text Table 4: Puppies Assignment

Group	Dosage Level (X of targeted dose)	Animal Numbers – F_1 Generation (Puppies)	
		Males	Females
1	0	(b) (4)	
2	½ X		
3	1X		
4	2X		

6.5 Housing

Animals were assigned to cages/pens in order of ascending animal mating number for blinding purposes.

Dams (F_0) were housed individually in ~3' × 6' pens a (b) (4) and in ~5' × 6' European cages at (b) (4), equipped with an automatic watering system due to the nature of this diet study involving pregnant animals and dams with their litter, which did not permit group housing.

Approximately 2 weeks prior to parturition, a nesting box was provided to each dam. In addition, a litter pan was given to the puppies from weaning until approximately 3 to 4 months of age.

After weaning, puppies selected for the F_1 generation were pair-housed in ~3' × 3'stainless-steel dog cages equipped with an automatic watering system, but were separated during the 6-8 hour daily feeding period starting the third week post-weaning, in order to acquire individual food consumption data. One male and one female were housed together in each group to harmonize the food consumption values between cages during the first two weeks post-weaning (of the youngest litter). Thereafter, puppies were pair housed by sex and by group. Throughout the weaning process and after weaning, dams were individually housed in ~3' × 3' stainless-steel dog cages equipped with an automatic watering system. Puppies not selected to continue on study remained in European cages until their release from the study approximately 2 weeks after weaning.

All pens/cages were clearly labeled with cage cards, indicating the study number, animal tattoo number, blinded animal assignment number, sex and replicate.

Due to space restrictions, at (b) (4), animals were housed in different rooms, but all rooms were of the same type, within the same building, and had the same environmental controls, water source, and daily routines for care and cleaning. Each room included animals from each treatment group as designated by unblinded technical staff not involved in data collection, such that the rooms were balanced for puppy sex, and treatment. Within each room at (b) (4), animals were assigned to cages by ascending animal arrival number and placed in a clockwise manner around the room in order to maintain blinding. Approximately 1 week after completion of weaning, selected pups, excluding spares, were consolidated into a single room.

At (b) (4), animals were assigned to pens by ascending animal mating number (i.e., in rows of ascending blinded animal assignment number) in order to maintain the study blinding.

6.6 Room Environment

At (b) (4), a commercial breeder facility, the temperature, humidity and air changes per hour were not controlled (set), but the temperature was monitored once daily. The light cycle was set to 14 hours light/10 hours dark.

At (b) (4), the animal room environment was set to maintain a relative humidity of 50 ± 20%; a light dark cycle of 12 hours light/12 hours dark, except during Study Plan-designated procedures; and 10 - 15 air changes per hour. The room temperature was set to maintain 21 ± 3°C from arrival until approximately 2 weeks prior to parturition when it was increased to maintain 24 ± 3°C until at least PPD 42. From PPD 43 (of the youngest litter) until the end of the study, the temperature was returned to 21 ± 3°C.

(b) (4)

At (b) (4) the temperature and relative humidity were monitored continuously. Room environmental conditions were reported to the Study Director, and excursions from the prescribed ranges are reported in section 12 *Deviations*. Records are kept on file at (b) (4).

Facility diagram, building orientation, ventilation and lighting procedures are presented in Appendix No. 66. The housing rooms at (b) (4) measured 14' × 33'.

6.7 Diet/Water

Throughout the pretreatment period until approximately 1 week prior to mating, animals received (b) (4), standard diet. For 3 to 14 days prior to Day 1 (day of first successful mating), the females received the reference/control diet, except during designated procedures. During the treatment period, animals in each group were provided access to the Sponsor-provided dietary mixtures as per section 5.5 *Administration of Diets*.

A very small amount of treats were provided to the puppies as part of the animal enrichment program. The provision of the treats was approved by the Study Director prior to being given. No treats were provided to the dams.

Municipal tap water, exposed to ultraviolet light and purified by reverse osmosis at (b) (4) only, was provided to the animals *ad libitum*, via automatic water system. A bowl of water was also placed in the cage until weaning. Periodic analyses of the purified municipal tap water was performed by a (b) (4) designated facility and the results are retained on file at (b) (4). Similarly, at (b) (4), periodic analyses of the municipal tap water were performed and the results provided to the Study Director and retained on file. Any identified contaminants in the diet or water were at concentrations that would not have interfered with the objectives of the study.

6.8 Acclimation/Socialization

While at the breeding facility, animals were socialized as per (b) (4), relevant standard procedures to ensure they were relaxed and calm when handled by caretakers in a laboratory setting.

There was no acclimation period upon arrival at the Test Facility, as daily oral dietary administration started at (b) (4) and was continued immediately after arrival. Nevertheless, the activities in the animal housing rooms were minimized for the first 7 days following arrival to accustom the animals to the laboratory environment.

Dams were socialized by the primary technicians (no more than 4) at least twice weekly throughout the gestation period starting 4 days following arrival at the Test Facility and stopped as soon as signs of parturition were observed. Only the primary technicians were allowed to handle the puppies (until 1 week old) outside the cage.

Secondary technicians (no more than 6) socialized with the dams at least once weekly during the gestation period starting 4 days following arrival at the Test Facility and stopped as soon as signs of parturition were observed. The secondary technicians manipulated the puppies only when handed over by a primary technician. For logistical convenience, once the youngest puppy in the room reached 1 week of age, both primary and secondary technicians were allowed to take the puppies out of the cage.

Puppies were also socialized as per SOP submission technique.

Throughout the study conduct at (b) (4), and especially prior to weaning, access to the housing rooms was restricted to the minimum feasible amount of personnel in order to minimize the stress to the animals.

7 IN-LIFE OBSERVATIONS

Signed and dated records of activities relating to the day-to-day running and maintenance of the study within the animal room as well as the activities relating to the observations and examinations outlined in this Study Plan were recorded. Observations were made and data collections were performed by blinded trained technicians (i.e., without knowledge of the treatment groups for individual animals). During the course of the study, additional evaluations to those described below and/or scheduled and considered necessary by the Study Director and the Veterinarian, as applicable, to assess health status were conducted and duly documented in the study file and included in this study report.

7.1 Mortality

Mortality checks were recorded concomitantly with the cage-side clinical signs observations (see below), during all phases of the study.

Pups in unrelievable pain or distress were euthanized. Animals pre-terminally euthanized or found dead were processed as detailed in section 8 *Terminal Procedures*.

7.2 Clinical Observations

Animals were observed for clinical signs of ill health or other changes. Observations were performed cage-side and during scheduled detailed clinical examinations. Additional clinical observations were conducted as warranted to properly monitor animals' health condition. Clinical observations were conducted by blinded trained technicians and per facility SOPs or (b) (4) at (b) (4), and study plan. Clinical findings were referred to the Clinical Veterinarian.

Clinical signs (ill health, behavioral changes, etc.) were recorded on all animals twice daily throughout the study. The nature of these observations included evaluation of general appearance, activity, and other indicators of changes in animal health and behavior, including fur condition, gait and mobility.

Litter checks were performed once daily (concurrently with a clinical sign activity) until PPD 56.

A detailed clinical examination (DCE) was performed on each animal on the day of estrous and on the day of treatment initiation, and once within the week prior to shipment (at (b) (4) concurrently with body weight measurements), and monthly thereafter at (b) (4). A DCE was also performed on the day prior to or on the day of release from the study.

Detailed clinical examinations were conducted per facility SOPs or (b) (4) at (b) (4) which described that during the detailed clinical examination, animals are observed while in the cage for behavior, general appearance, coordination, etc., and then removed from the cage for close evaluation of general condition of the whole body including, but not limited to, head, thoracic, and abdominal areas through examination and palpation. Body temperature, heart rate and respiratory rate (counts per minute) were also evaluated.

For all puppies, height and head circumference were also measured weekly starting on PPD 7.

In addition, a detailed examination (including body temperature, heart rate and respiratory rate) was performed on all puppies assigned to the F_1 generation, by blinded technical staff starting on PPD63 (1 week post-weaning) and once monthly thereafter, including within 3 days prior to release from the study. This evaluation was conducted per facility SOPs which included assessment of the general body condition, autonomic and central nervous system, somatomotor activity, gait, skin/fur condition, lymph nodes, eyes, mucus membranes, respiration, behavior, circulatory system, state of hydration, and lungs, bladder, reproductive system and gastrointestinal auscultation and/or palpation. Particular attention was directed to observations of central nervous system signs (seizures, tremors, or salivation), vomiting and diarrhea. Additional observations were performed as deemed necessary.

Animals whose health condition warranted further evaluation were examined.

7.3 Medical treatments

Medical treatments were administered as needed over the course of the study. They were not considered to have an impact on the test item treatment since they were either provided at short durations on a few occasions, and/or were non-systemic. The specific treatments administered are presented in Appendix No. 4.

7.4 Body Weights

Body weights were recorded for all dams on the day of estrous and on the day of treatment initiation (at (b) (4) concurrently with DCE), and weekly thereafter.

Puppies were weighed every 3 or 4 days, i.e., PPD 0, 4, 7, 10, 14, 17, 21, etc., until weaning (in grams, 4 digits), and weekly thereafter (in kilograms, with 2 decimals).

A body weight measurement was also performed on dams and puppies on the day prior to release from the study.

7.5 Food Consumption

Individual food intake was measured on all animals daily except on days of food deprivation (dams only) throughout the study, starting at initiation of feeding the reference/control diet (3-14 days prior to treatment start). In addition to the daily food consumption, achieved intakes were calculated at (b) (4) on a weekly basis. Throughout the phase conducted a (b) (4), any spilled food was also weighed daily for each cage, unless clearly contaminated with liquid or solid material (e.g. water, urine, feces, etc.). The amount of contaminated food (excluded from the spillage measured value) was visually estimated and documented.

The average of daily individual achieved intake of the test item in mg/kg/body weight per week was calculated for both generations based on daily food consumption, taking into account any spilled food weight using the following formulas:

- On dams from Day 1 until puppies are 5 weeks of age (without feeding pan)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

- On dams with puppies, from 5 weeks of age until weaning (with feeding pan, including puppies body weight), and for the first two weeks post-weaning (2 puppies/cage)

$$\frac{\text{Dietary concentration (mg/kg/cage) x food consumption (kg)}}{\text{Start-week body weight (kg/cage)}}$$

- On selected puppies, from the third week post-weaning (1 puppy/cage during feeding)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

For reporting purposes, weekly average of daily food consumption and achieved intakes are presented.

On occasion, no daily food consumption data was obtained/reportable for some dams and/or puppies due to various reasons. Similarly, there were also a few occasions were the amount of spilled food was not weighed for some animals. It occurred no more than twice per animal, except for dam (b) (4) (5 occurrences). See Appendices No. 17 and 18 (dams) and Appendix No. 48 (puppies) for details. These deviations were not considered to have had an impact as these were isolated occasions, especially compared to the long study duration, with only a few animals concerned, furthermore spread across groups.

7.6 Parturition Observations

Dams were observed for parturition at least 3 times daily starting from GD 55 until GD 71 (as applicable), as per standard operating procedures. Body temperature was measured twice daily (12 ± 1 hour apart) starting on GD 55 until the first signs of parturition were observed. Body temperature was also measured daily from GD 52 to 54 for baseline acquisition. The time of onset and completion of delivery was recorded for each animal when possible. The day parturition was completed was termed as PPD 0. Any signs of difficulty in parturition were recorded.

On GD 54, dam (b) (4) presented vaginal discharge, but no contractions; however, the presence of live fetuses was confirmed by ultrasound. On GD 55, a malformed, still-born foetus was expelled, which was rapidly consumed by the dam. Another ultrasound was performed to confirm remaining fetuses were alive. On GD 56, the animal displayed decreased activity, an elevated body temperature (38.9°C), greenish-black liquid feces, tremors, decreased capillary refill time and retching. Intravenous administration of fluids and antibiotics was started immediately due to a suspected infection. This animal's food consumption was severely decreased from GD 52 to 55 (2 to 3 grams daily), justifying the addition of 100 mL warm water to the bowl in an attempt to stimulate its appetite. On GD 57, dam (b) (4) was still exhibiting decreased activity and markedly reduced appetite (less than 50 grams daily); therefore, 156 grams of canned food and 50 mL of Ensure® were provided. On GD 57, the abdomen was noticed as no longer distended and another ultrasound examination confirmed that the animal was no longer in gestation. No material was found in the cage, suggesting that the dam probably consumed any expelled fetuses as whelping was ongoing overnight, and there were no witnesses of the process.

The parturition process went well for dam (b) (4) (low dose) which had 9 puppies; however, by PPD 2, they were cannibalized or not nursed by the dam. Similarly, there were no issues with the parturition of dam (b) (4) however, all puppies from that litter died shortly after birth, up to PPD 5, due to a lack of nursing, which was confirmed by the absence of milk in the stomach observed at necropsy.

All other dams displayed normal maternal behavior.

On GD 63, mid dose dam (b) (4) was suspected to present fetus retention, after a relatively long whelping process of approximately 12 hours. The presence of a dead puppy remaining in the uterus was confirmed via an ultrasound examination. Oxytocin was administered and the animal monitored; however, the dead puppy had to be removed by caesarian section. Antibiotics were provided prophylactically as presented in Appendix No. 4 *Medical Treatments*.

7.7 Litter Size

Following littering, the number of live, dead and malformed puppies at birth of F_1 generation puppies was recorded daily from PPD 0 until weaning on PPD 56. Gross abnormalities were recorded.

7.8 External Sex Determination Puppies (F_1 Generation)

The number of male and female puppies in each litter was determined as per (b) (4) OP, by visually judging the ano-genital distance and/or presence of a vulva or penis.

7.9 Standardization of Litter (Culling)

Any dams with a litter of more than 6 puppies on PPD 1 was randomly adjusted to 6 puppies.

On PPD 4, the size of each litter was further adjusted by eliminating extra puppies by random selection to yield 4 puppies/litter (with at least 1 male and 1 female puppy where the number of puppies allowed).

The culled puppies were randomly selected and were euthanized by intracardiac injection of sodium pentobarbital solution (240 mg/mL – dose volume based on the SOP, unless the animal`s body weight was less than 0.5 kg, in which case the dose volume was 0.6 mL).

The puppies were identified as per relevant (b) (4) standard operating procedures.

7.10 Weaning

The puppies were weaned on PPD 56 and separated from the dams. One puppy/sex/litter was randomly retained for the F_1 assessments.

Starting on PPD 49, the daily period of separation of the puppies from their mother was introduced. The duration was gradually increased until complete separation on PPD 56. While separated from their mother during the weaning process, the puppies had access to a bowl of electrolyte solution.

7.11 Clinical Pathology

Clinical pathology evaluations (hematolo and clinical chemistry) were performed on all dams (F_0) once during pretreatment (at (b) (4)) and at weaning.

In addition, coagulation and urinalysis were performed on all F_1 generation puppies during Weeks 13 and 34; while hematology and clinical chemistry evaluation was performed at weaning and every two months thereafter for a total of 4 occasions during the growth phase.

Blood samples were collected from a jugular vein. Food was removed overnight prior to blood collections (required for clinical chemistry). Urine was collected overnight (targeted 10 hours ± 1 hour) from individually housed (in stainless-steel dog cages) animals that were deprived of food and water. The urine collection period was extended in the event a sufficient urine sample volume was not collected within the time frame permitted. Repeat collection for hematology and/or coagulation was performed with or without food deprivation.

a) **Hematology**

The following parameters were measured on blood samples collected into tubes containing K_3-EDTA as anticoagulant.

Cell morphology *	Platelet count
Hematocrit	Red blood cell count
Hemoglobin	Red cell distribution width
Mean corpuscular volume	Reticulocyte counts (absolute and relative) **
Mean corpuscular hemoglobin	White blood cell count (WBC)
Mean corpuscular hemoglobin concentration	WBC differential (absolute and relative)

* *Manual reading of smears for morphology check only was carried out as necessary, in accordance with* (b) (4) *tandard operating procedures. At* (b) (4), *when manual readin o smears for morphology check was required, it was performed by* (b) (4) *designated laboratory* (b) (4) (b) (4)

** *Not analyzed for occasion performed at* (b) (4) *(pretreatment) due to oversight.*

b) **Coagulation**

The following parameters were measured on blood samples collected into tubes containing citrate as anticoagulant.

Sample Appearance (when abnormal)	Fibrinogen
Activated partial thromboplastin time	Prothrombin time

c) **Clinical Chemistry**

The following parameters were measured on blood samples collected into tubes containing clotting activator gel. At (b) (4), the obtained serum was separated into two aliquots. One aliquots was shipped to (b) (4) designated laboratory (b) (4) for analysis of the parameters with an '*' below. The other aliquot was analyzed at (b) (4) (b) (4) for the remaining parameters.

Sample Appearance (when abnormal)	Creatine kinase
A/G ratio (calculated)	Gamma glutamyltransferase (GGT)
Alanine aminotransferase	Globulin (calculated)
Albumin	Glucose
Alkaline phosphatase	Lactate dehydrogenase (LDH)*
Amylase	Magnesium
Aspartate aminotransferase	Phosphorus (inorganic)
Bile acids (total)**	Potassium
Bilirubin (total)	Sodium
Total Calcium	Total protein
Chloride	Triglycerides*
Cholesterol (total)	Urea
Creatinine	

** *Not analyzed for occasion performed at* (b) (4) *(pretreatment) due to oversight.*

d) **Urinalysis**

The following parameters were measured on urine samples:

Bilirubin	Nitrites
Blood	pH
Color and appearance	Protein
Glucose	Specific gravity
Ketones	Urobilinogen
Leukocytes	Volume
Microscopic analysis (sediments)	

7.12 Buccal Mucosal Bleeding Time

Buccal mucosal bleeding time was measured on all F_1 Generation puppies during Week 34, on the same day (+/- 1 day) as coagulation assessments.

7.13 Bioanalysis

Blood samples (a target of 3 mL each) were collected from dams during the pretreatment period for a baseline (at (b) (4)), after 4 to 5 weeks of treatment (at (b) (4)) and at weaning (a (b) (4)) F_1 generation puppies at weaning and during Weeks 13 and 34, at approximately the same time on each occasion.

Each blood sample was collected by jugular venipuncture into tubes containing K_2-EDTA as anticoagulant and kept on wet ice pending centrifugation. Samples were centrifuged at 1500 g RCF for targeted 10 minutes. Centrifugation was refrigerated (set to +4°C) at (b) (4), but not at (b) (4) where it was performed at room temperature.

Plasma was transferred into 2 separate tubes, placed on dry ice pendin stora e in a freezer set to maintain -70°C until shipment. One set of samples was shipped b (b) (4) overnight on dry ice, to the Sponsor-designated laboratory for analysis at the following address:

(b) (4)

Samples were analyzed using a validated assay (OMQ-MTD-003, Whole Plasma Fatty Acid Concentrations) for measurement of DHA and EPA plasma concentrations.

Following confirmation of safe and intact receipt of the first set of samples, the second set of the duplicate samples was shipped to the Sponsor (DSM Nutritional Products AG, Columbia, MD, USA) on dry ice, for possible future analysis.

7.14 Remaining Sample Disposal Policy Statement

All remaining unanalyzed biological samples were discarded prior to finalization.

8 TERMINAL PROCEDURES

At weaning, for dams and puppies not selected for the growth phase, or two weeks after weaning of the youngest litter (for spare puppies), all dams and all puppies not selected for the growth phase of the study (once ability to thrive of selected puppies was confirmed, i.e., 2 weeks post-weaning of the youngest litter) were transferred to the (b) (4) animal colony. Similarly, at the completion of the study, all selected puppies were transferred to the (b) (4) animal colony.

In addition, dam (b) (4) with no puppies after whelping completion, were released from the study and transferred to (b) (4) animal colony.

There were no dams found dead or euthanized for humane reasons throughout the course of the study.

Any puppies found dead or euthanized for humane reasons were processed as per relevant standard operating procedures. Necropsy of the puppies consisted of an external macroscopic examination, including identification of all clinically recorded lesions, as well as a detailed internal examination, and processed as per standard operating procedures. Grossly abnormal tissues were retained.

In order to avoid autolytic changes, the macroscopic examination of the carcass was conducted, as soon as possible, on all puppies which died or were euthanized prematurely. Any puppy found dead or euthanized outside regular working hours, necropsy was completed as soon as possible after the time of death. Pending necropsy, the carcass was stored in a refrigerator (set to 2-8°C).

Any necropsy data generated were not included in the report, but retained on file.

8.1 Histopathology

No histopathological preparation or evaluation was performed.

9 DATA HANDLING AND REPORTING

9.1 Data Capture

This report includes tabulated data commencing one to two weeks prior to the start of dosing. Data from one week prior to the start of dosing is considered adequate for baseline comparison. Any data that may have been collected prior to this period are maintained in the study file.

The following data capture systems were used during the conduct of this study.

In-life data collection	Provantis Module 9.3.0.0 (at [redacted], none at [redacted])
Pathology	Provantis Module 9.3.0.0 (at [redacted], none at [redacted])
Clinical pathology	Provantis Module 9.3.0.0 (at [redacted], CEDRIC [redacted], custom-designed animal management database)
Analytical chemistry	Agilent OpenLab CDS, version C.01.07
Bioanalytical	Shimadzu Lab Solutions, version 5.81
Statistical analysis	SAS 9.2 and 9.3 (at [redacted]) Minitab™ statistical software and R statistical software version 3.4.3 (at DSM, for Bioanal sis
Room environment	Siemens Insight 3.13 (at [redacted], none at [redacted])

Various parameters, not mandated by the Study Plan that were automatically measured and recorded by the instrumentation, but were not reported.

Manual or computerized recording (in-life data collection and pathology, if any) in accordance with the standard operating procedures was used to ensure data capture as necessary. At [redacted] most data were manually collected and subsequently entered in Provantis (b [redacted] for re ortin ur oses. All data collected at [redacted] were transferred to [redacted] prior to and/or at shipment of the animals. A quality control verification of the raw data was performed prior to unblinding of the animal identification information.

9.2 Data Analysis

The statistical analysis approach for this study was designed with reference to Guidance for Industry #226: Target Animal Safety Data Presentation and Statistical Analysis. The statistical reporting was done in compliance with the Guidance for Industry #197: "Documenting Statistical Analysis Programs and Data Files".

Data recorded at unscheduled occasions were reported on an individual basis, but were not included in the analysis described below.

Whenever a continuous variable was measured on more than one pup per litter, an average per litter and sex was computed, reported and the statistical analysis was performed using the average per litter and sex.

Continuous variables specified in the study plan and collected during the conduct of the study were subjected to calculation of group means, standard deviations, minimum and maximum values and were reported by group and sex on each occasion. The calculation of group descriptive statistics were also presented by group on combined occasions and/or combined sexes when a non-significant occasion and\or sex interaction with the treatment effect was detected by the respective statistical analysis.

Categorical and dichotomous data specified in the study plan and obtained during the conduct of the study were reported as individual results and, as deemed appropriate for interpretation, as group incidences by group on occasion and combined occasions for each sex and combined sexes.

The individual food consumption was reported and analyzed as weekly average of daily food intake and as weekly average of achieved food intake.

To keep the statistical model as simple as possible and, considering that the inclusion of data from both sexes and across time in the same analysis would have increase the power of the analysis, considering the group and the sex were the most relevant factors of interest and considering that the inclusion of more factors may had over parameterize the statistical model, only the group, the sex and the time effects were considered as fixed factors in the statistical models.

Statistical analysis was independently performed for the three periods: gestation, pre and post weaning.

To get a data distribution more closely to a normal one, data transformation was used before doing the statistical comparisons when the data distribution was clearly skewed, e.g. for percentages approaching 0% or 100%.

<u>One-Way ANOVA/ANCOVA</u>

A one-way analysis of variance (ANOVA) was performed for the following datasets:

- average of pre-treatment individual results of body weights F_0;
- average of pre-treatment individual results of food consumption F_0;
- average of pre-treatment individual results for body temperature F_0;
- average of pre-treatment individual results for heart rate F_0;
- average of pre-treatment individual results for respiratory rate F_0;
- percentage live pups by litter, percentage malformed pups per litter at PPD 0;
- clinical pathology parameters of F_0 during pretreatment and, for parameters without baseline values, at weaning.

A one-way analysis of covariance (ANCOVA) was performed for the following datasets:

- clinical pathology parameters of F_0 at weaning

Two-Way ANOVA

A two-way analysis of variance (ANOVA) was performed for the following datasets:

- body weight for F_1 at PPD 0

Two-Way Repeated Measures ANOVA/ANCOVA

A two-way repeated measures analysis of variance (ANOVA) was performed for the following datasets:

- body weight for F_0 during post-partum (lactation phase);
- body weight changes for F_0 during gestation and post-partum (lactation phase);
- body temperature for F_0 during post-partum (lactation phase);
- heart rate for F_0 during post-partum (lactation phase);
- respiratory rate for F_0 during post-partum (lactation phase);
- food consumption for F_0 and F_1 combined (by cage) during post-partum (PPD 0 to weaning);
- food consumption F_1 during the first 2 weeks post-weaning

A two-way repeated measures analysis of covariance (**ANCOVA**) was performed for the following datasets:

- post-start of treatment results of body weights F_0 during gestation
- post-start of treatment results of food consumption F_0 during gestation
- post-start of treatment results of body temperature F_0 during gestation;
- post-start of treatment results of heart rate F_0 during gestation;
- post-start of treatment results of respiratory rate F_0 during gestation

Three-Way Repeated Measures ANOVA

A three-way repeated measures analysis of variance (ANOVA) was performed for the following datasets:

- body weight and body weight change for F_1 post-weaning;
- food consumption for F_1 after the first 2 weeks post-weaning;
- numerical clinical pathology data for F_1;
- body temperature for F_1 post-weaning;
- heart rate for F_1 post-weaning;
- respiratory rate for F_1 post-weaning;
- height and height change for F_1 post-weaning;
- head circumference and head circumference change for F_1 post-weaning.

A three-way nested repeated measures analysis of variance (ANOVA) was performed for the following datasets (pups nested within litter) including only the puppies selected at culling:

- body weight and body weight change for F_1 pre-weaning;
- height and height change for F_1 pre-weaning;
- head circumference and head circumference change for F_1 pre-weaning.

Log-rank test

The Log-rank test was performed for the following data set:

- buccal mucosal bleeding time for F1;

Statistical methods

Log-rank test

The statistical analyses for bleeding time were performed on sexes combined due to the low number of animals. All animals still bleeding at the end of the observation period (30 minutes) were censored at 30 minutes. Inter-group differences of the time to event curve estimates were tested using the Log-Rank test. The log rank test was applied to all groups in order to assess the significance of the overall group effect.

One-Way ANOVA/ANCOVA

The following statistical group comparison did not include groups with less than three observations or with zero variance.

For each data set, a one-way ANOVA/ANCOVA was performed with group as fixed effect. In addition, for the ANCOVA models, the pre-treatment average was used as covariate. When significant differences among the group means are indicated by the model's overall *F*-test ($p \leq 0.10$), a *t*-test was used to perform the group mean comparisons between the control diet group and each test item treated group.

Two-Way ANOVA

The fixed effects in the model were the group, the sex, their interaction and litter nested within group.

When the model indicated that the group-by-sex interaction was significant ($p \leq 0.10$), the group effect was assessed within each sex using *F*-test on least-squares means. When there was no significant group-by-sex interaction, then the group effect was assessed for each sex using the *F*-test from the model.

When the group effect was significant ($p \leq 0.10$), *t*-test on least-squares means was performed to compare control diet group with each of the test item treated groups.

Two-Way Repeated Measures ANOVA/ANCOVA

The average of pre-treatment results was used as covariate in the analysis of the F_0 generation gestation period.

The fixed effects in the model were the group, the time and their interaction with the animal as subject and, when applicable, the pre-treatment as covariate. For the pre-weaning period, subject was the puppy nested within litter. The repeated measures analysis of variance was performed using each of the following four covariance structures: the first-order autoregressive [AR(1)], the heterogeneous first-order autoregressive [ARH(1)], the compound symmetry (CS) and the heterogeneous (CSH) in order to determine which one would best express the pattern of measurement correlations across time. A common covariance matrix for all groups was used. The Kenward and Roger's method was used when computing the denominator degrees of freedom for the tests involving the fixed effects. When the final Hessian was not positive definite or computational limitation/convergence problems were encountered while fitting a model, the model was not considered in the following steps. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) was selected.

When the retained two-way repeated measures ANOVA/ANCOVA model indicated that the group-by-time interaction was significant ($p \leq 0.10$), the group effect was assessed within each time point using *F*-test on least-squares means. When no significant group-by-time interaction, then the group effect was assessed across pooled time points using the *F*-test from the retained model.

When the group effect was significant ($p \leq 0.10$), *t*-test on least-squares means was performed to compare control diet group with each of the test item treated groups.

Three-Way Repeated Measures ANOVA/ANCOVA

The fixed effects in the model was the group, the sex, the time and their two-way and three-way interactions with the animal as subject. For the pre-weaning period, subject was the puppy nested within litter. The repeated measures analysis of variance was performed using each of the following six covariance structures: the spatial power [SP(POW)], the spatial anisotropic power [SP(POWA)], the first-order autoregressive [AR(1)], the heterogeneous first-order autoregressive [ARH(1)], the compound symmetry (CS) and the heterogeneous (CSH) in order to determine which one best expressed the pattern of measurement correlations across time. A common covariance matrix for all group-sex levels was used. The Kenward and Roger's method was used when computing the denominator degrees of freedom for the tests involving the fixed effects. When the final Hessian was not positive definite or computational limitation/convergence problems were encountered while fitting a model, the model was not considered in the following steps. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) was selected.

When the retained model indicated that the group-by-sex-by-time interaction was significant ($p \leq 0.05$), the group effect was assessed within each sex-time combination using F-test on least-squares means. When there was no significant group-by-sex-by-time interaction ($p > 0.05$), then the group-by-sex and the group-by-time interactions were assessed using the F-test from the retained model.

When the group-by-sex interaction was significant ($p \leq 0.10$), the group effect was assessed within each sex using F-test on least-squares means. When the group-by-time interaction was significant ($p \leq 0.10$), the group effect was assessed within each time using F-test on least-squares means. When both group-by-sex and group-by-time interactions were not significant ($p > 0.10$), then the group effect was assessed on pooled sexes and pooled time points using the F-test i.e., the main group effect from the retained model.

For all analyses, the pairwise group comparisons were assessed at an alpha level of 0.10. Significant differences from group mean comparisons were reported as $p \leq 0.10$, $p \leq 0.05$, $p \leq 0.01$, where p represented the t-test probability. Least-square means related to the pairwise group comparisons were presented with p-values.

Profile plots

For continuous variables measured repeatedly, the individual and group mean variations across time were presented in graphs.

9.3 Archives

All data and samples that were generated during this study at (b) (4), the original copy of the study plan, study plan amendments, and the final report are retained for approximately 5 years, at th (b) (4) designated archive facility.

(b) (4) agrees to give the Sponsor sufficient advance notification of any intended disposal of such materials after the 5-year holding period, to allow the Sponsor to secure alternative storage facilities.

All stud material generated by the (b) (4), will be retained in the archives of (b) (4).

All study material generated by (b) (4) was transferred to (b) (4) or archiving.

9.4 Multisite

For any portion of the study conducted by a Test Site, the Study Director ensured that a qualified Principal Investigator was identified by the site conducting that portion of the study, prior to the start of the study phase analysis (excluding for analysis performed a (b) (4)).

For any portions of the study conducted by a test site (i.e.: analytical, bioanalytical), a sub-report was provided by the Principal Investigator responsible of the data interpretation to the Study Director for inclusion in the study report.

9.5 Standard Operating Procedures

The standard o eratin rocedures and the Study Specific Procedures (SSPs) used in this study b [redacted] (b) (4) and the external sub-contractors are maintained on-file at the respective facility locations.

10 RESULTS

10.1 Analysis of Diets

(Appendix No. 2)

Fatty acid analysis of dietary samples collected throughout the study confirmed acceptable levels of EPA+DHA at Study Day 1 (b) (4), at the arrival of animals to (b) (4) and at 2 and 6 months thereafter. At Month 4, a recovery of the Low dose diet (82%) was outside of the range ±15% of the CoA concentrations. At Month 8, recovery values for all diets, including the control, did not meet the acceptance criteria of ±15% of the CoA concentrations. The same was true for the control and High dose diet at the study completion. However, recoveries for Low and Mid dose diets were ≥85% at the end of the study.

To determine a reason for low recoveries at Month 8 and higher recoveries observed at the study completion compare to Month 8 data, a decision to re-analyze samples at the lab performed the original analysis was made. The retention samples were sent to (b) (4) and were analyzed as one batch to determine DHA + EPA potencies. Although recovery values at most timepoints were below original values determined shortly after samples collection, generally, they were above 80% and were consistent across different diets and timepoints. It should be mentioned that the acceptance criteria used by industry for solids is recovery values of 100±20% where recovery is measured by dividing the found concentration by the nominal value (Whitmire et al., 2010). The diets recoveries were above 80% either at the original analysis or re-analysis (or both) and, therefore, were considered acceptable to ensure proper dosing of animals.

Text Table 5: DHA+EPA Potency Determination for Control and Dose Diets

	Day 1		Animal Arrival		Month 2		Month 4		Month 6		Month 8		End	
Diet (Code)	*	**	*	**	*	**	*	**	*	**	*	**	*	**
Control (CD907)	90	***73***	87	***82***	98	***82***	***76***	91	92	***82***	***68***	***82***	***70***	***82***
Low Dose, 0.5X (CD165)	99	***78***	95	***80***	101	***80***	***82***	***83***	87	***80***	***78***	***80***	85	***83***
Mid Dose, 1X (CD049)	95	***82***	114	***82***	98	***78***	94	***84***	93	***83***	***84***	87	91	***84***
High Dose, 2X (CD610)	93	***83***	93	***81***	96	85	88	***82***	90	85	***76***	***83***	***71***	***84***

* = % of Target *(DSM)*

** = % of Target (b) (4)

Values in bold and italic were below the acceptance criteria of ±15% (recovery below 85%), while values in red were below the ±20% (recovery below 80%).

10.1.1 Peroxide Value (PV) Determination

Peroxide values were consistently below 10 mEq/Kg throughout the entire duration of the study.

Text Table 6: Peroxide Value Determination for Control and Dose Diets in mEq/Kg

Diet	Day 1	Animal Arrival	Month 2	Month 4	Month 6	Month 8	Last Day
Control Diet	2	2	2	3	4	5	6
Low Dose, 0.5X	2	3	2	3	6	6	6
Mid Dose, 1X	2	3	3	3	4	5	6
High Dose, 2X	2	3	3	8	5	7	5

10.2 RESULTS F_0 Generation

10.2.1 Mortality F_0 Generation

There were no dams found dead nor preterminally euthanized. However, three dams were released from the study shortly after completion of the parturition process since they were left with no live puppies.

Text Table 7: Dams Released from Study

Group	Dose Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Dam No.	Parturition Day (GD)	Day of Release	Reason for Release/Comments
2. AOCED - CDS003	½X	0.75	(b) (4)	60	PPD2	Post-partum infection possibly due to placenta retention, leading to pup cannibalism and/or pups FD/UE due to lack of nursing
3. AOCED - CDS004	1X	1.5		67	PPD5	Pups FD due to lack of nursing
4. AOCED - CDS005	2X	3.0		57	*	No longer pregnant / Pups cannibalism during parturition (not observed directly) possibly due to prematurity

UE: Unscheduled Euthanasia; FD: Found Dead; NA: Not Applicable;
* Animal (b) (4) was released 6 days after observation of terminated gestation (recorded as GD63 although the animal was no longer pregnant).

These three cases, across different dose groups, were not considered related to the administration of AOCED diets, and were considered likely incidental in nature given their dissimilar etiology.

Data collected from the released dams are presented in the tables and appendices; however, they are not discussed further in this report, since these dams did not produce a F_1 Generation required for the subsequent phases of the study.

10.3 Clinical Observations – F_0 Generation – Gestation and Lactation Periods

(Tables No. 1 and No. 2, Appendices No. 5 and No. 6)

No clinical signs were considered related to the administration of AOCED during the gestation or the lactation periods of the F_0 females during this study.

Variations in stool consistency, reported as soft/loose/liquid stool and brown liquid/mucoid material in cage tray, were observed in all groups, including controls. Similarly, reduced/absent fecal output was observed across groups throughout the gestation and lactation periods. Fecal changes are considered common in laboratory-housed members of this species, especially during pregnancy and/or parturition.

Other clinical signs observed in the dams during the course of the gestation and lactation periods were considered incidental since they occurred across groups including control, are common in laboratory-housed dogs, were transient, and/or showed no relationship to dose levels in incidence or severity.

10.4 Body Temperature – F_0 Generation – Gestation and Lactation Periods

(Tables No. 3 and No. 4; Appendices No. 7 and No. 8; Figures No. 1, No. 2, No. 11 and No. 12)

There were no AOCED-related effects on body temperatures during the gestation or the post-partum periods of the F_0 dams at any dose level.

Body temperature individual variations were considered incidental since similarly observed in some individual control animals, were transient and/or reflected the normal inter-animal variation in this species.

10.5 Heart Rate – F_0 Generation – Gestation and Lactation Periods

(Tables No. 5 and No. 6; Appendices No. 9 and No. 10; Figures No. 3, No. 4, No. 13, and No. 14)

There were no AOCED-related effects on heart rates during the gestation or the post-partum periods of the F_0 dams at any dose level.

Individual heart rate variations were considered incidental since similarly observed in some individual control animals, were transient and/or reflected the normal inter-animal variation in this species.

10.6 Respiratory Rate – F_0 Generation – Gestation and Lactation Periods

(Tables No. 7 and No. 8; Appendices No. 11, No. 12, Figures No. 5, No. 6; No. 15 and No. 16)

There were no AOCED-related effects on respiratory rates during the gestation or the post-partum periods of the F_0 dams at any dose level.

Individual respiratory rate variations were considered incidental since similarly observed in some individual control animals, were transient and/or reflected the normal inter-animal variation in this species.

10.7 Body Weight – F_0 – Gestation and Lactation Periods

(Tables No. 9 to 12; Appendices No. 13 to 16; Figures No. 7, No. 8, No. 17 and No. 18)

There were no AOCED-related effects on body weights or body weight changes during the gestation or the post-partum periods of the F_0 dams at any dose level.

Body weight and body weight gain individual variations were considered incidental since similar values were observed in some individual control animals, were transient and/or reflected the normal inter-animal variation in this species.

10.8 Food Consumption – F_0 Generation – Gestation and Lactation Periods

(Tables No. 13 and No. 14; Appendices No. 17 and No. 18; Figures No. 9, No. 10, No. 19 and No. 20)

There was no AOCED-related effect on food consumption for F_0 females during the gestation or the lactation periods in this study.

Individual food consumption fluctuations were considered incidental since similar food consumption was noted in some individual control animals, resulted in values that were within the range of values observed across groups pre-dose, and/or reflected the normal inter-animal variation in this species.

10.9 Achieved AOCED Intake – F_0 Generation – Gestation and Lactation Periods

(Table No. 49; Appendix No. 63; Figures No. 21, No. 22, No. 23 and No. 24)

The average of daily individual achieved intake of AOCED in mg/kg/body weight per week, calculated based on daily food consumption and taking into account any spilled food weight and reported per week, was overall dose proportional both during the gestation and the lactation periods. The achieved AOCED intake at the low dose and the high dose levels were generally approximately half and twice the mid dose of 1X (1.5% of AOCED in the diet on DM basis), respectively.

10.10 Clinical Pathology – F_0 Generation – Gestation and Lactation Periods

The Clinical Pathology Abbreviations, Methods and Units are presented in Appendix No. 19.

10.10.1 Hematology – F_0 Generation

(Tables No. 15 and No. 16, Appendices No. 20 and No. 21)

No changes were noted in hematology related to the addition of Algal Oil containing EPA and DHA (AOCED) at any dose to the diet of the pregnant and lactating females during this study.

Differences in hematology between AOCED-fed animals and control animals were considered incidental because many differences were noted in control animals and were consistent with normal biological and/or analytical variability and potentially associated with a different location of analysis.

10.10.2 Clinical Chemistry – F_0 Generation

(Tables No. 17 and No. 18, Appendices No. 22 and No. 23)

No changes were noted in clinical chemistry related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the pregnant and lactating females during this study.

Differences in clinical chemistry between AOCED-fed animals and control animals were not notable and any changes during the study that occurred in were also noted in control animals and were consistent with normal biological and/or analytical variability and were considered incidental.

10.11 Maternal Performance – F_0 Generation

(Table No. 19, Appendix No. 24)

There was no AOCED-related effects on maternal performance.

The percentage of live puppies at birth was overall similar across groups, ranging from 89% in the control group, to 100% in the high dose group.

10.12 Bioanalysis – F_0 Generation – Gestation and Lactation Periods

(Appendix No. 62)

DHA, EPA and ARA fatty acid profiles from plasma were assessed in the F_0 generation at pretreatment, Gestation Day 28 (GD28) and Postpartum Day 56 (PPD56).

At pretreatment, DHA and EPA levels were not significantly different across groups.

At GD 28, DHA levels in all three dose groups (½X, 1X and 2X) were all significantly higher than that in the control group. There were no statistical differences between the low, mid and high dose DHA levels at this time point. Dose-dependent differences were observed in EPA levels, with the mid and high dose groups (1X and 2X) showing significantly higher EPA levels than the control group level, while the low dose group (½X) EPA levels were comparable to the control group levels. The mid dose group (1X) EPA levels did not differ from the low and high dose group (½X and 2X) levels; and the high dose group (2X) levels were significantly higher than that of the low dose group (½X). There were no differences in ARA levels between the control, low, mid and high dose groups.

At PPD 56, DHA levels in all three dose groups (½X, 1X and 2X) were all significantly higher than that in the control group. There were no statistical differences between the low, mid and high dose group DHA levels at this time point. Dose-dependent increases were observed in EPA levels in the AOCED-treated groups (½X, 1X and 2X). Although the low dose group (½X) EPA levels increased more than two-fold compared to the control, the difference did not reach statistical significance. The mid and high dose group (1X and 2X) EPA levels were significantly higher than that of the control and the low dose (½X) groups, and differences between the mid and the high dose groups (1X and 2X) were statistically significant. The low and mid dose group (½X and 1X) ARA levels were statistically the same as in the control group. The high dose group (2X) ARA levels were significantly lower than the control and low dose (½X) group levels but were the same as the mid dose (1X) ARA levels at this timepoint.

For DHA, there was a significant effect of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p<0.001$). All treatment groups increased significantly more than the control group at all timepoints (all $p<0.001$ and increase >200 *μg/mL* versus the control group, except low dose group at GD 28 with $p=0.004$, where the increase over time versus the control group was 110.48 *μg/mL*).

For EPA, there was a significant effect of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p<0.001$). For the low dose group (½X), the changes from pretreatment to GD 28 and to PPD 56 were not significantly different versus the control group (17.510 *μg/mL*, $p = 0.521$ for GD 28 and 48.698 *μg/mL*, $p = 0.083$ for PPD 56). For the mid dose group (1X), the increase from pretreatment to GD 28 was significant (71.469 *μg/mL*, $p=0.014$) versus the control group. From Pretreatment to PPD 56 the increase versus the control group was even higher (138.62 *μg/mL*, $p<0.001$). For the high dose group (2X), the increase from pretreatment to GD 28 was significant (96.903 *μg/mL*, $p=0.001$) versus the control group. From Pretreatment to PPD 56 the increase versus the control group was even higher (235.76 *μg/mL*, $p<0.001$).

For ARA, there was a significant effect of time ($p<0.001$), no significant effect of dose ($p<0.443$) but significant dose-time interaction ($p<0.001$). For the low dose group (½X), the changes from Pretreatment to GD 28 and to PPD 56 were not significantly different versus the control group (-204.562 *μg/mL*, $p = 0.061$) but were significantly different from Pretreatment to PPD 56 (-256.381 *μg/mL*, $p = 0.022$). For the mid dose group (1X), the decrease from pretreatment to GD 28 was significant (-226.306 *μg/mL*, $p=0.04$) versus the

control group. From Pretreatment to PPD 56 the decrease versus the control group was even higher (-495.068 *µg/mL*, p<0.001). For the high dose group (2X), the decrease from pretreatment to GD 28 was significant (-265.004 *µg/mL*, p=0.018) versus the control group. From Pretreatment to PPD 56 the decrease versus the control group was even higher (-540.477 *µg/mL*, p<0.001).

10.13 RESULTS – F_1 Generation – Lactation Period (PPD0 to 56)

10.13.1 Puppy Viability

Means of viability index at birth and survival indices are presented in Text Table 9 below.

There were no detrimental AOCED effects on the puppy viability pre-culling on PPD4 and survival indices on PPD6 to 56 were comparable between groups. On the contrary, the viability and survival indices were generally higher in groups administered AOCED, especially at the highest dose (2X) where only a single death was observed out of 38 born puppies.

Text Table 9: Mean PPD0 Viability and PPD1 to 56 Survival Indices

Group	1	2*	3*	4
Dose Level (X of targeted dose)	0	½X	1X	2X
Target Dosage Level (% of AOCED in the diet on DM basis)	0	0.75	1.5	3.0
PPD0 Viability Index (%)	89.3	96.1	96.4	100
PPD1 Survival Index (%)	82.6	85.0	82.42	100
PPD2 Survival Index (%)	86.0	100	88.0	100
PPD3 Survival Index (%)	82.7	100	84.0	95.8
PPD4 Survival Index (%)	82.7	100	84.0	100
PPD5 Survival Index (%)	100	100	80	100
PPD6 to 56 Survival Index (%)	100	100	100	100

* Including litter from dams (b) (4) and (b) (4) which were ultimately released from the study due to mortality of their whole litter.

Text Table 10: F_1 Generation Mortality up to PPD4

Group	Dose Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Number of Litters*	Number of Born Puppies on PPD0*	Average Number of Puppies per Litter on PPD0*	Number of Deaths*
1. Control Diet	0	0	5	38	7.6	11
2. AOCED - CDS003	½ X	0.75	4 (5)	33 (42)	8.3 (8.4)	1 (9)
3. AOCED - CDS004	1X	1.5	4 (5)	30 (36)	7.5 (7.2)	7 (13)
4. AOCED - CDS005	2X	3.0	4	38	9.5	1

* Values in bracket ( ) includes litters from dams (b) (4) and (b) (4) which were ultimately released from the study due to mortality of their entire litter.

There was only one mortality after PPD 4 culling: the last live puppy of dam (b) (4) died on PPD5, leading to release of this dam from the study.

10.14 Clinical Observations – F_1 Generation – Lactation Period (PPD0 to 56)

(Table No. 20, Appendix No. 26)

There were no clinical observations for F_1 puppies from birth (PPD0) to weaning (PPD56) that were considered attributable to AOCED administration to the F_0 dam during this study.

On the day of weaning, PPD56, puppy (b) (4) from high dose dam (b) (4), exhibited red buccal discharge, retching, labored and increased respiration, as well as being cold to touch. These clinical signs were observed shortly after blood sampling and therefore were considered procedure-related. Given the animal condition, it was released from the study on PPD56 and replaced by spare puppy (b) (4), to continue on to the growth phase.

Clinical signs for puppies included, but were not limited to, skin changes (bruises, dryness, redness, lump, scabbed and/or wounded), tail kinked, firm/soft swelling of flank or cervical dorsal areas, and fur thin/dull/stained. Most adverse clinical observations of decreased activity, weakness, recumbency, body thinness, cold to touch, signs of dehydration, etc., were noted prior to PPD5, generally in puppies that did not survive. These observations were considered incidental since they occurred across groups including control animals, are common in puppies of this age and species, and/or showed no relationship to dose levels in incidence or severity.

10.15 Body Weight – F_1 Generation – Lactation Period (PPD0 to 56)

(Tables No. 21 to 24; Appendices No. 27 to 32; Figures No. 25 to 36)

There were no variations in body weights or body weight changes of F_1 puppies from birth to weaning that were considered attributable to AOCED administration to the F_0 dam during this study.

From birth onward during the lactation period, the mean body weights of low and mid dose puppies, ½X and 1X, were increased compared to controls in both sexes, reaching statistical significance on most measurement occasions. Given the lack of a dose-response, these increases were considered incidental and not related to the administration of AOCED.

Fluctuations in body weights and body weight gains including some that resulted in statistically significant differences between treated groups versus control group, were considered incidental since they did not present any dose-related trend, they resulted in values that were within the range of values observed across groups including control, and/or reflected the normal inter-animal variation in this species.

10.16 Head Circumference – F_1 Generation – Lactation Period (PPD0 to 56)

(Tables No. 25 to 28; Appendices No. 33 to 38; Figures No. 37 to 48)

There were no AOCED-related effects on head circumference or head circumference changes of F_1 puppies from PPD7 to weaning (PPD56) that were considered attributable to AOCED administration to the F_0 dam during this study.

From PPD7 onward during the lactation period, the mean litter head circumference of low and/or mid dose puppies, ½X and 1X, was increased compared to controls in both sexes, reaching statistical significance on most measurement occasions, especially during the first half of the lactation phase. By PPD56, the group-mean litter head circumference was overall similar across groups including control, due to a slightly lower increases in head circumference observed throughout the phase at the low and mid dose groups compared to the control group. Given the lack of a dose-response, these increases were considered incidental and not related to the administration of AOCED.

Other head circumferences or head circumference changes individual variations were considered incidental since similarly observed in some individual control animals, showed no dose-related pattern, and/or reflected the normal inter-animal variation in this species.

10.17 Height – F_1 Generation – Lactation Period (PPD0 to 56)

(Tables No. 29 to 32; Appendices No. 39 to 44; Figures No. 49 to 60)

There were no AOCED-related effects on the height or height changes of F_1 puppies from PPD7 to weaning (PPD56) that were considered attributable to AOCED administration to the F_0 dam during this study.

Any variations in height or height changes including some that resulted in statistically significant differences between treated groups versus control group were considered incidental since similar values were observed in some individual control animals, showed no dose-related pattern, and/or reflected the normal inter-animal variation in this species.

10.18 RESULTS F_1 – Growth Phase

10.18.1 Mortality F_1 Generation – Growth Phase (PPD56 to PPD238)

There were no puppy deaths during the growth phase.

10.19 Clinical Observations – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Table No. 33, Appendix No. 45)

There were no AOCED-related clinical observations for F_1 puppies during the growth phase in this study.

Any clinical signs noted on puppies during the growth phase, including sporadic changes in stool consistency, presence in the cage tray of material of various color and consistency including undigested food, were considered incidental since they occurred across groups including control animals, are common in laboratory-housed puppies of this species, and/or showed no relationship to dose levels in incidence or severity.

10.20 Body Temperature – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Table No. 41; Appendix No. 53; Figures No. 91 to 94)

There were no AOCED-related effects on the body temperature during the growth of the F_1 puppies at any dose level.

Individual body temperature variations were considered incidental since similar values were observed in some individual control animals, were transient and/or reflected the normal inter-animal variation in this species.

10.21 Heart Rate – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Table No. 42; Appendix No. 54; Figure No. 95 to 98)

There were no AOCED-related effects on heart rates during the growth of the F_1 puppies at any dose level.

Individual heart rate variations, including those reaching statistical significance, were considered incidental since similar values were observed in some individual control animals, were transient and/or reflected the normal inter-animal variation in this species.

10.22 Respiratory Rate – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Table No. 43; Appendix No. 55; Figures No. 99 to 102)

There were no AOCED-related effects on the respiratory rate during the growth of the F_1 puppies at any dose level.

Individual respiratory rate variations, including those reaching statistical significance, were considered incidental since similarly observed in some individual control animals, were transient and/or reflected the normal inter-animal variation in this species.

10.23 Body Weight – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Tables No. 34 and No. 35; Appendices No. 46 and No. 47; Figures No. 61 to 68)

There were no AOCED-related effects on body weights or body weight changes for F_1 puppies during the growth phase in this study.

From weaning onward during the growth period, the mean body weights of low and/or high dose puppies, ½X and 2X, were increased compared to controls in both sexes, reaching statistical significance on most measurement occasions from Day 182 onward. Consequently, the overall mean body weight gain for the whole growth phase (PPD238 compared to PPD56) was generally above control mean in the low and high dose groups (½X and 2X). Given the lack of a dose-response, these increases were considered incidental and not related to the administration of AOCED.

Any fluctuations in body weights and body weight gains including some that resulted in statistically significant differences between treated groups versus control group, were considered incidental since they did not present any dose-related trend, they resulted in values that were within the range of values observed across groups including control, and/or reflected the normal inter-animal variation in this species.

10.24 Head Circumference – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Tables No. 36 and No. 37; Appendices No. 49 and No. 50; Figures No. 75 to 82)

There were no AOCED-related effects on head circumferences or head circumference changes during the growth of the F_1 puppies at any dose level.

Any fluctuations in head circumferences or head circumference changes including some that resulted in statistically significant differences between treated groups versus control group, were considered incidental since they did not present any dose-related trend, they resulted in values that were within the range of values observed across groups including control, and/or reflected the normal inter-animal variation in this species.

10.25 Height – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Tables No. 38 and No. 39; Appendices No. 51 and No. 52; Figures No. 83 to 90)

There were no AOCED-related effects on heights or height changes during the growth of the F_1 puppies at any dose level.

Any fluctuations in heights or heights changes including some that resulted in statistically significant differences between treated groups versus control group, were considered incidental since they did not present any dose-related trend, they resulted in values that were within the range of values observed across groups including control, and/or reflected the normal inter-animal variation in this species.

10.26 Food Consumption – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Table No. 40; Appendix No. 48; Figures No. 69 to 74)

There were no AOCED-related effects on food consumption for F_1 puppies during the growth phase in this study.

The group-mean food consumption from combined Weeks 3 to 26 post-weaning was comparable across groups, including controls, in both sexes.

Fluctuations in food consumption including some that resulted in statistically significant differences between treated groups versus control group, were considered incidental since they did not present any dose-related trend, they resulted in values that were within the range of values observed across groups including control, and/or reflected the normal inter-animal variation in this species.

10.27 Achieved AOCED Intake – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Table No. 49; Appendix No. 63; Figures No. 103 to 108)

The average of daily individual achieved intake of AOCED in mg/kg/body weight per week, calculated based on daily food consumption and taking into account any spilled food weight and reported per week, was overall dose proportional during the puppies growth phase. The achieved AOCED intake at the low dose and the high dose levels were generally approximately half and twice the mid dose of 1X (1.5% of AOCED in the diet on DM basis), respectively.

The mean weekly food consumption post-weaning was occasionally slightly decreased at the mid dose (1X) when compared to the other groups, hence the achieved AOCED intake between the low and the mid dose group (½X vs 1X) was slightly below 2-fold, while between the mid and the high dose group (1X vs 2X) the achieved intake was slightly above 2-fold. Given the absence of AOCED-related effects on any of the evaluated parameters at any dose levels including at the highest dose of 2X, it was considered that these minor sporadic variations in achieved AOCED intake had no impact on the study.

10.28 Clinical Pathology – F_1 Generation – Growth Phase (PPD56 to PPD238)

The Clinical Pathology Abbreviations, Methods and Units are presented in Appendix No. 19.

10.28.1 Hematology and Coagulation – F_1 Generation

(Tables No. 44 and No. 46; Appendices No. 56 and No. 58)

No changes were noted in hematology related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the offspring (Generation F_1) at any dose during this study. Some parameters varied during the study in AOCED-dosed animals, but similar variability was also noted within the control group and therefore considered incidental.

No changes were noted in coagulation parameters.

Differences were noted in many hematology parameters over the different time points during the study. However, between AOCED-fed animals and controls, there was no notable difference. Therefore, this variability in parameters was consistent with normal biological (growth) and/or analytical variability, and was considered incidental.

10.28.2 Clinical Chemistry – F_1 Generation

(Table No. 45, Appendix No. 57)

No changes were noted in clinical chemistry parameters related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the offspring (Generation F_1 males and females) during this study.

Urea concentrations were higher on PPD56 in the high dose males and females when compared with controls, but this did not correspond with any increases in creatinine. Therefore, this was considered prerenal in cause and not associated with the administration of AOCED. Creatinine values were higher in all animals with primary increases by PPD168 and peaking at PPD224. This was an expected result due to increased muscle mass during the growth period and was noted in all groups, including control.

Differences in clinical chemistry between AOCED-fed animals and control animals were not notable, and any variability that occurred during the study was also noted in control animals and was consistent with normal biological (growth) and/or analytical variability and was considered incidental.

10.28.3 Buccal Mucosal Bleeding Time – F_1 Generation

(Table No. 47; Appendix No. 59; Figure No. 109)

No changes noted in the buccal mucosal bleeding times were considered related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the offspring (Generation F_1 males and females) during this study.

There were no statistically significant differences among the groups, sexes combined, with most individual values within the range of values observed in the concurrent control group, or to historical controls. However, the mean value of the control group was markedly high, with mean bleeding times of approximately 27 to 24 minutes in control males and females, respectively.

The buccal mucosal bleeding time test is considered a less sensitive test compared to blood sample analysis for coagulation parameters. This test does not involve the coagulation system with fibrin formation and deposition. It only identifies whether platelets are present in adequate numbers and functioning correctly.

Given that all platelet numbers were within reference values for these animals (refer to Appendix No. 56), as well as coagulation parameters (refer to Appendix No. 58), and in the absence of petechiae or hematomas developing from the handling and/or blood collection, it is considered that all animals had normal platelet activity and therefore, these buccal mucosal bleeding time values should be regarded with caution, and not interpreted independently from the clinical pathology results.

10.28.4 Urinalysis – F_1 Generation

(Table No. 48, Appendix No. 60)

No changes were noted in urinalysis parameters related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the offspring (Generation F_1) during this study.

10.29 Bioanalysis – F_1 Generation – Growth Phase (PPD56 to PPD238)

(Appendix No. 62)

DHA, EPA and ARA fatty acid profiles from plasma, were assessed in the F_1 generation at Postpartum Day 56 (PPD56), Week 13 and Week 34. Sex interaction with respect to dose and time were explored but no significance was found so sexes were combined.

At PPD56, the F_1 DHA and EPA levels were significantly higher than in the control group at all dose levels (½X, 1X, 2X) indicating that the F_0 generation fatty acid status affected the F_1 generation status. For DHA, differences between groups were statistically significant between the low and mid dose groups (½X and 1X) but not between the mid and high dose groups. There was a dose dependent increase in EPA concentrations across the three doses. At PPD56, the low and mid dose group (½X and 1X) ARA levels did not differ from control group levels and were equivalent to each other; while, the high dose group ARA level was significantly lower than those in other dose groups and the control.

At Week 13 of age, the F_1 DHA and EPA levels in all treated groups (½X, 1X, 2X) were higher than in the control. DHA levels increased significantly between the low and mid dose group (½X and 1X) but not between the mid and high dose group (1X and 2X). The increases in EPA levels were dose dependent across all three dose levels. At Week 13, the ARA levels were significantly lower than that in the control group at all dose levels (½X, 1X, 2X), and the decreases were dose dependent.

At Week 34 of age, DHA and EPA levels in all treated groups (½X, 1X, 2X) remained higher than control levels. DHA levels did not differ significantly between the low and mid dose groups (½X and 1X) but were different between the mid and high dose levels (1X and 2X). The increases in EPA levels were dose dependent across all three dose levels. At Week 34, the mid and high dose group (1X and 2X) ARA levels were significantly lower than the control group level. The low dose group (½X) ARA levels did not differ from that in the control. The mid dose group (1X) ARA level did not differ from the low and high dose group levels (½X and 2X). The high dose group (2X) level was significantly lower than that in the low dose (½X).

For DHA, there was a significant effect of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p<0.001$). For the low dose group (½X), the changes from PPD 56 to Week 13 and Week 34 were not significantly different versus the control group (-24.62 *µg/mL*, $p = 0.101$ for week 13 and -18.841 *µg/mL*, $p = 0.207$ for week 34). For the mid dose group (1X),

the change from PPD 56 to Week 13 was not significant (-27.191 *μg/mL*, p=0.071) versus the control group. From PPD 56 to Week 34, the decrease was significantly different versus the control group (additional decrease by 45.432 *μg/mL*, p=0.003). For the high dose group (2X), the change from PPD 56 to Week 13 was not significant (12.455 *μg/mL*, p=0.402) versus the control group. From PPD 56 to Week 34 the change was significantly different versus the control group (38.14 *μg/mL*, p=0.012).

For EPA, there were significant effects of time (p<0.001), dose (p<0.001) and dose-time interaction (p<0.001). For the low dose group (½X), the increases from PPD 56 to Week 13 and Week 34 were not significantly different versus the control group (5.687 *μg/mL*, p = 0.578 for Week 13 and 8.498 *μg/mL*, p = 0.407 for Week 34). For the mid dose group (1X), the increases from PPD 56 to Week 13 and Week 34 were not significantly different versus the control group (10.709 *μg/mL*, p = 0.297 for Week 13 and 6.592 *μg/mL*, p = 0.521 for Week 34). For the high dose group (2X), the increases from PPD 56 to Week 13 and Week 34 were significantly different versus the control group (34.327 *μg/mL*, p = 0.001 for Week 13 and 58.959 *μg/mL*, p<0.001 for Week 34).

For ARA, there were significant effects of time (p<0.001), dose (p<0.001) and dose-time interaction (p=0.004). For the low dose group (½X), the changes from PPD 56 to Week 13 and Week 34 were not significantly different versus the control group (-33.96 *μg/mL*, p = 0.489 for Week 13 and -58.669 *μg/mL*, p = 0.234 for Week 34). For the mid dose group (1X), the changes from PPD 56 to Week 13 and Week 34 were significantly different versus the control group (-116.878 *μg/mL*, p = 0.02 for Week 13 and -181.825 *μg/mL*, p<0.001 for Week 34). For the high dose group (2X), the changes from PPD 56 to Week 13 and Week 34 were not significantly different versus the control group (4.837 *μg/mL*, p = 0.921 for Week 13 and -28.138 *μg/mL*, p = 0.566 for Week 34).

11 CONCLUSION

In conclusion, the results of this study showed that Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old) was well-tolerated at ½X, 1X, and 2X the recommended dose.

12 REFERENCES

Whitmire *et al*., NonClinical Dose Formulation Analysis Method Validation and Sample Analysis. The AAPS Journal, Vol. 12, No. 4, December 2010

13 DEVIATIONS

Aside from any study plan deviations that were discussed within the relevant sections of the report, there were occasional procedural deviations that were minor and did not impact the integrity or outcome of the study. Such instances of study plan deviations were documented and acknowledged by the Study Director within the study records. These minor deviations are summarized below.

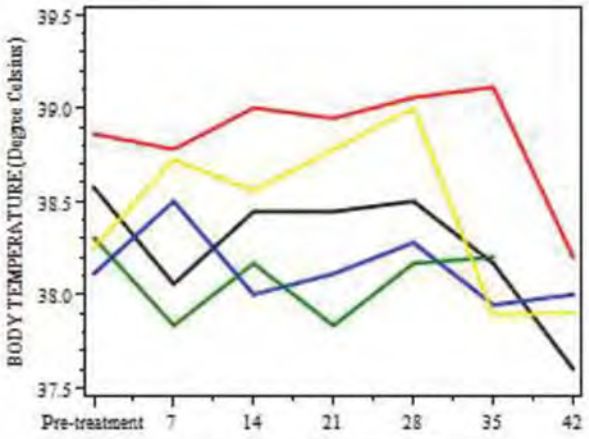
DEVIATION	STUDY PLAN SECTION
On occasion, the puppies had access to food for slightly less or slightly more than the targeted 6 to 8 hours daily; the magnitude of the deviations was negligible (deviating by less than 10 minutes) and/or only concerned spare animals ultimately released from the study.	Administration of Diets
On isolated occasions during the growth phase, the check mark confirming that the diet ID was performed at the moment of feeding was not filled out. However, given that the other procedures involved in bowl preparation and feeding were properly performed, with a card identifying the animal/cage being placed in each bowl prepared, it is reasonable to assume that the puppies were provided the correct diet on these days.	
There were a few occasional excursions from the targeted room environment conditions (i.e., relative humidity ranging for 30-70%, temperature between 18 to 24°C, and 10 to 15 air changes per hour). However, the deviations were of small magnitude and of short duration, without a detrimental effect to animals.	Room Environment
On one occasion (June 24, 2017), the building temperature and humidity check was not performed. On another occasion (August 2, 2017), the building temperature was not recorded on the examination sheet of dam No. 14 (became No. 4502).	Room Environment (at (b) (4))
Unblinded personnel performed the PM health observation/mortality check on one occasion (Day 1); however, all 16 dogs enrolled at that time were on the control diet.	Animal Assignment and Blinding Procedure (at (b) (4))
There were minor, occasional, deviations from the socialization schedule by some primary technicians (socialization performed less than twice weekly) or secondary technicians (at least weekly socialization not performed). The animals were nevertheless exposed to these technicians throughout the gestation phase and no particular signs of stress were observed in the dams.	Acclimation/ Socialization
Blood collection forms were not filled for the hematology collection performed on in July 2017 (pretreatment).	Clinical Pathology (at (b) (4))
An additional body temperature measurement was performed on two dams due to technical oversight. The data was retained on file, but not reported.	Parturition Observations
For some puppies on isolated occasions, the bodyweight value recorded was aberrant and therefore was excluded. Sufficient body weight data are available to allow for proper assessment of animal growth.	Bodyweights

DEVIATION (cont.)	STUDY PLAN SECTION
For detailed clinical examinations (DCE) animals should be observed while in the cage for behavior, general appearance, coordination, etc., and then be removed from the cage for close evaluation of general condition of the whole body including (but not limited to) head, thoracic, and abdominal areas through examination and palpation. Body temperature (BT), heart rate and respiratory rate (counts per minute) should also be evaluated. However, on a few occasions, the activity was not done properly (some endpoints not evaluated) by (b) (4) personnel. Nevertheless, sufficient data was obtained from these animals to allow for proper assessment of their overall health condition, as the frequency of DCE - including BT - was higher at (b) (4) than mandated by the Study Plan. Similarly, on isolated occasions, the AM clinical signs activity was omitted for a few dams.	Clinical Observations (at (b) (4)
For some puppies on isolated occasions, the weekly head circumference or height value recorded was aberrant and therefore was excluded. Still sufficient data are available to allow for proper assessment of animal growth.	Clinical Observations
On a single occasion, the technician who performed the AM cage side clinical signs was not blinded; however, all animals were normal (no clinical signs entered in Provantis) at the time they were observed by the unblinded technician; therefore, any knowledge of animals` dose level was irrelevant.	
On two occasions during the growth phase, the PM cage side clinical signs activity was omitted.	
For a few puppies, the Week 34 plasma samples (both sets of aliquot) were left on dry ice after collection instead of being transferred to the freezer (set to -70°C) and were found the following morning on the bench with all dry ice evaporated. The validation confirmed that the samples are able to sustain 3 freeze/thaw cycles and 24 hours at room temperature; therefore, these samples were still suitable for analysis.	Bioanalysis
Plasma samples were analyzed for arachidonic acid (ARA) though it was not mandated by the study plan.	
The interpretation of the bioanalysis data was not performed by (b) (4), (b) (6) at DSM Nutritional Products R&D Analytics in Switzerland; but by (b) (4), (b) (6) at DSM Nutritional Products in Maryland, USA.	
According to the Study Plan, the diet analysis was to be performed by (b) (4), (b) (6) (b) (4); however, only the analysis of the primar sam les was performed at that Test Site. The retention samples were analyzed at (b) (4). Furthermore, the diet analysis data interpretation was not performed by (b) (4), (b) (6) (b) (4), but at another DSM site and by another Principal Investigator, i.e., by (b) (4), (b) (6) at DSM Nutritional Products in Maryland, USA.	Analysis of Diets
Diet samples' peroxide values were determined and reported though it was not mandated by the study plan.	
The Multisite section of the Study Plan indicates that the Study Director will ensure that a qualified Principal Investigator is identified by the site conducting that portion of the stud rior to the start of the study phase analysis, which was not done for the PI at (b) (4) as the Study Director was only informed of these analysis at the reporting stage. For the bioanalysis performed at (b) (4), the Principal Investigator ((b) (b) (4)) did not issue a report. Similarly, for the diet analysis performed at DNP (b) (4) and at (b) (4), the Principal Investigators (b) (4), (b) (6) and (b) (4), (b) (6)) did not issue a report. Instead, details pertaining to the work performed at these laboratories as well as the data they generated were incorporated into the Interpretation Reports produced by DSM (b) (4), (b) (6)).	Multisite

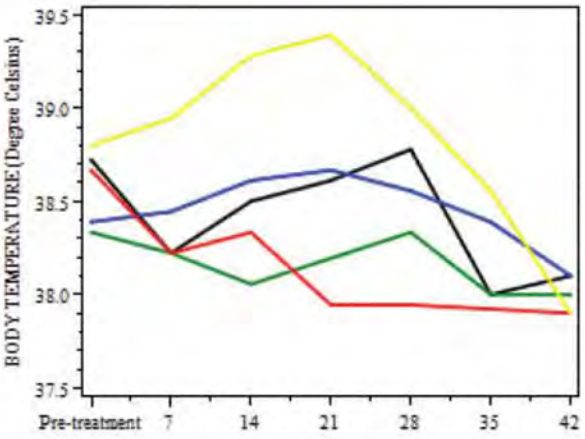
FIGURES
F0 GENERATION

FIGURE NO. 1

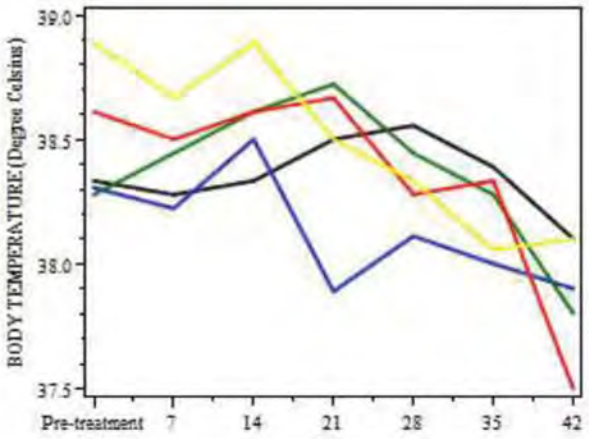
GENERATION F0, GESTATION
Individual - Females



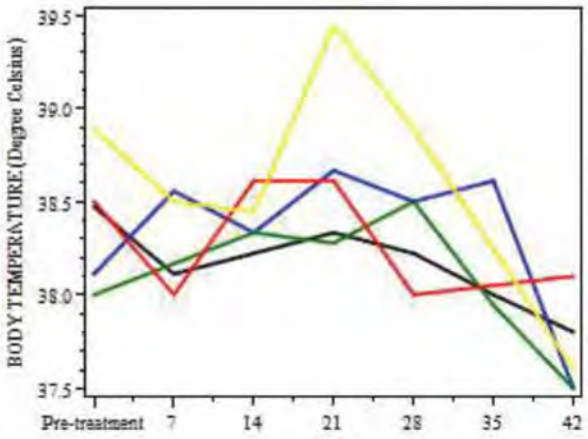
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 2

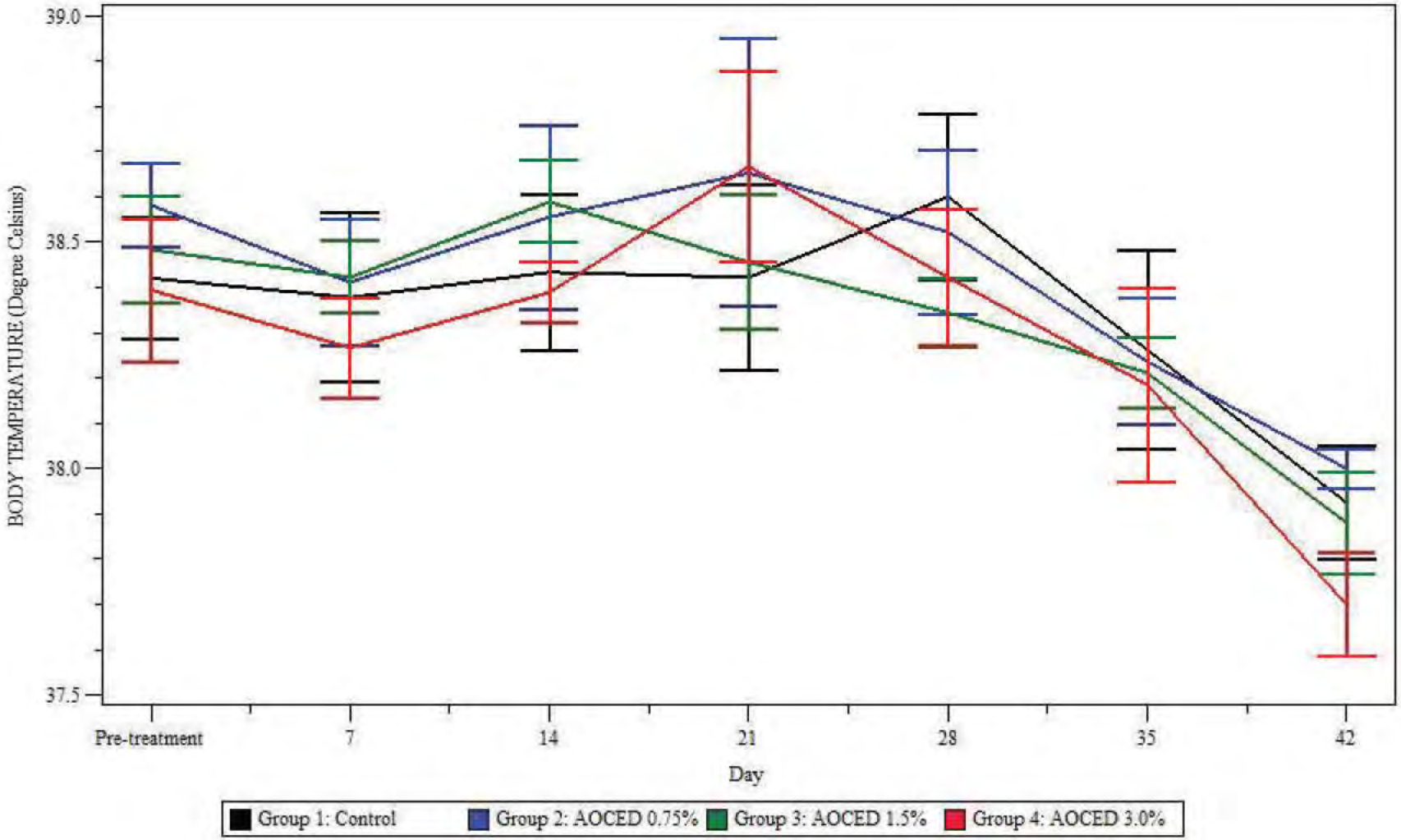
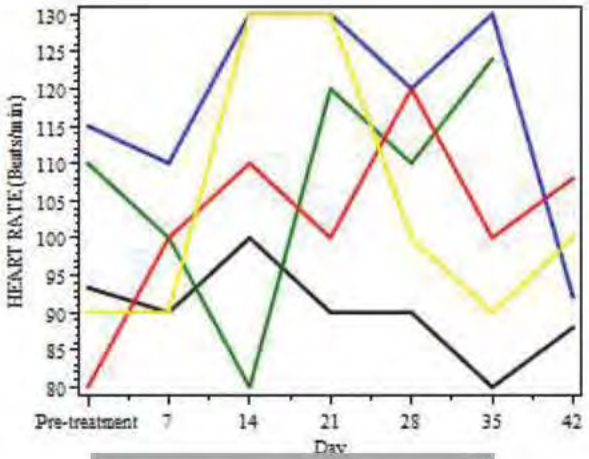

GENERATION F0, GESTATION
Females
Treatment Means ± SEM
BODY TEMPERATURE (Degree Celsius)
39.0
38.5
38.0
37.5
Pre-treatment
7
14
21
28
35
42
Day
Group 1: Control
Group 2: AOCED 0.75%
Group 3: AOCED 1.5%
Group 4: AOCED 3.0%

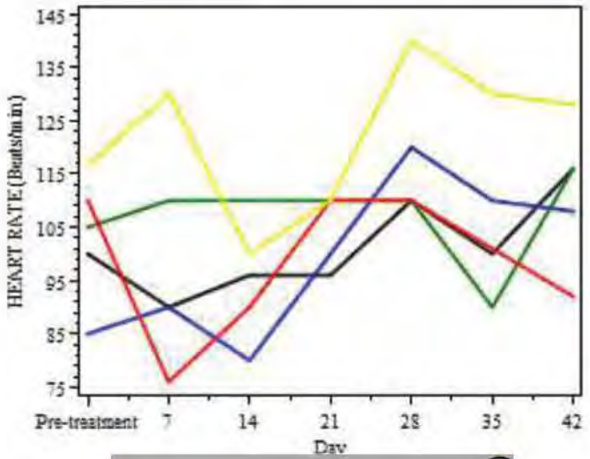
FIGURE NO. 3

[redacted] (b) (4)

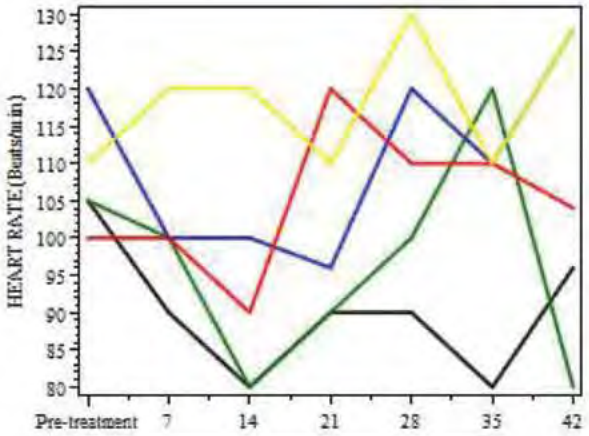
GENERATION F0, GESTATION
Individual - Females



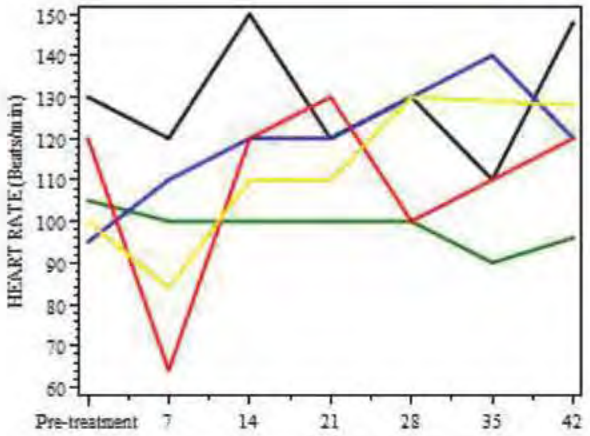
[redacted] (b) (4)



[redacted] (b) (4)



[redacted] (b) (4)



[redacted] (b) (4)

FIGURE NO. 4

(b) (4)

GENERATION F0, GESTATION
Females
Treatment Means ± SEM

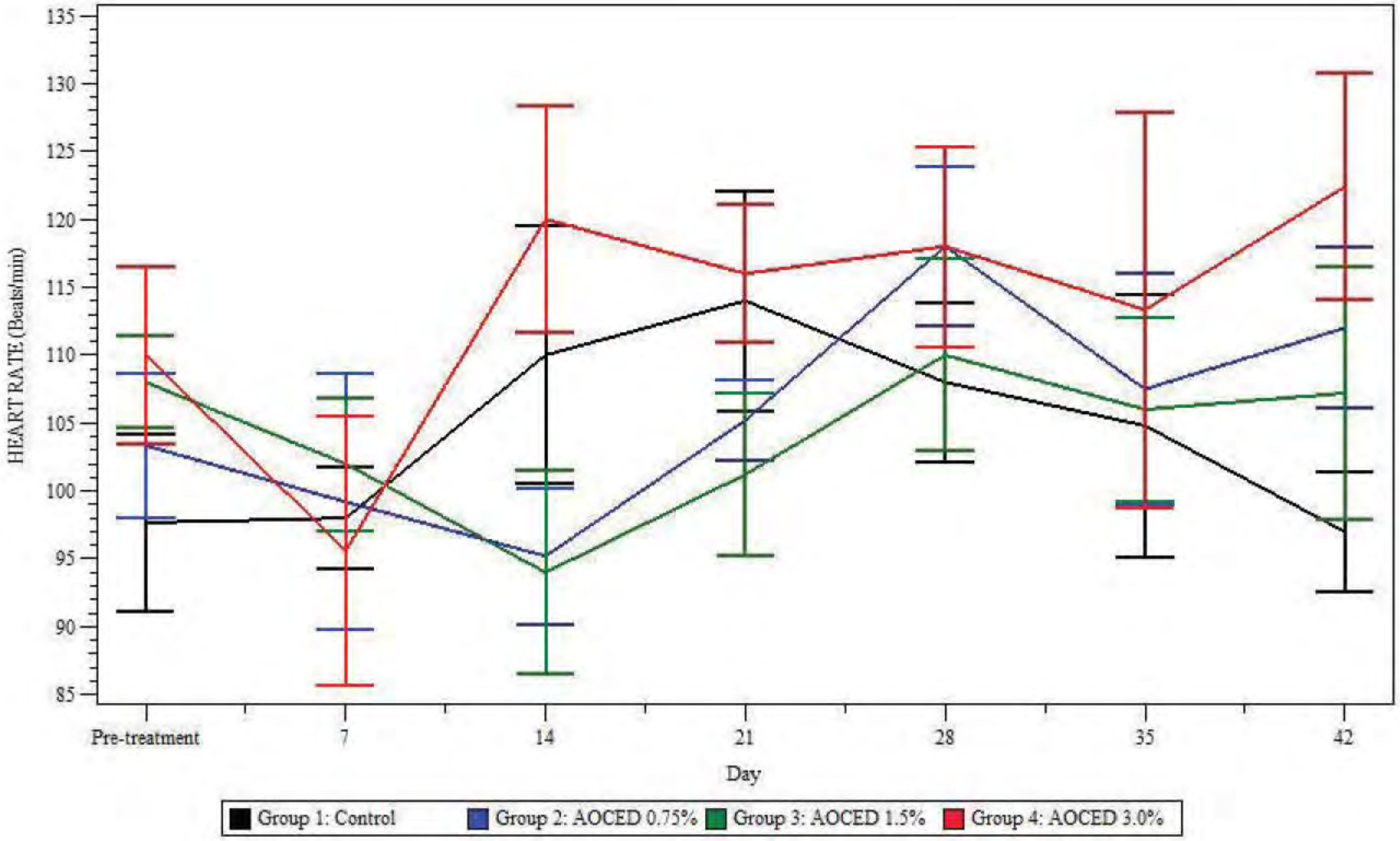
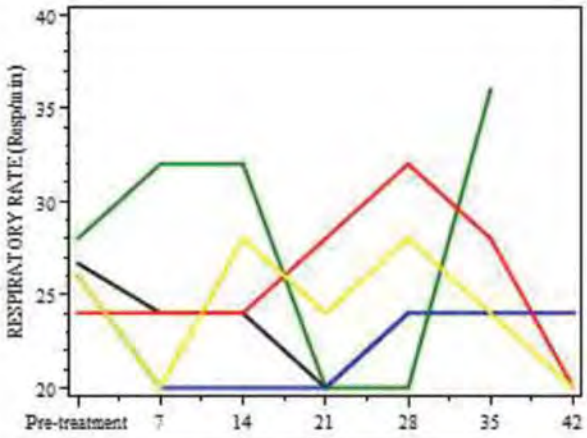
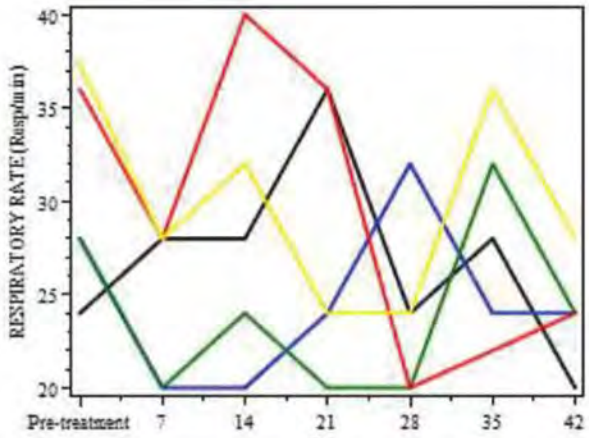


FIGURE NO. 5

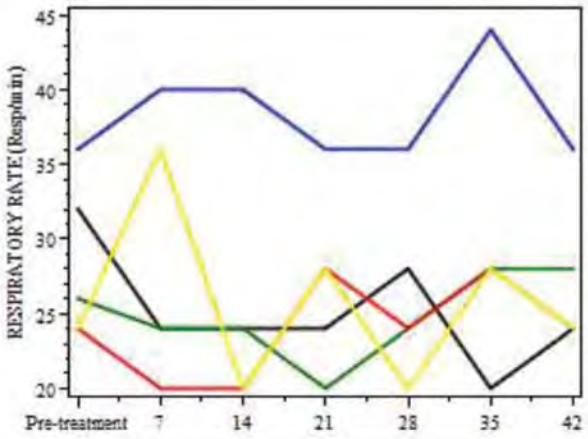
GENERATION F0, GESTATION
Individual - Females



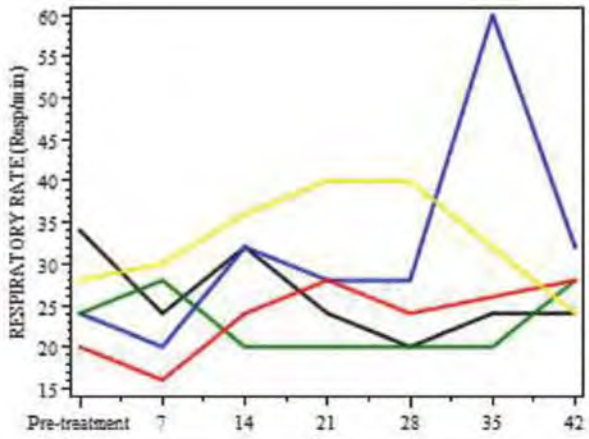
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 6

(b) (4)

GENERATION F0, GESTATION
Females
Treatment Means ± SEM

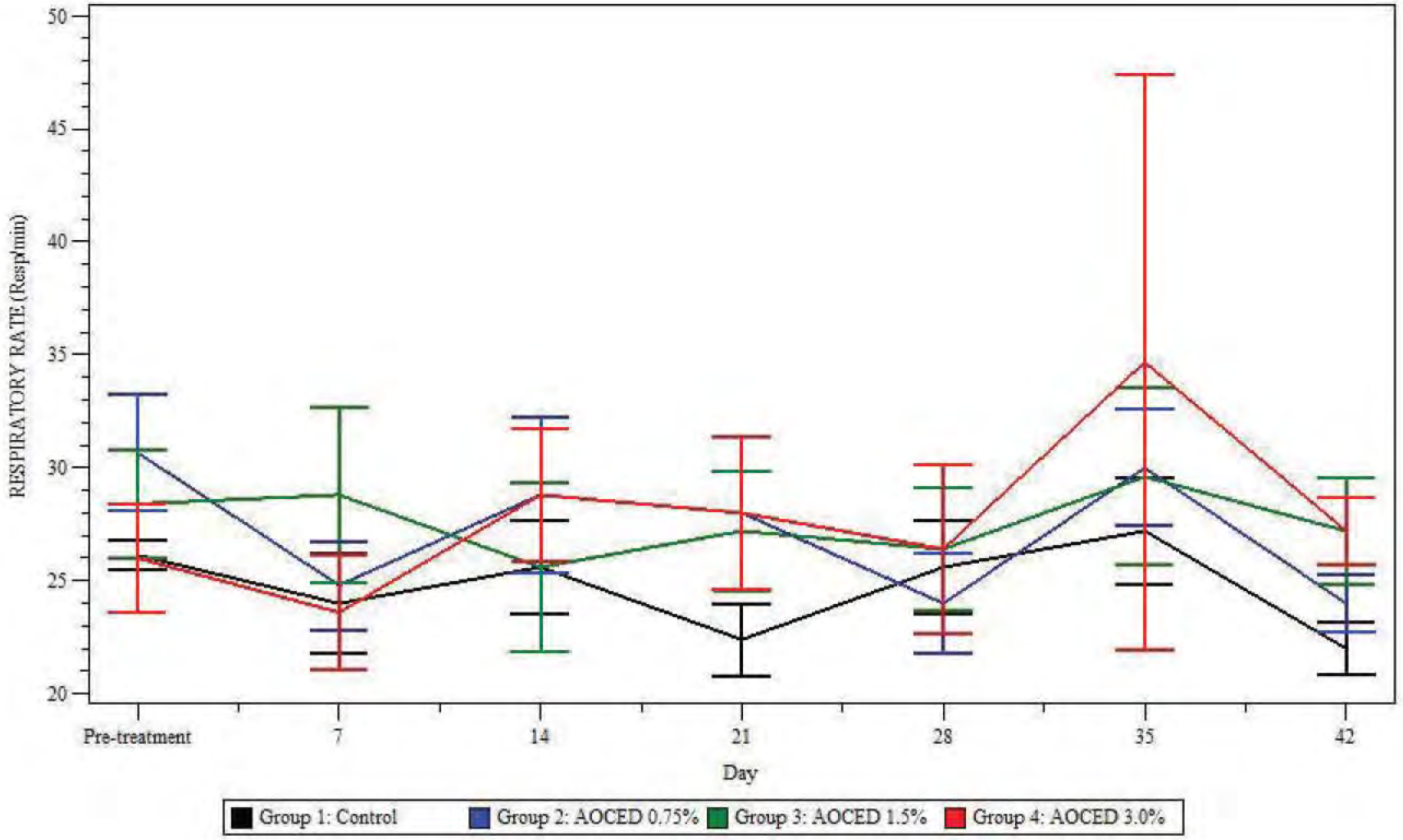
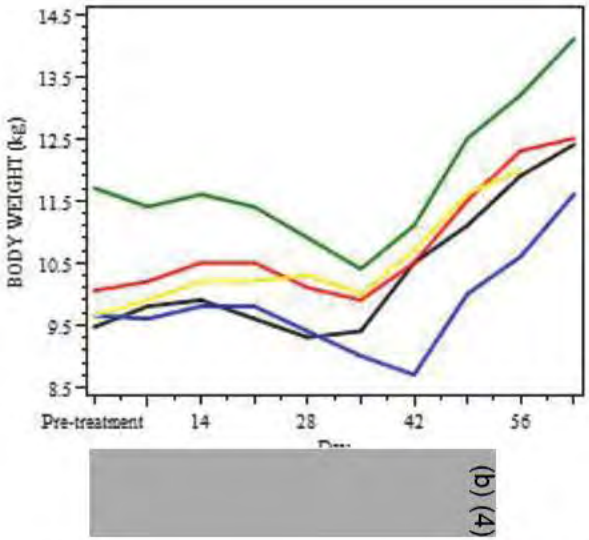


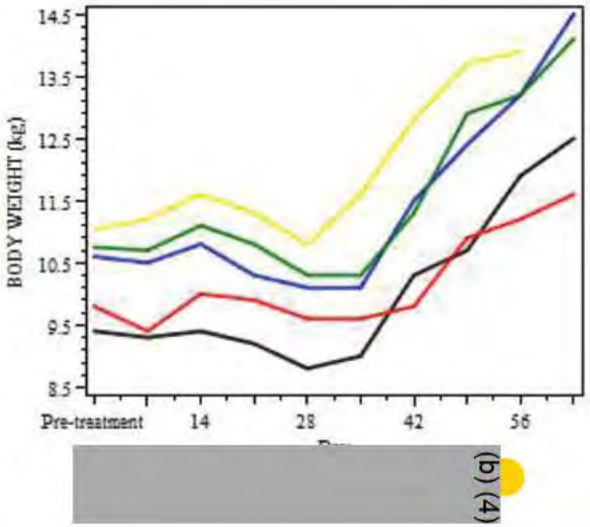
FIGURE NO. 7

(b) (4)

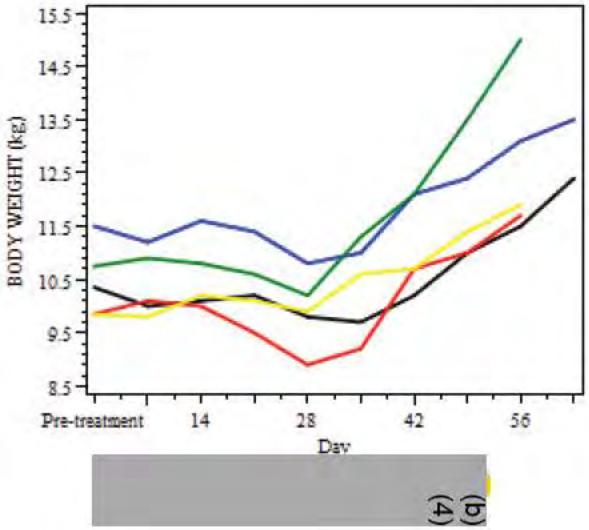
GENERATION F0, GESTATION
Individual - Females



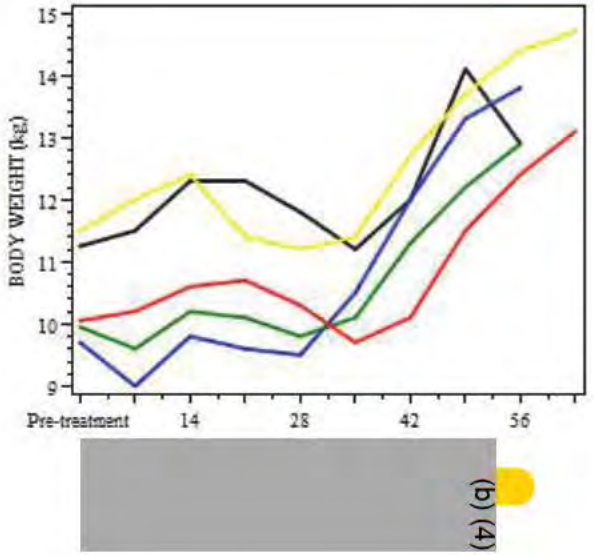
(b) (4)



(b) (4)



(b) (4)



(b) (4)

73 of 1567

FIGURE NO. 8

[redacted] (b) (4)

GENERATION F0, GESTATION
Females
Treatment Means ± SEM

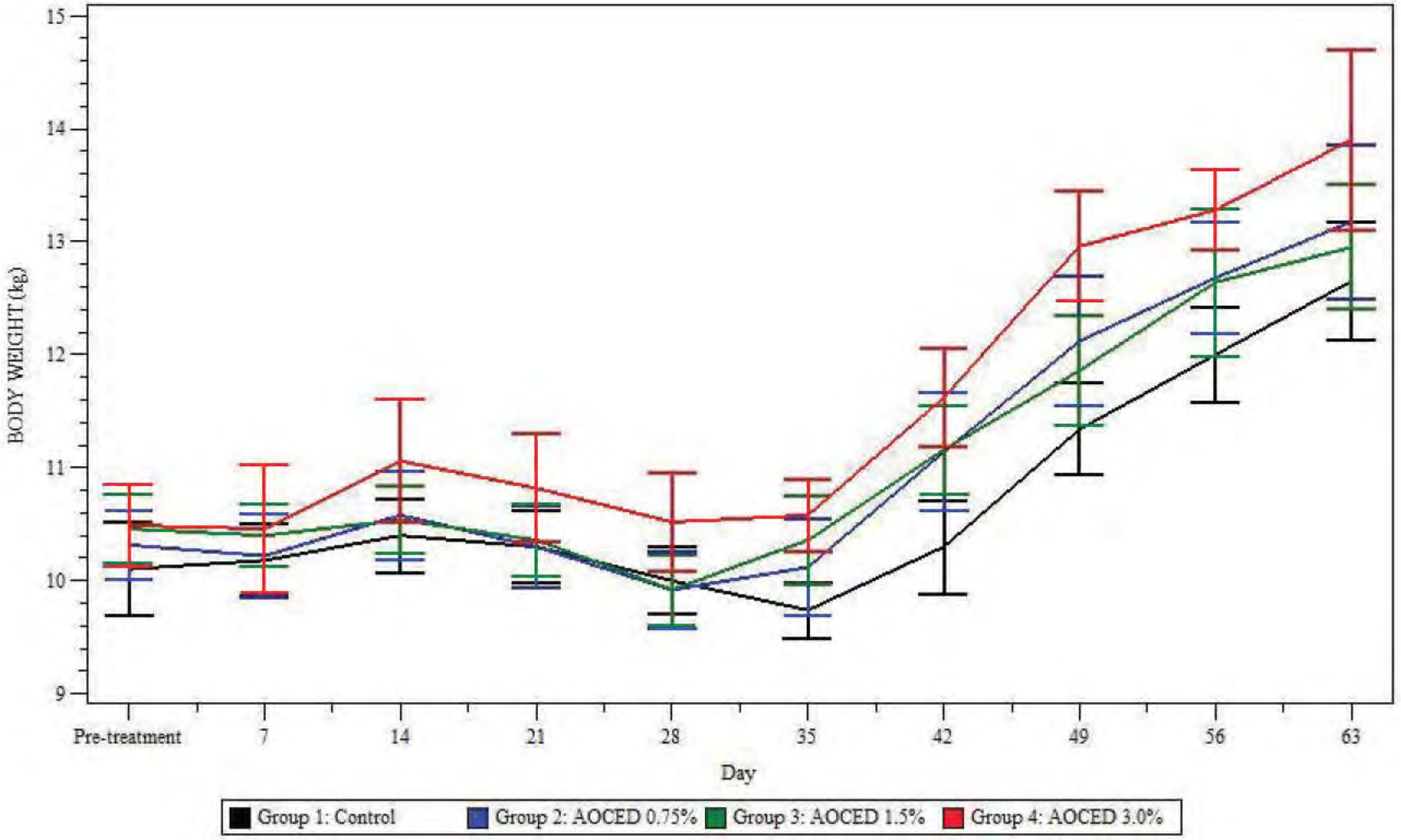
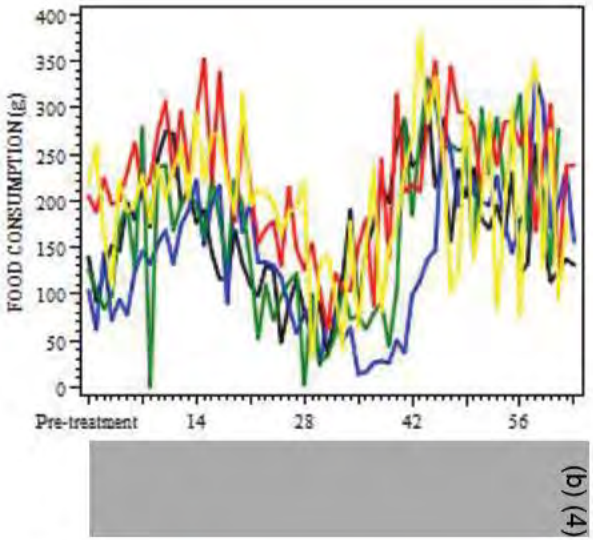
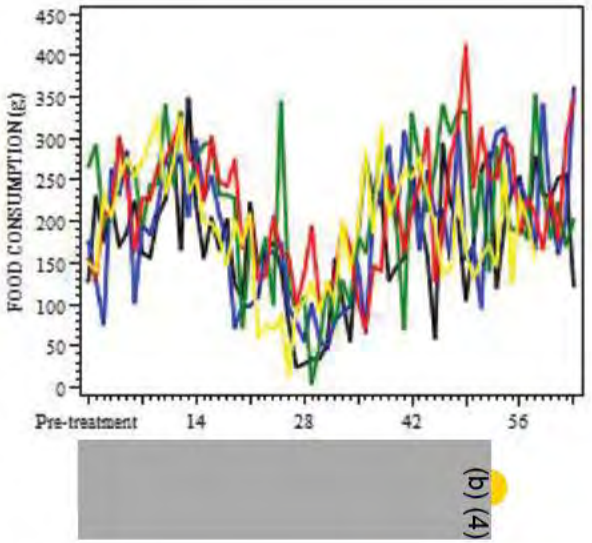
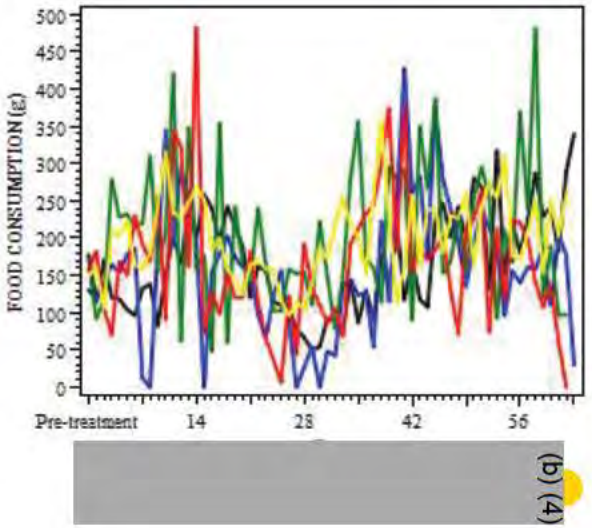


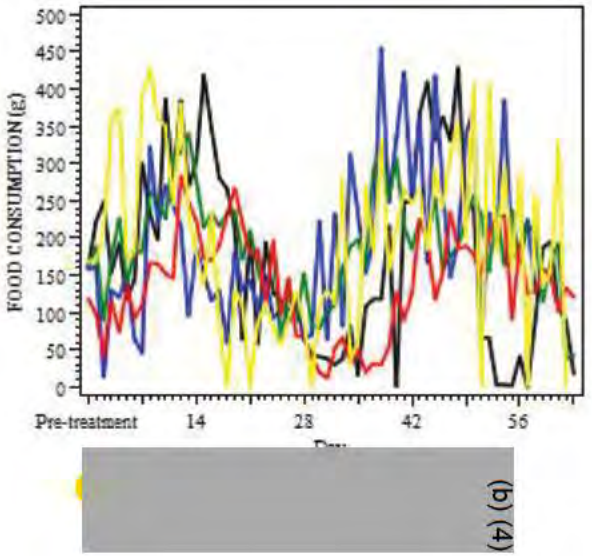
FIGURE NO. 9

GENERATION F0, GESTATION
Individual - Females









(b) (4)

FIGURE NO. 10

(b) (4)

GENERATION F0, GESTATION
Females
Treatment Means ± SEM

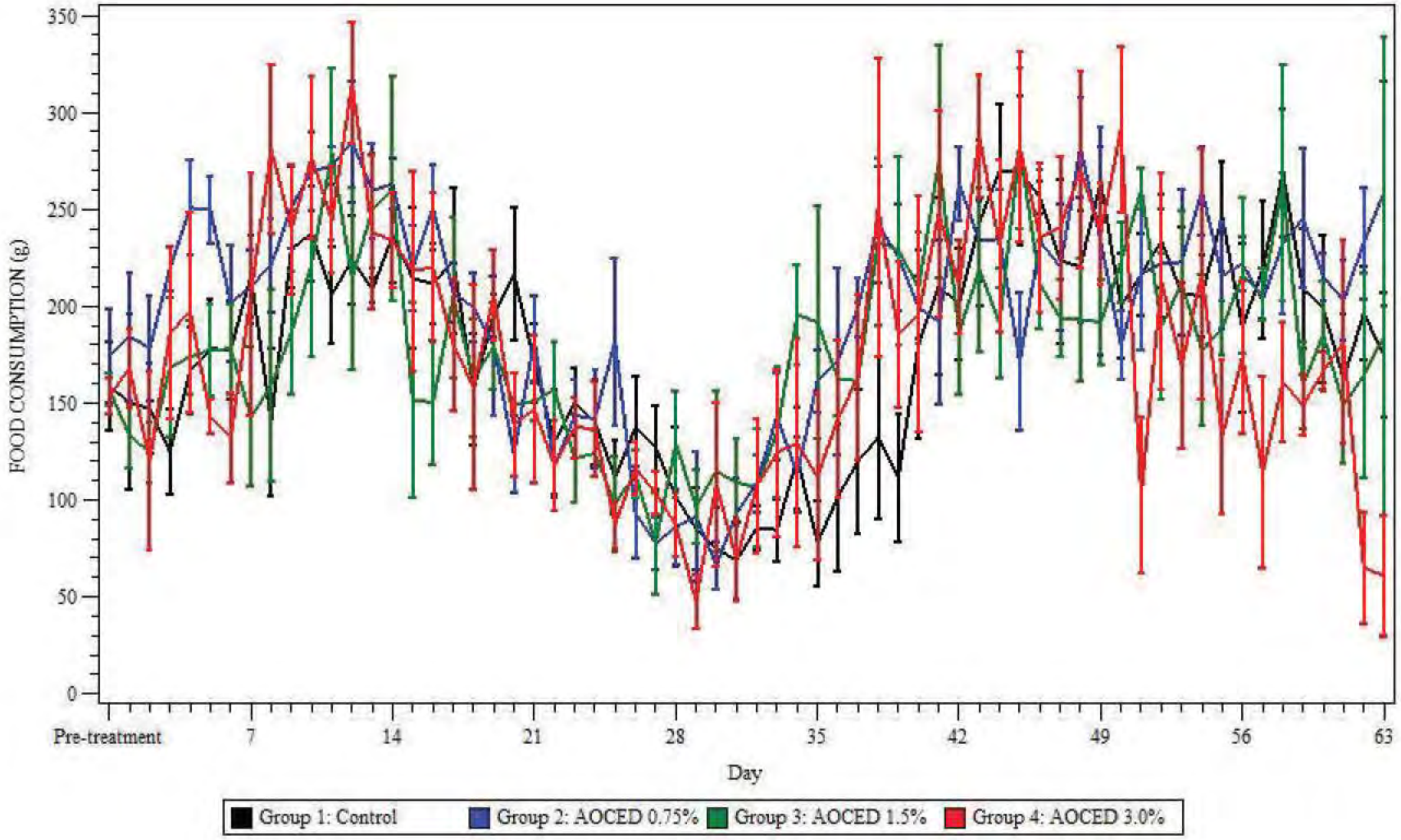
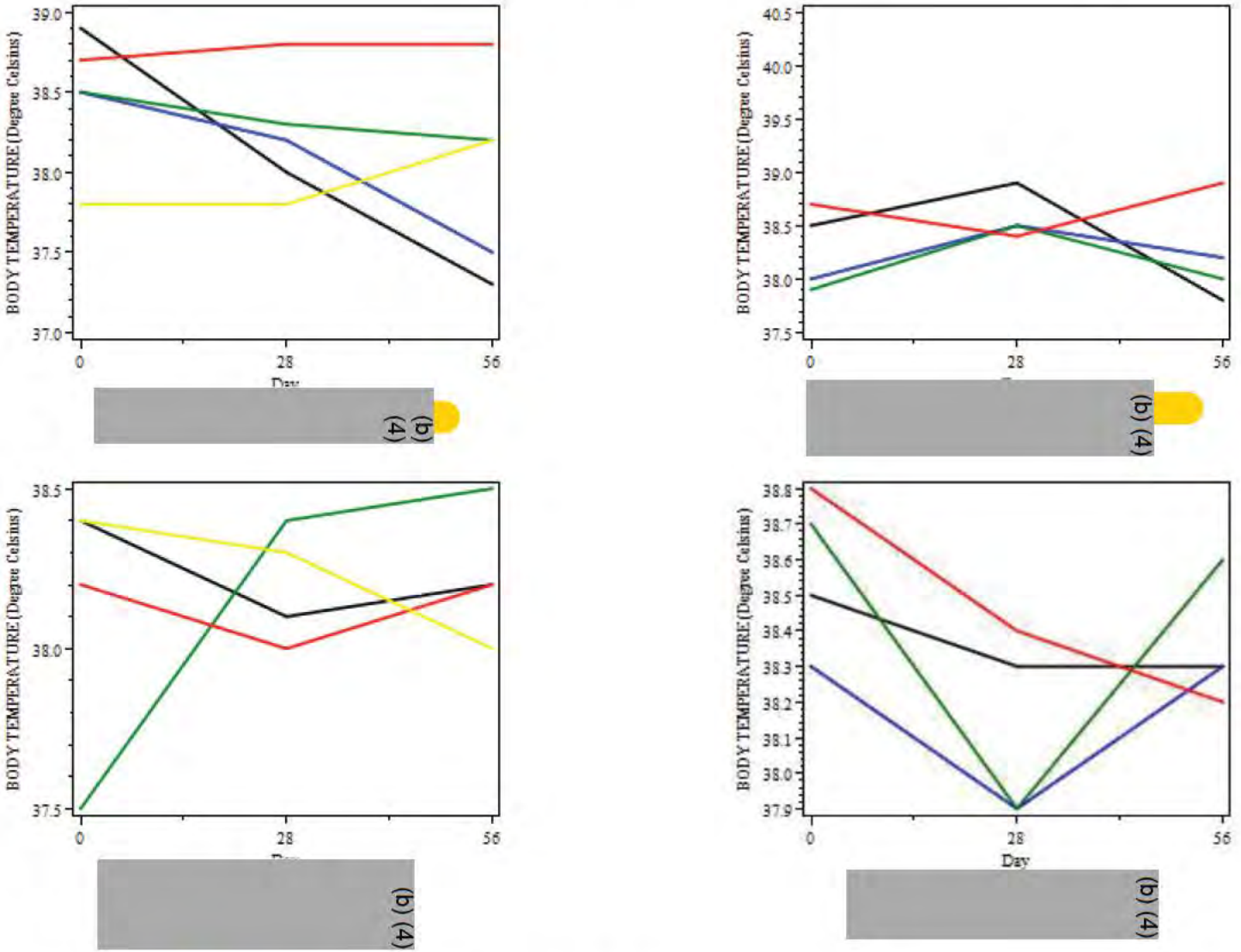


FIGURE NO. 11

(b) (4)

GENERATION F0, LACTATION
Individual - Females



Animal (b) (4) ere released on Day 2 and 5 respectively, therefore they were not present on the graph

FIGURE NO. 12

(b) (4)

GENERATION F0, LACTATION
Females
Treatment Means ± SEM

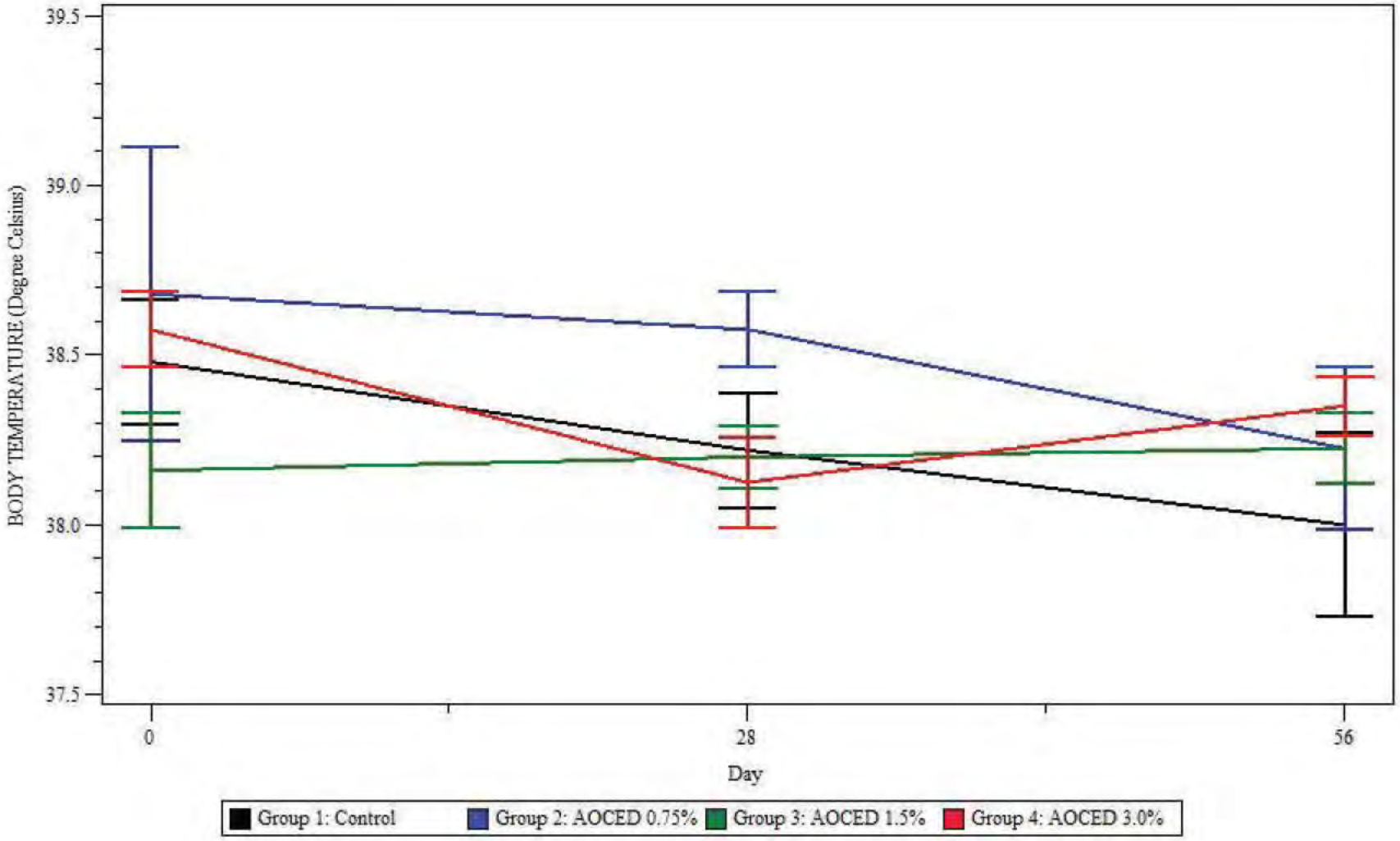
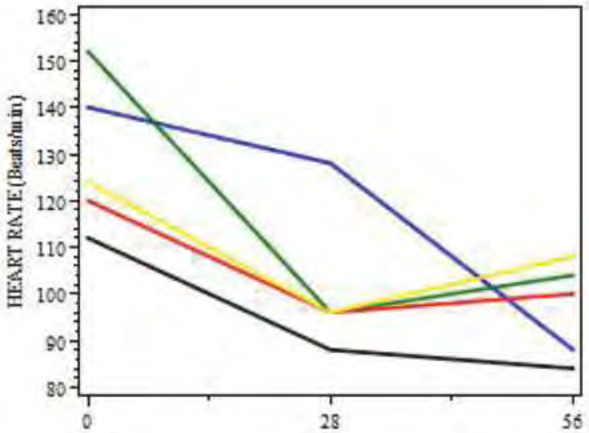


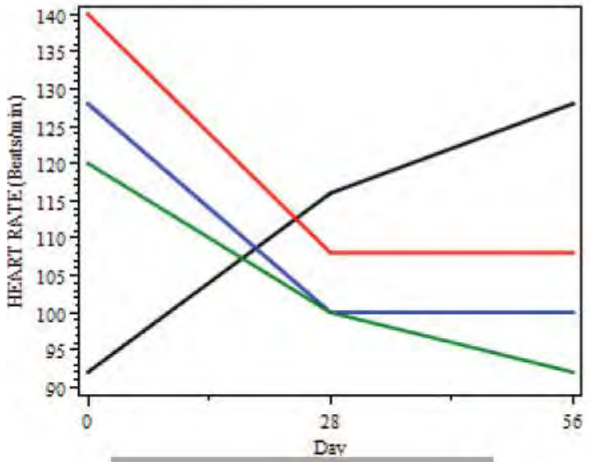
FIGURE NO. 13

(b) (4)

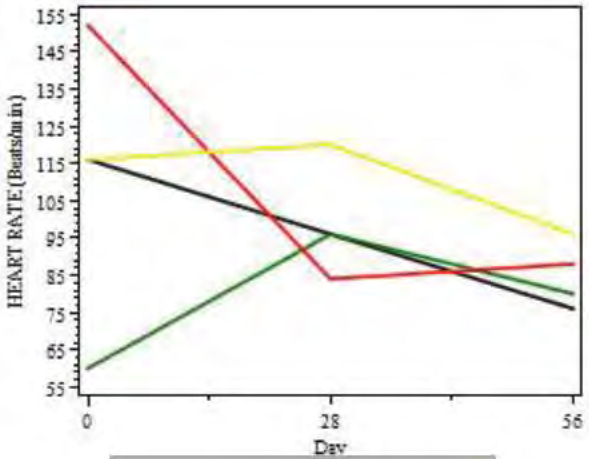
GENERATION F0, LACTATION
Individual - Females



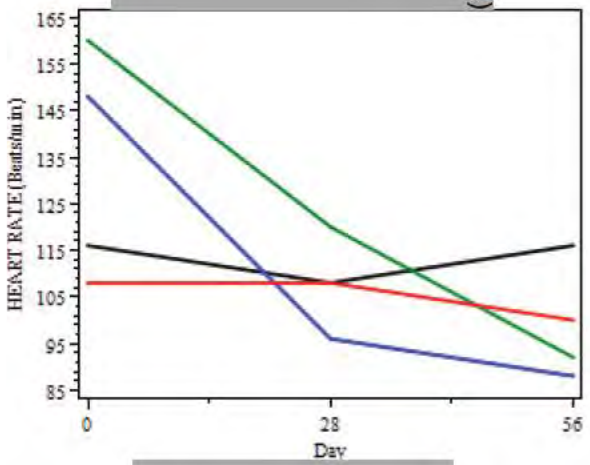
(b) (4)



(b) (4)



(b) (4)



(b) (4)

Animals (b) (4) ere released on Day 2 and 5 respectively, therefore they were not present on the graph

FIGURE NO. 14

(b) (4)

GENERATION F0, LACTATION
Females
Treatment Means ± SEM

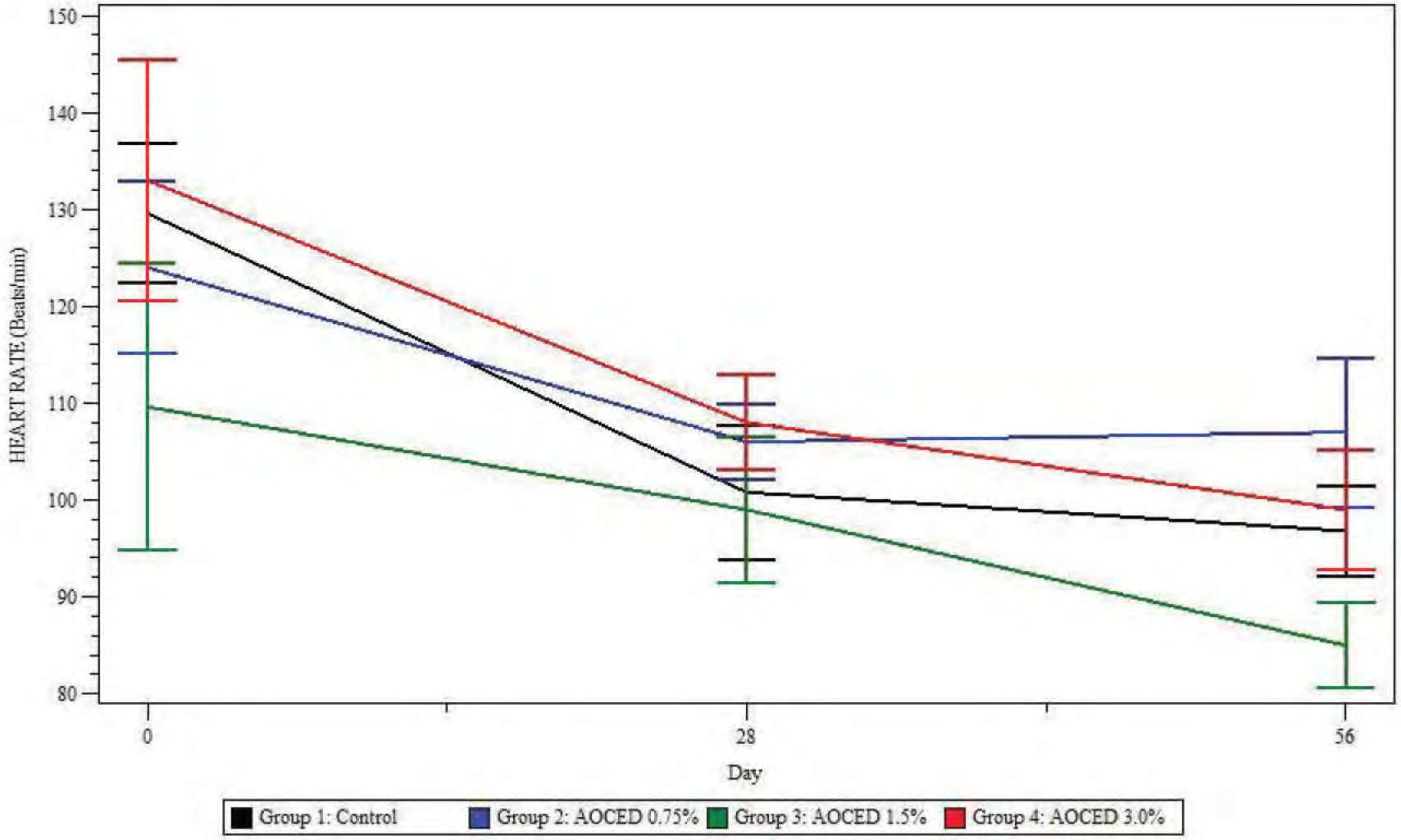
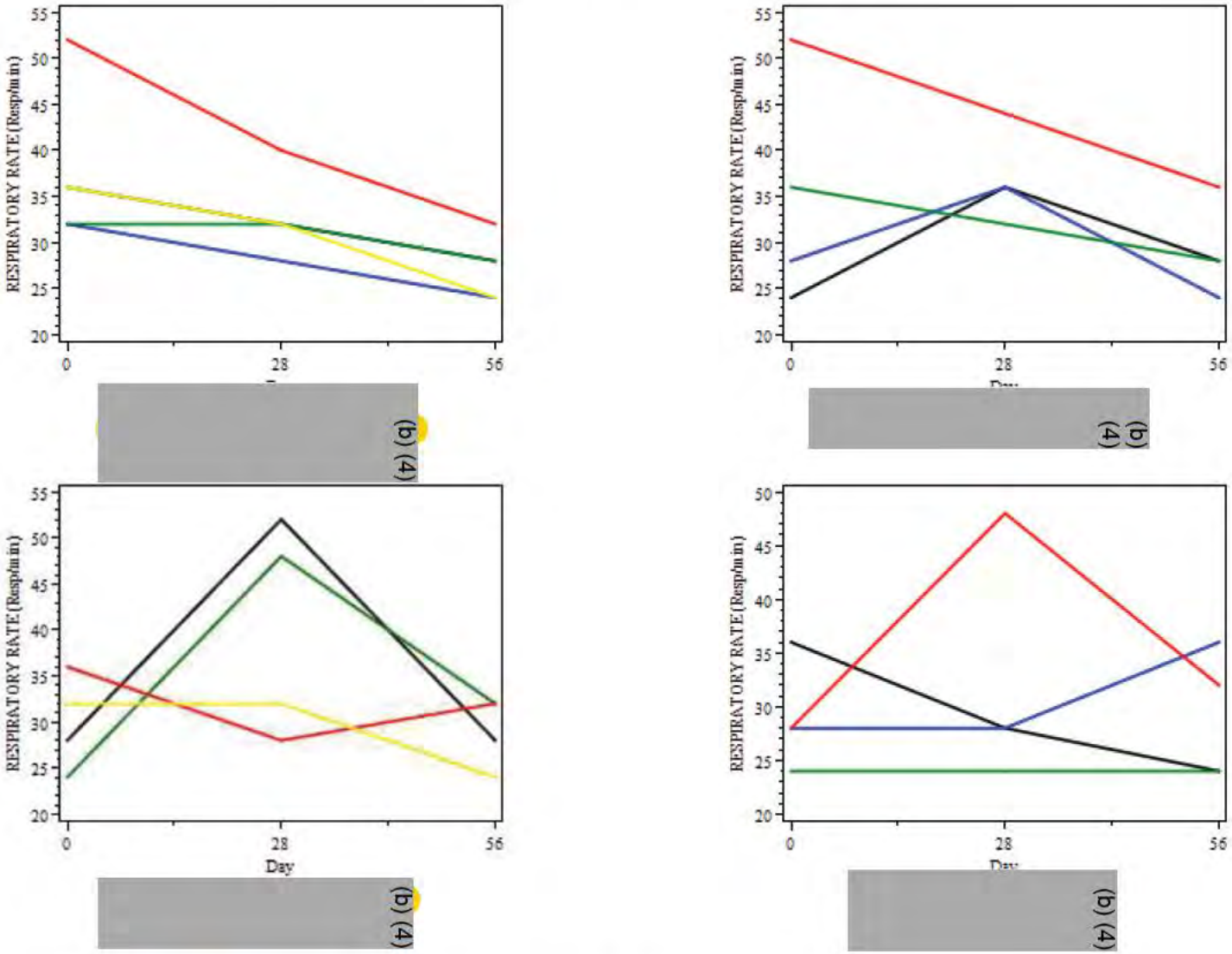


FIGURE NO. 15

(b) (4)

GENERATION F0, LACTATION
Individual - Females



Animal (b) (4) and (b) (4) were released on Day 2 and 5 respectively, therefore they were not present on the graph

FIGURE NO. 16

(b) (4)

GENERATION F0, LACTATION
Females
Treatment Means ± SEM

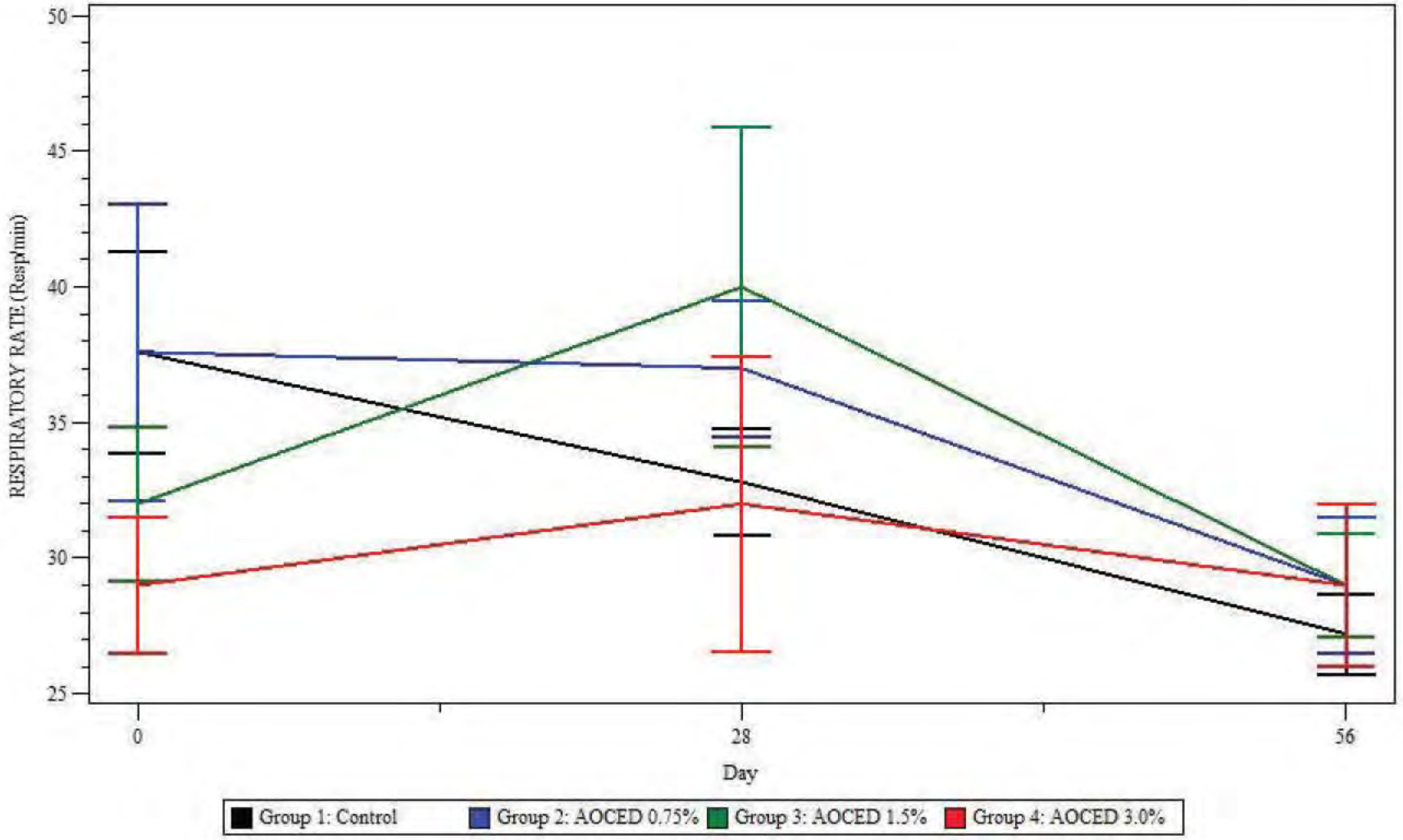
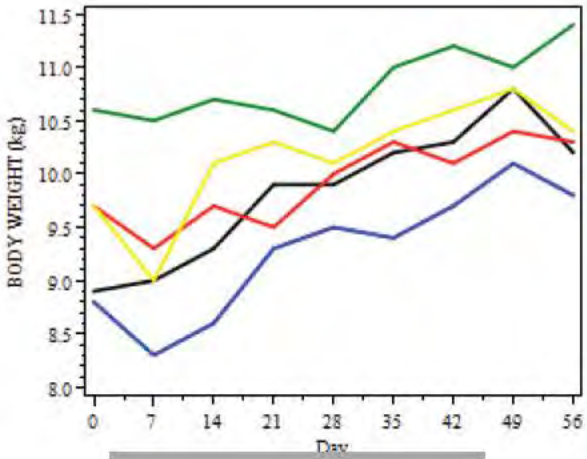


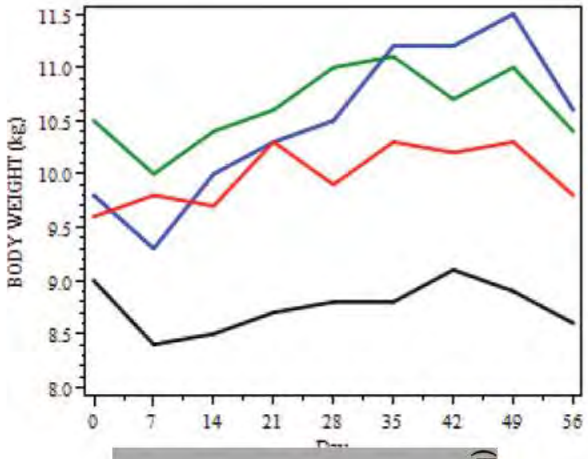
FIGURE NO. 17

(b) (4)

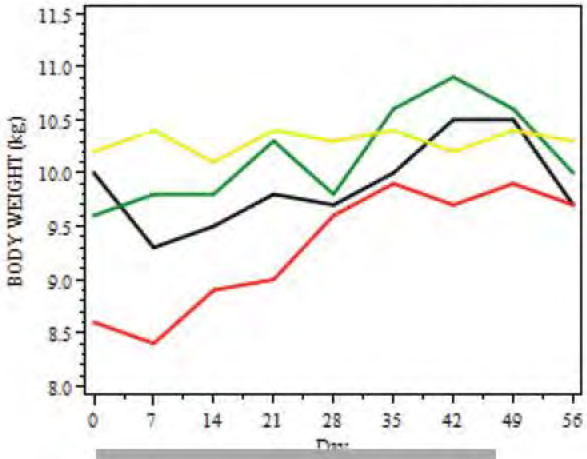
GENERATION F0, LACTATION
Individual - Females



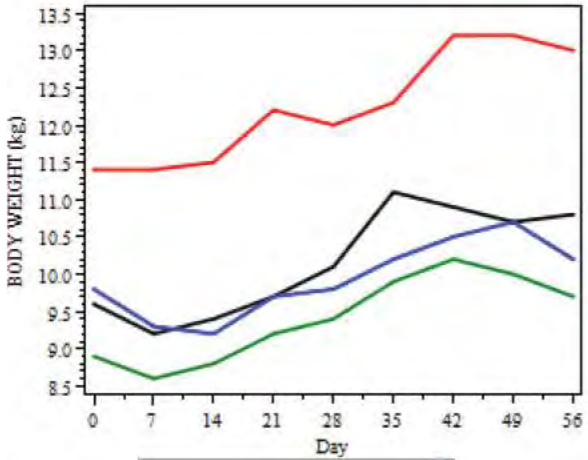
(b) (4)



(b) (4)



(b) (4)



(b) (4)

Animals (b) (4) and (b) (4) were released on Day 2 and 5 respectively, therefore they were not present on the graph

FIGURE NO. 18

[redacted] (b) (4)

GENERATION F0, LACTATION
Females
Treatment Means ± SEM

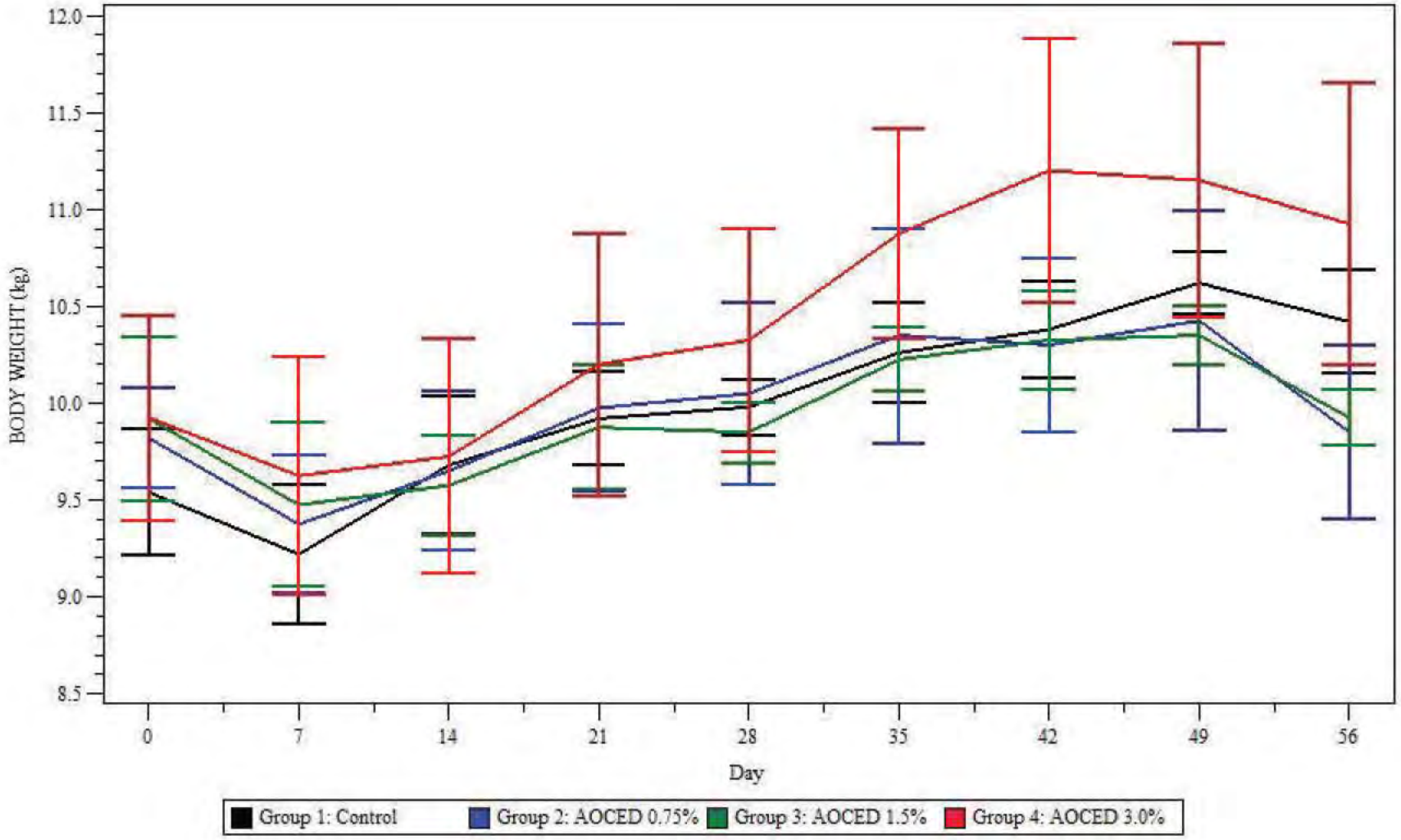
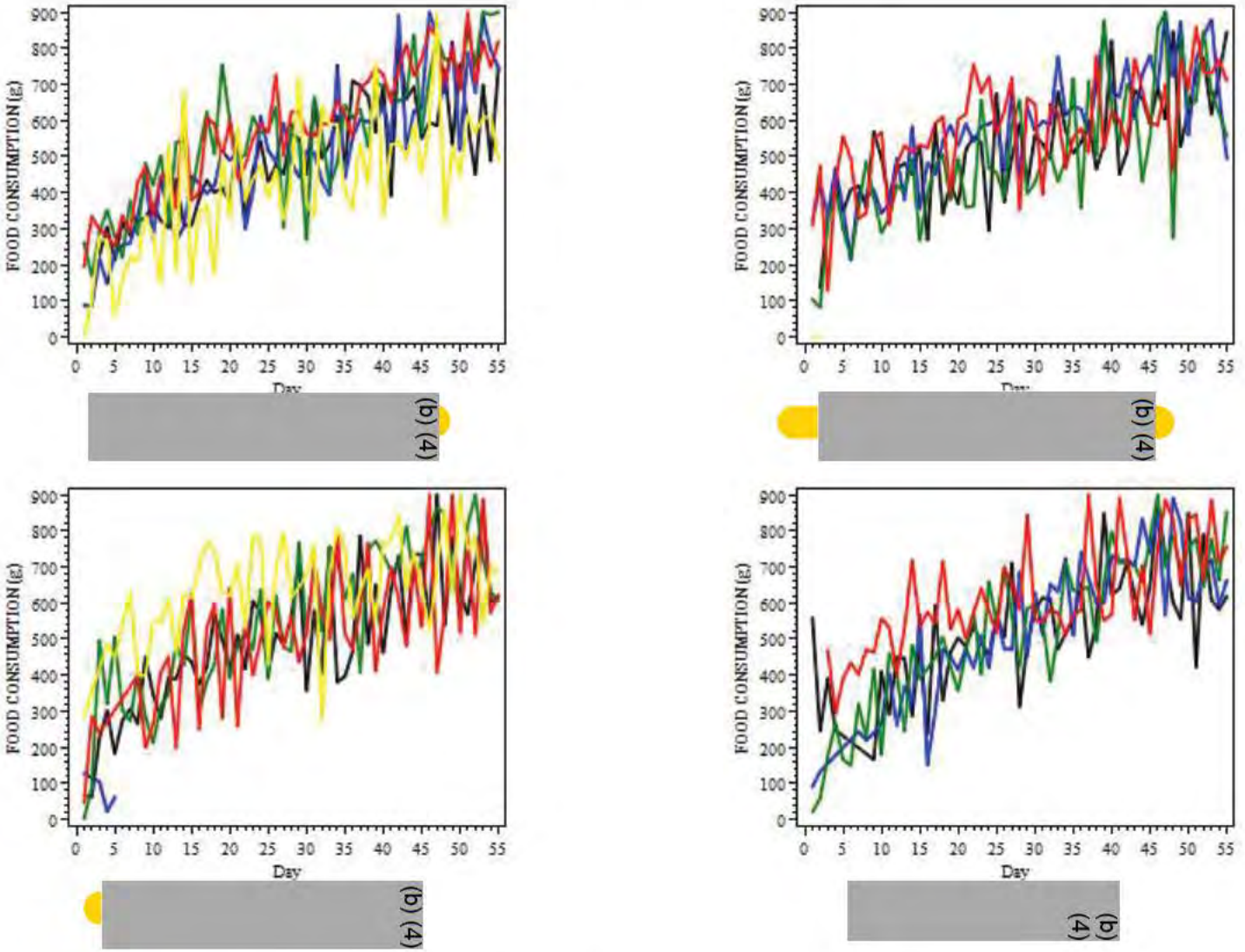


FIGURE NO. 19

(b) (4)

GENERATION F0, LACTATION
Individual - Females



Animals (b) (4) was released on Day 2, therefore it was not present on the graph

FIGURE NO. 20

(b) (4)

GENERATION F0, LACTATION
Females
Treatment Means ± SEM

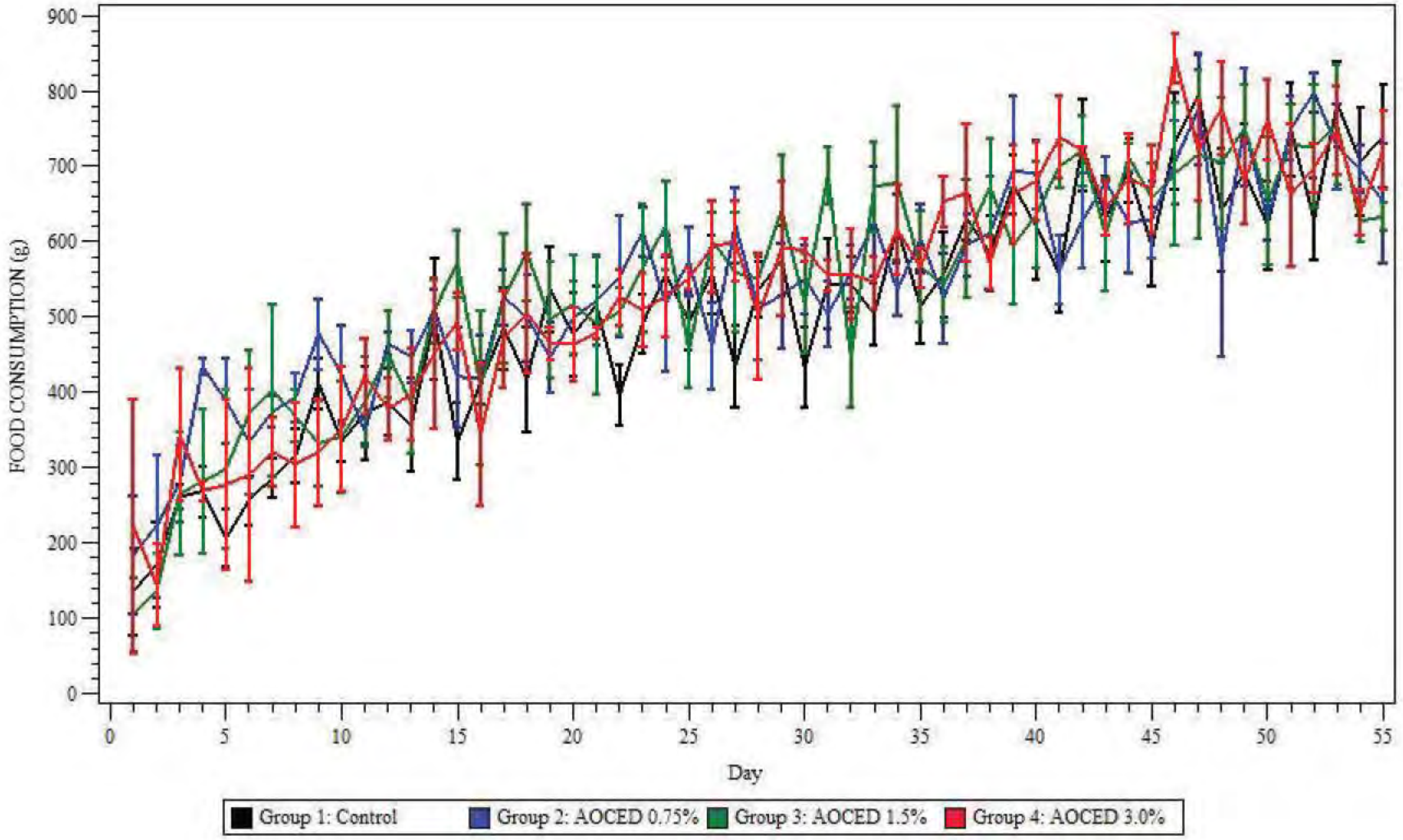
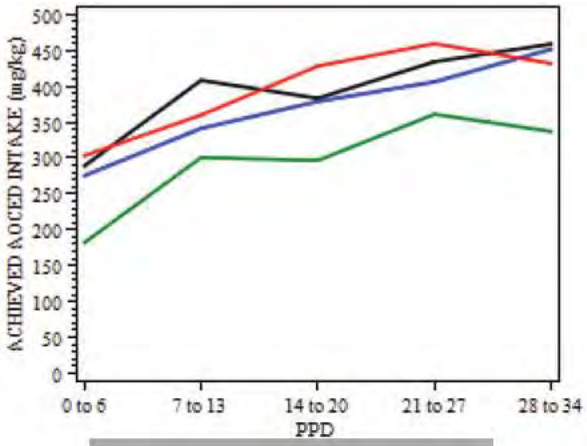


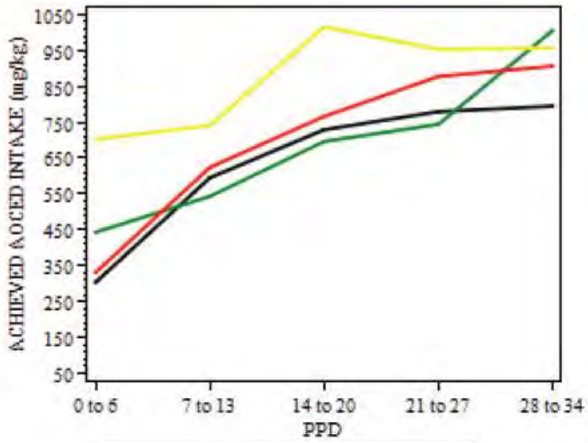
FIGURE NO. 21

(b) (4)

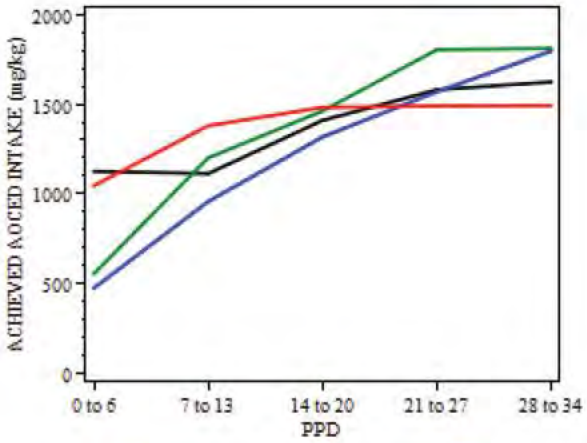
GENERATION F0, LACTATION PPD0 to PPD35
Individual - Females



(b) (4)



(b) (4)



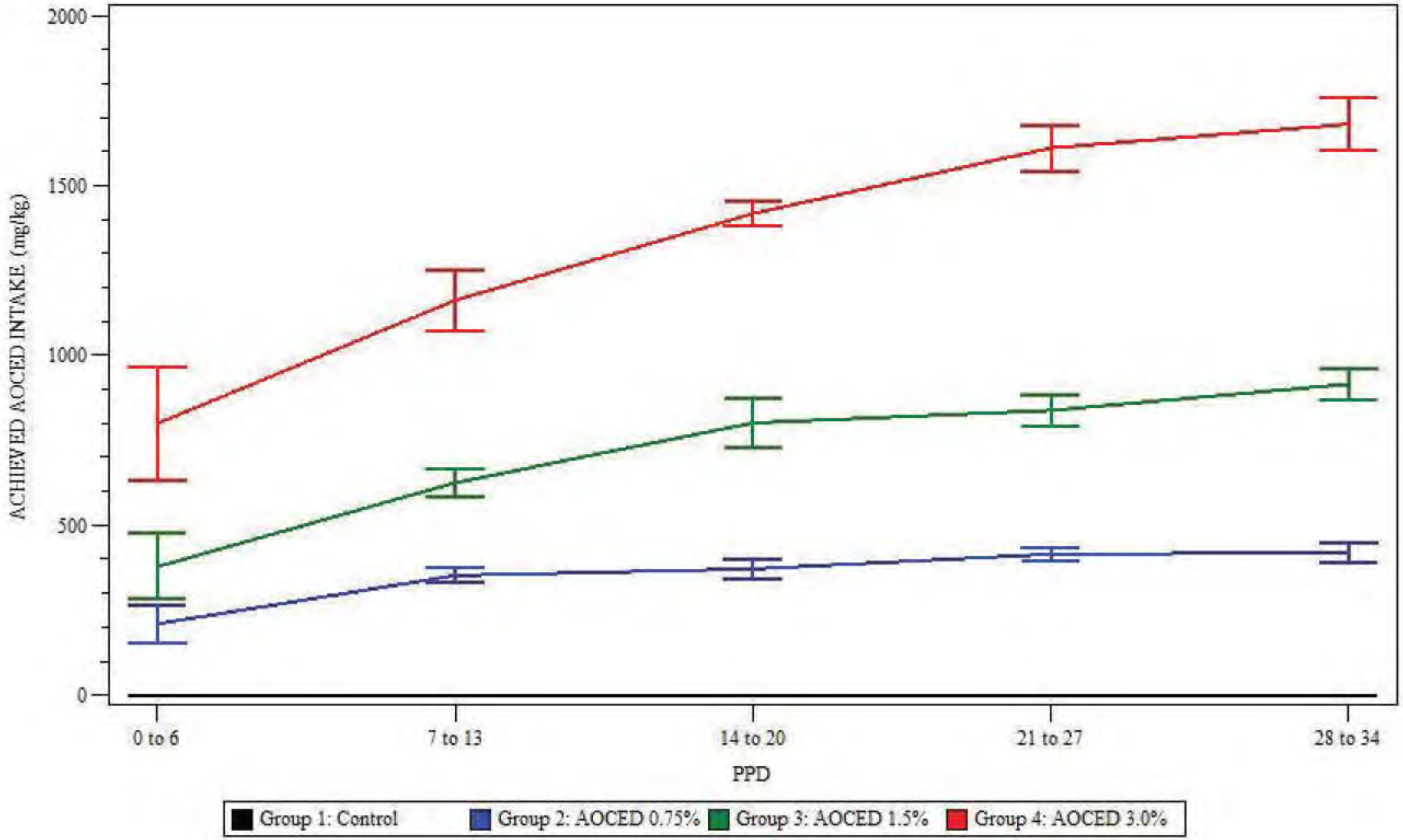
(b) (4)

Animals (b) (4) and (b) (4) were released on Day 2 and 5 respectively, therefore they were not present on the graph

FIGURE NO. 22

(b) (4)

GENERATION F0, LACTATION PPD0 to PPD35
Females
Treatment Means ± SEM

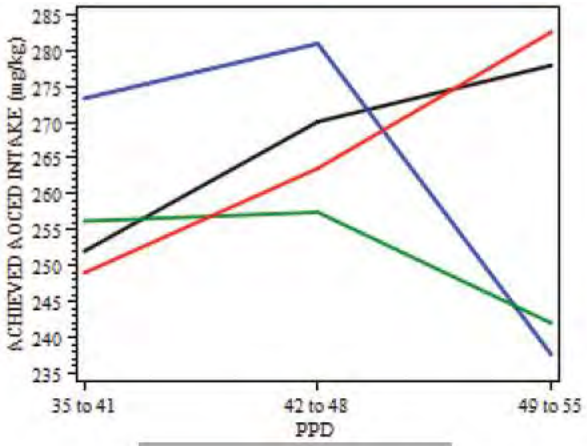


FIGURES
F0 AND F1 GENERATIONS - LACTATION

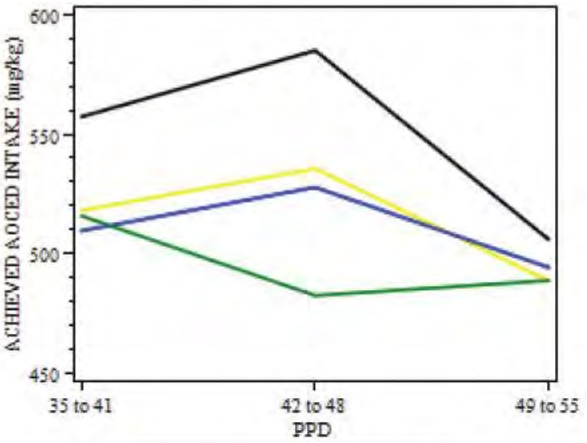
FIGURE NO. 23

(b) (4)

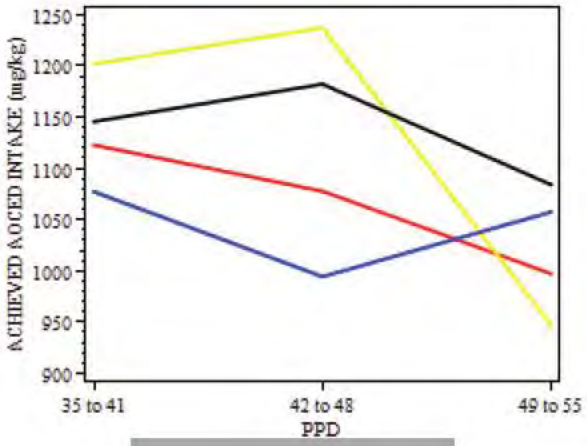
GENERATION F0 AND F1, LACTATION PPD35 to PPD55
Individual - Females



(b) (4)



(b) (4)

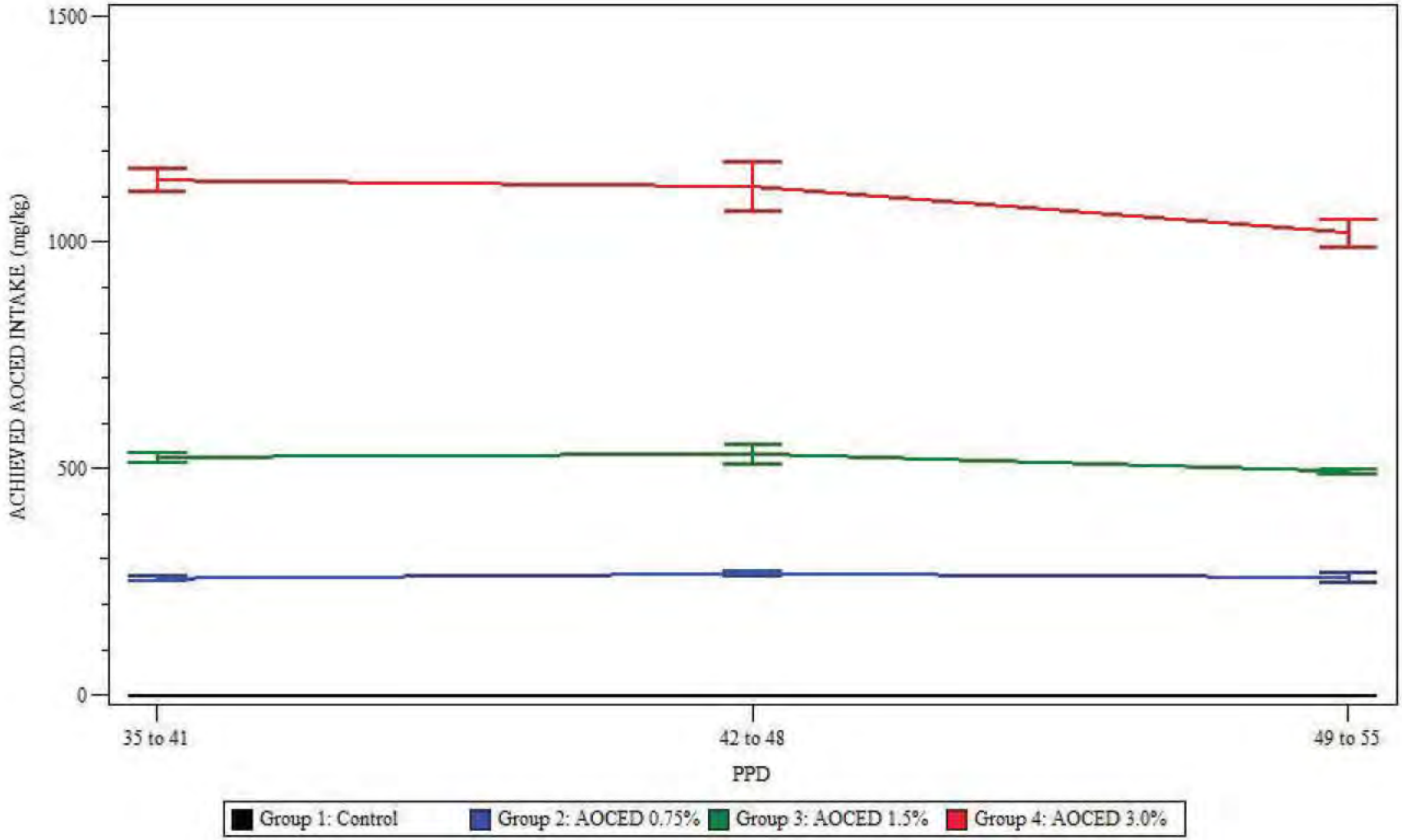


(b) (4)

FIGURE NO. 24

(b) (4)

GENERATION F0 AND F1, LACTATION PPD35 to PPD55
Females
Treatment Means ± SEM



FIGURES
F1 PUPPIES PRE-WEANING

FIGURE NO. 25

GENERATION F1, LACTATION
MALE PUPS
Litter Means

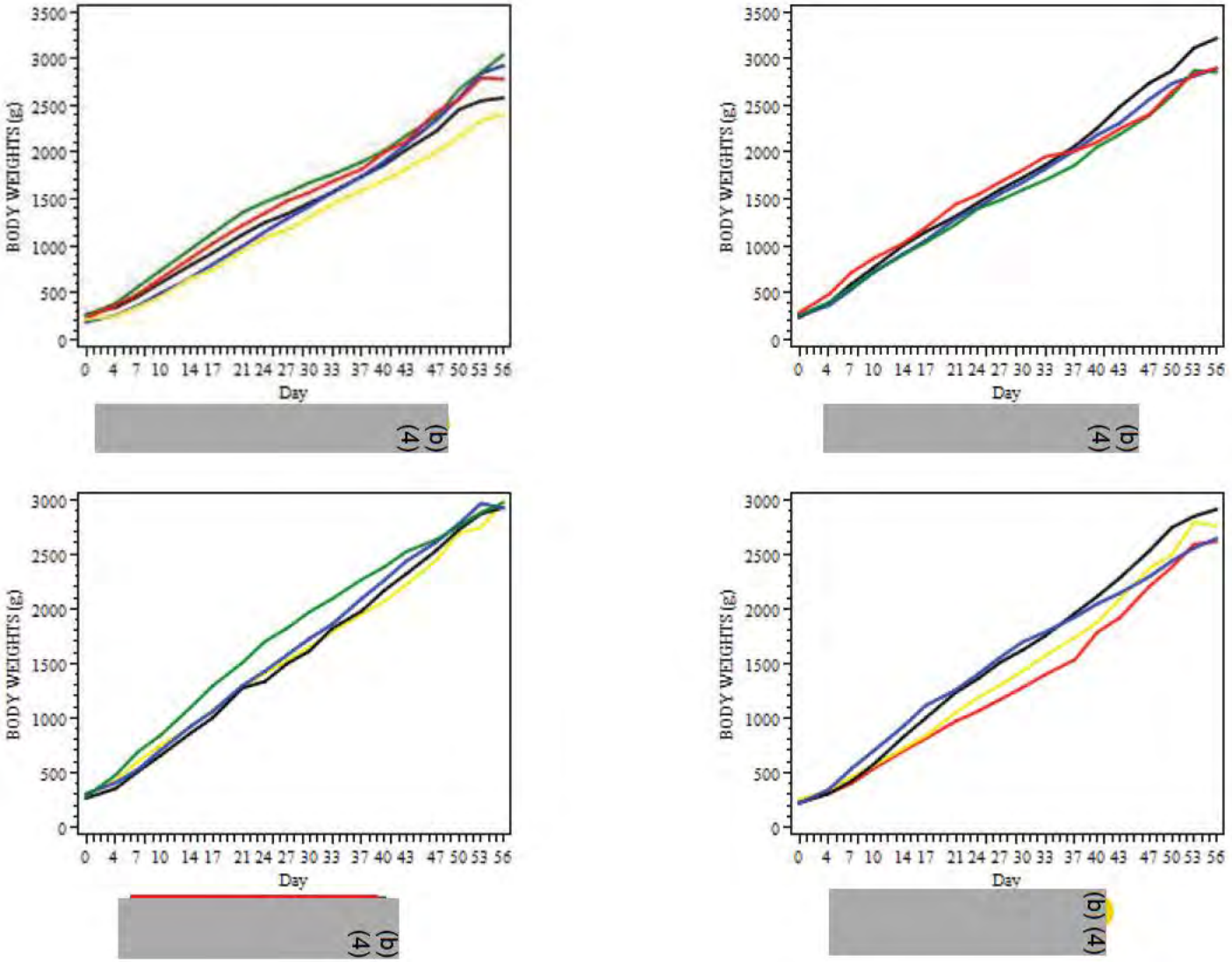
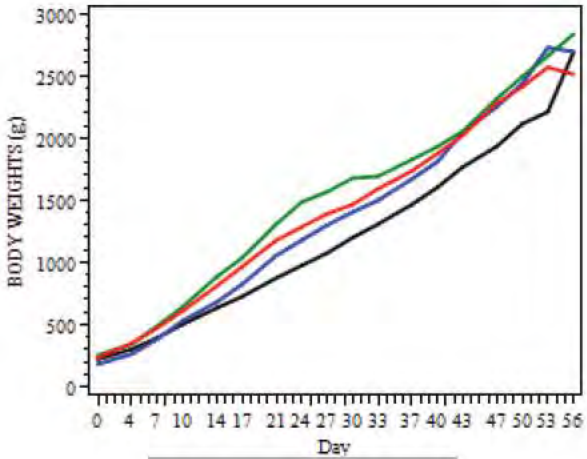


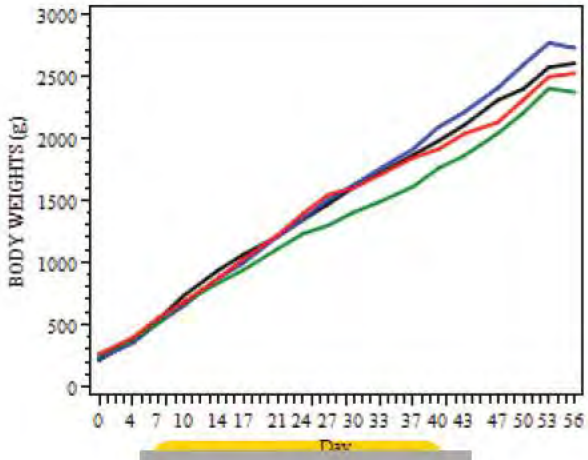
FIGURE NO. 26

(b) (4)

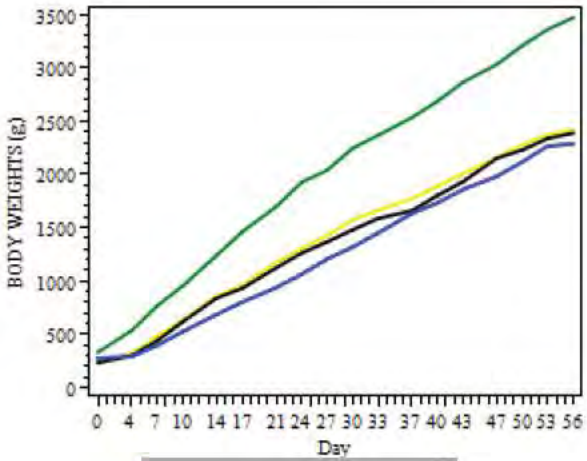
GENERATION F1, LACTATION
FEMALE PUPS
Litter Means



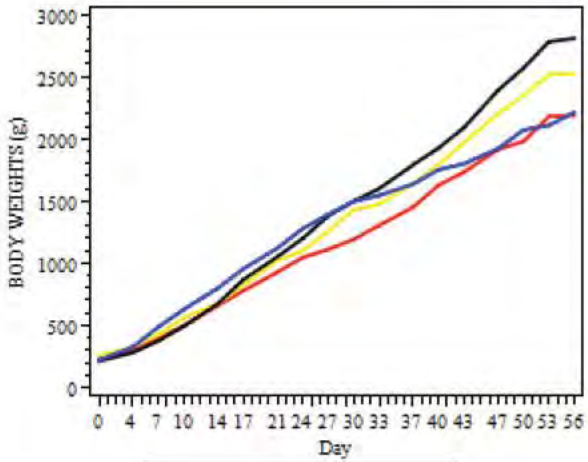
(b) (4)



(b) (4)



(b) (4)

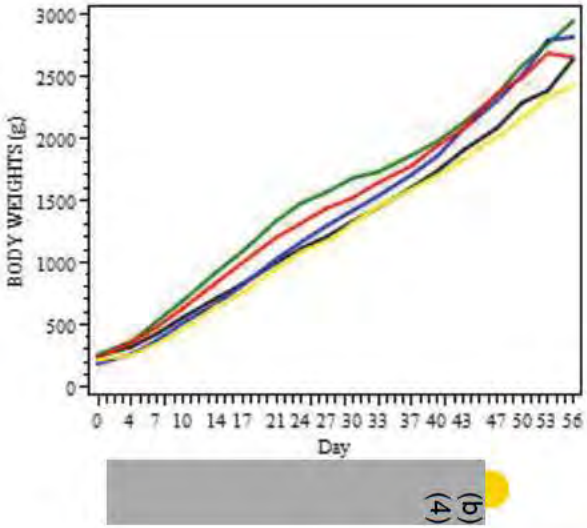


(b) (4)

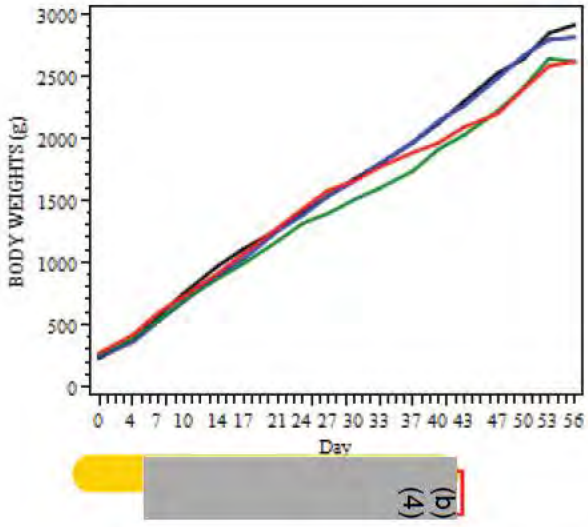
FIGURE NO. 27

(b) (4)

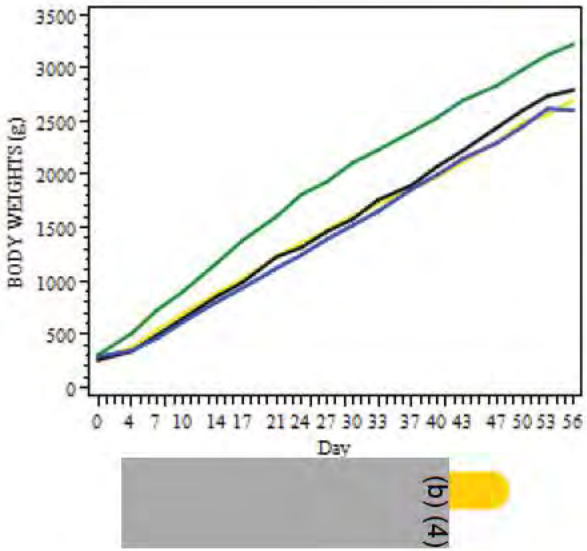
GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Litter Means



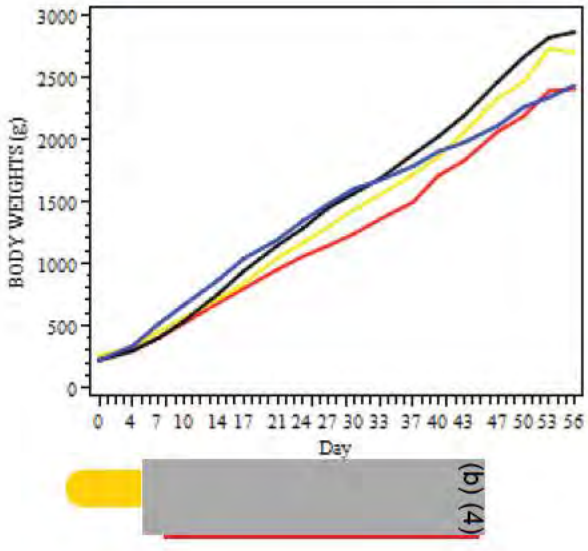
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 28

(b) (4)

GENERATION F1, LACTATION
MALE PUPS
Treatment Means based on Litter Means ± SEM

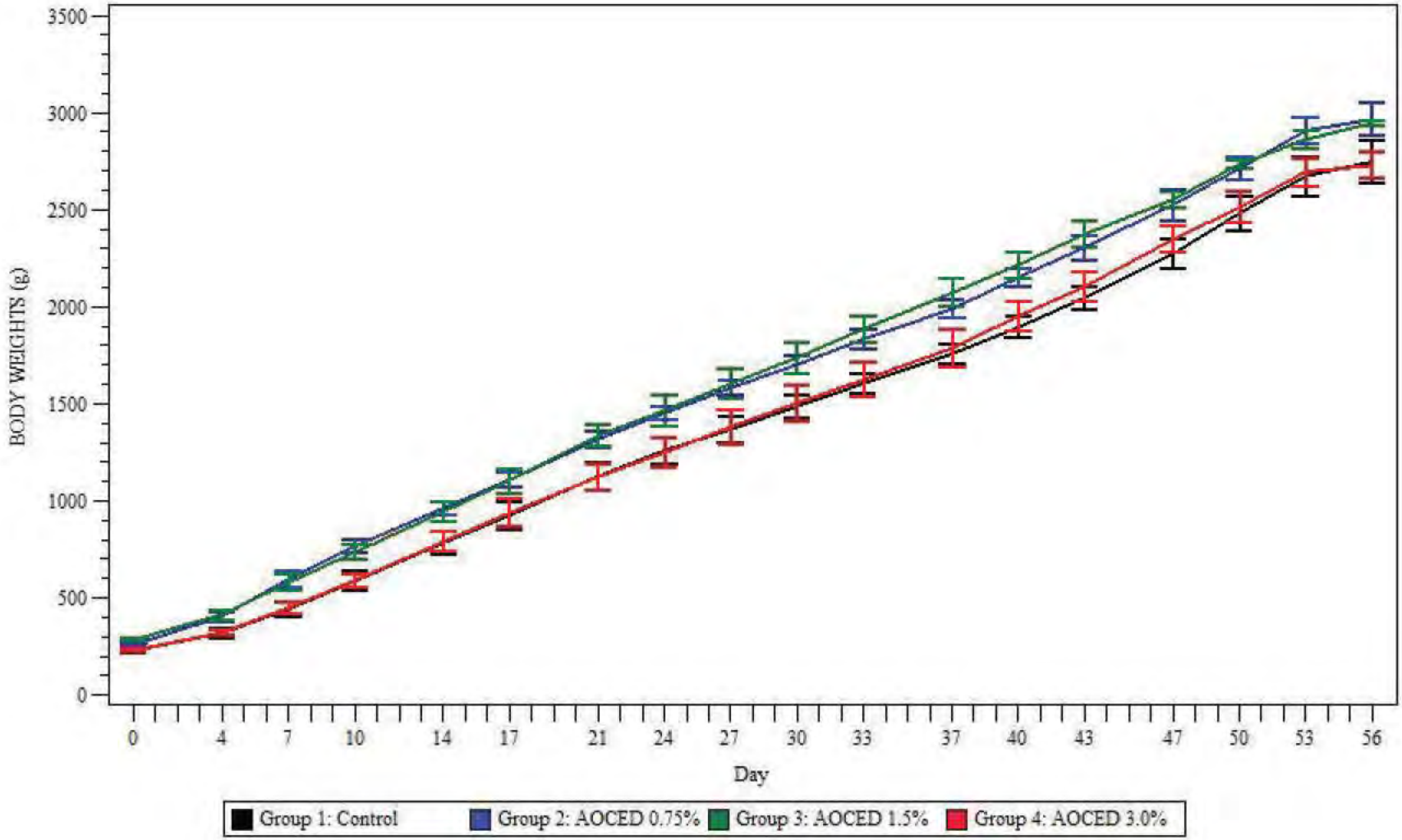


FIGURE NO. 29

(b) (4)

GENERATION F1, LACTATION
FEMALE PUPS
Treatment Means based on Litter Means ± SEM

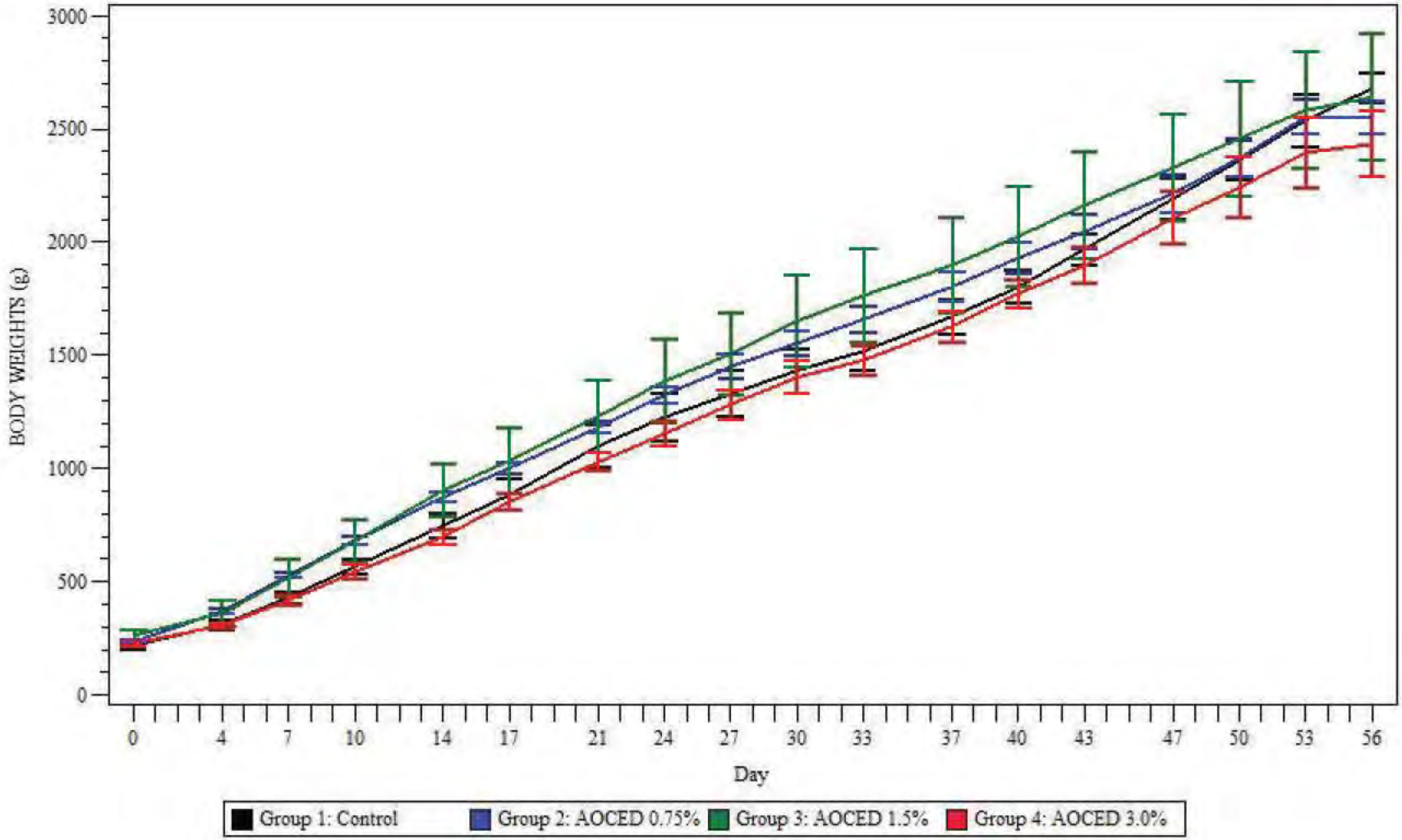


FIGURE NO. 30

(b) (4)

GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Treatment Means based on Litter Means ± SEM

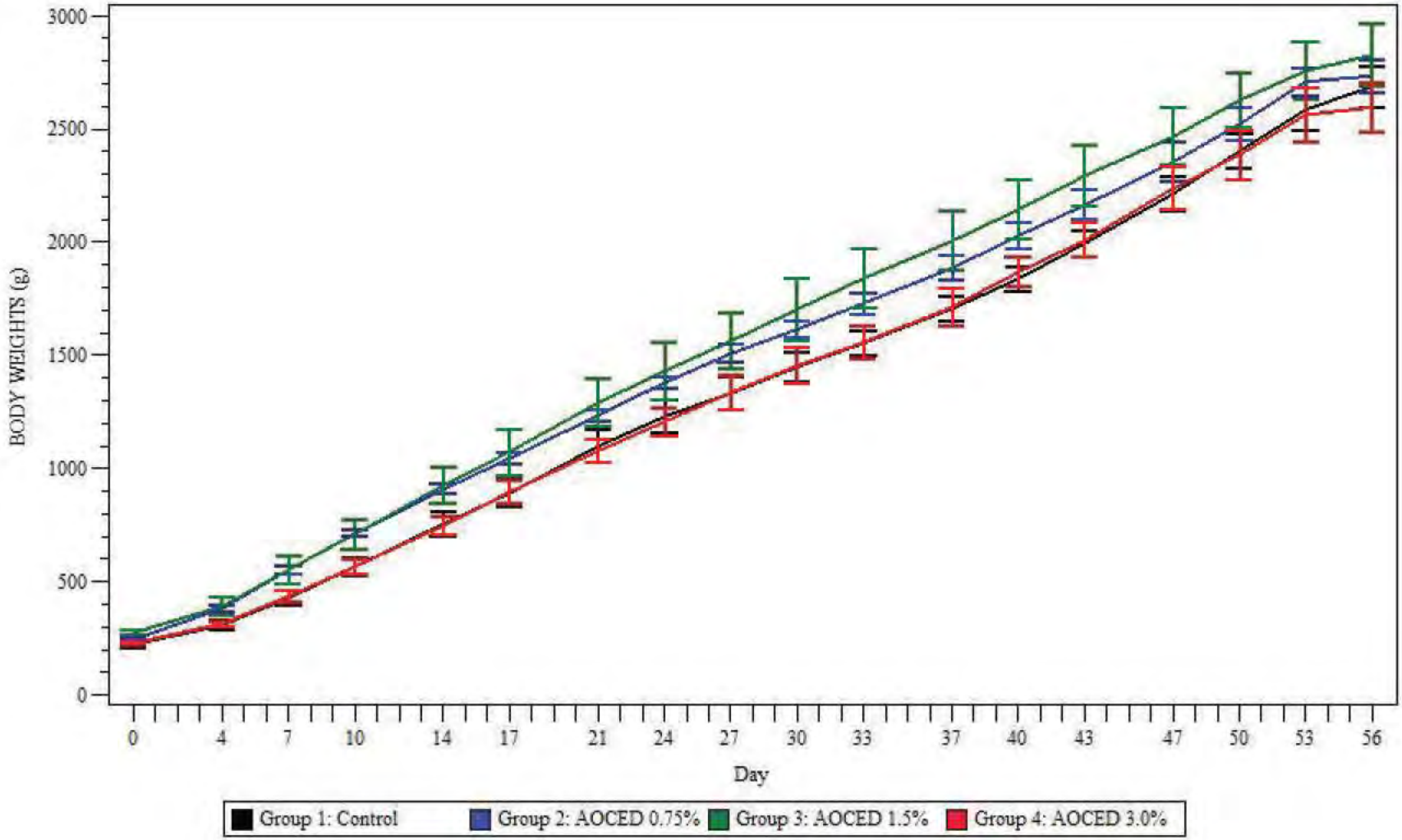
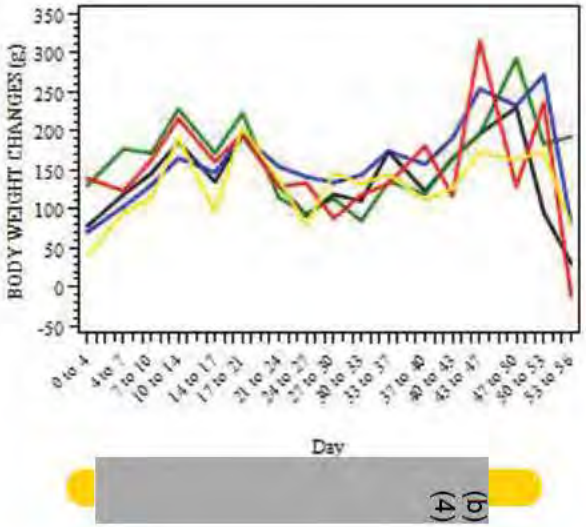
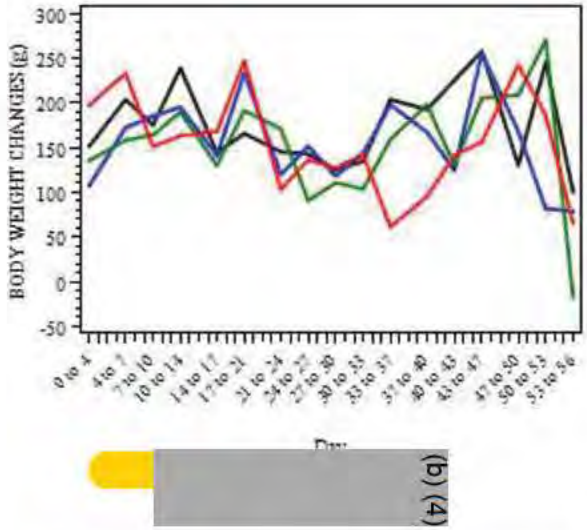


FIGURE NO. 31

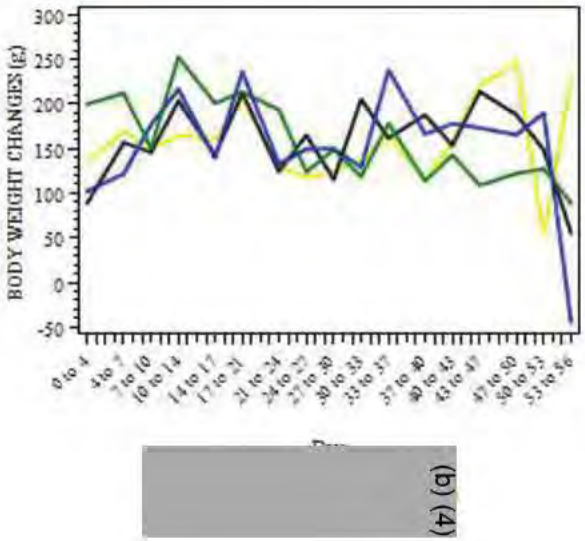
GENERATION F1, LACTATION
MALE PUPS
Litter Means



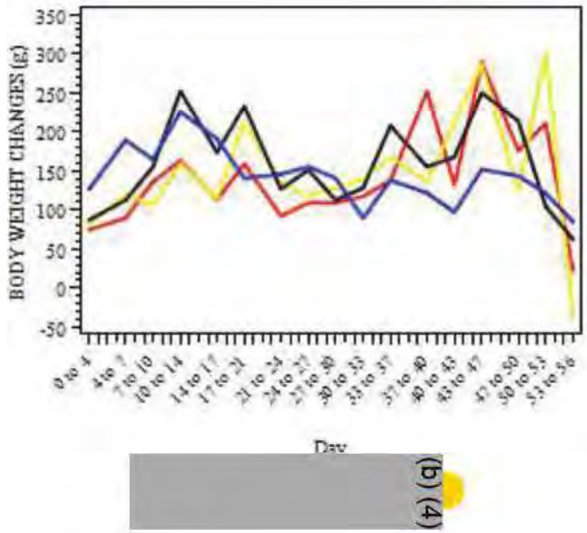
(b) (4)



(b) (4)



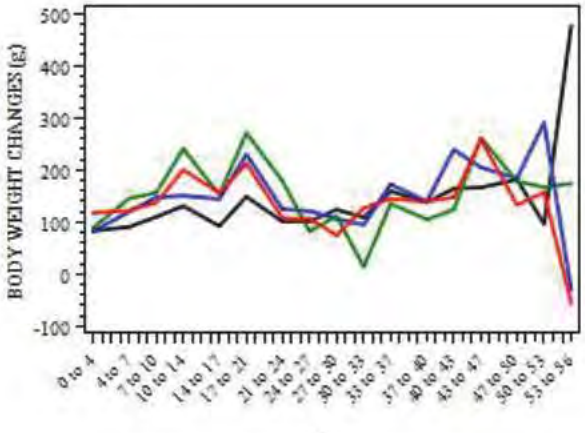
(b) (4)



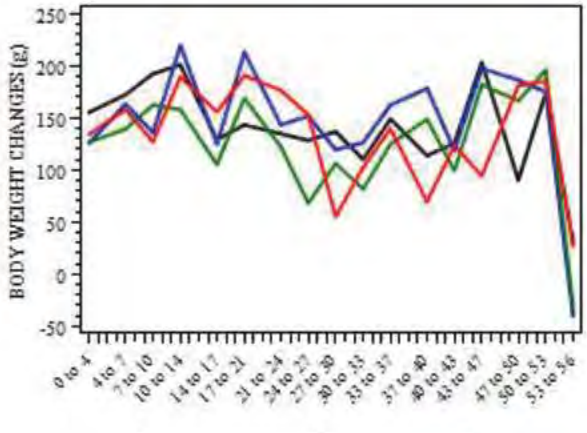
(b) (4)

FIGURE NO. 32

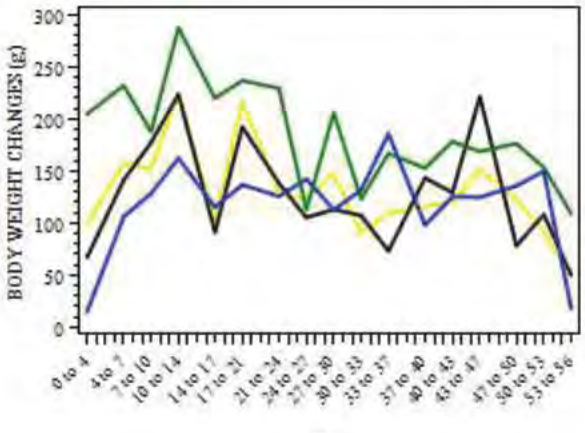
GENERATION F1, LACTATION
FEMALE PUPS
Litter Means



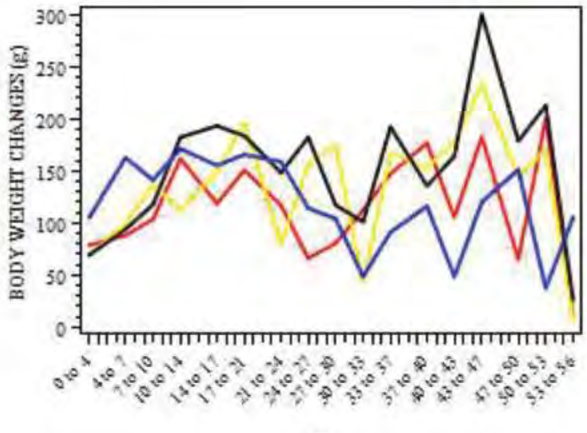
(b) (4)



(b) (4)



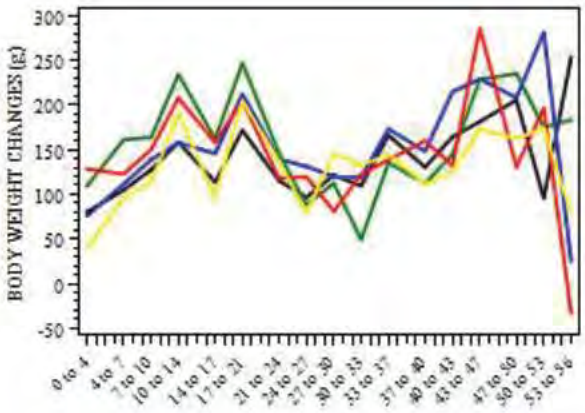
(b) (4)



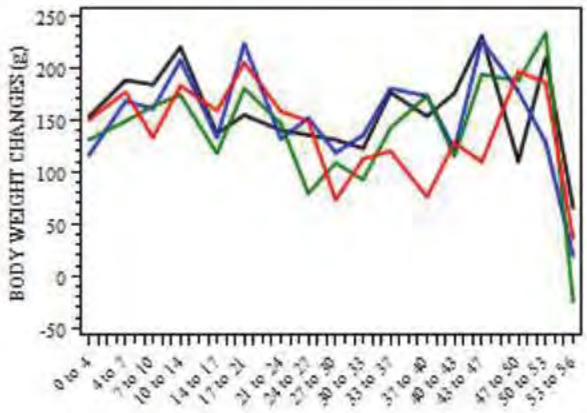
(b) (4)

FIGURE NO. 33

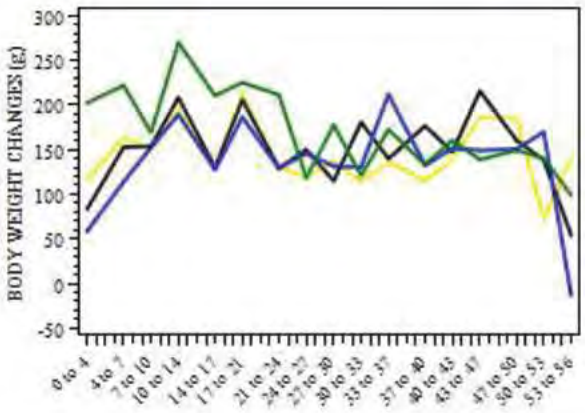
GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Litter Means



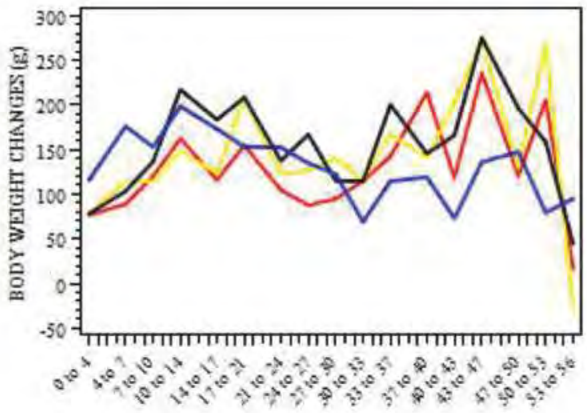
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 34

(b) (4)

GENERATION F1, LACTATION
MALE PUPS
Treatment Means based on Litter Means ± SEM

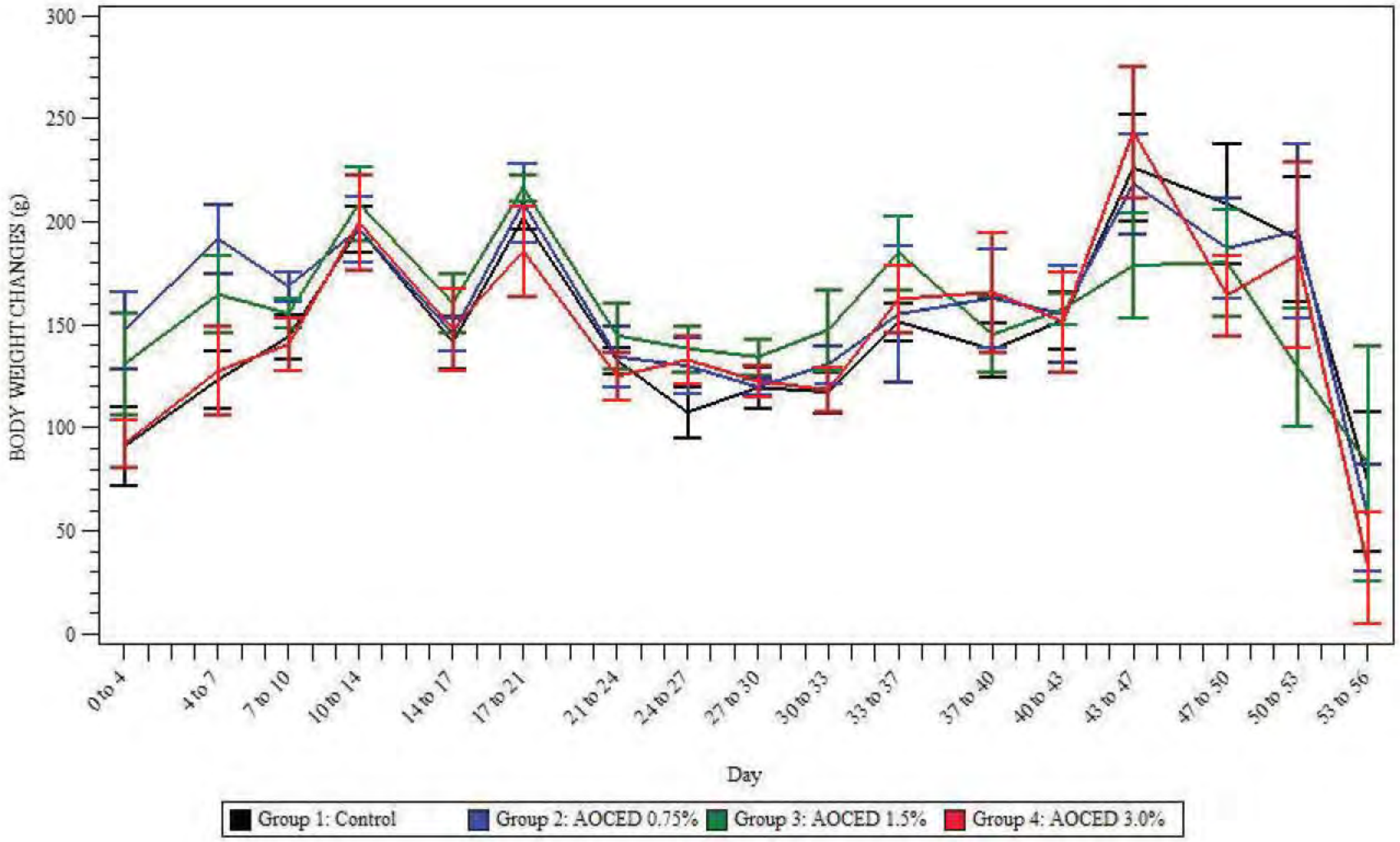


FIGURE NO. 35

(b)(4)

GENERATION F1, LACTATION
FEMALE PUPS
Treatment Means based on Litter Means ± SEM

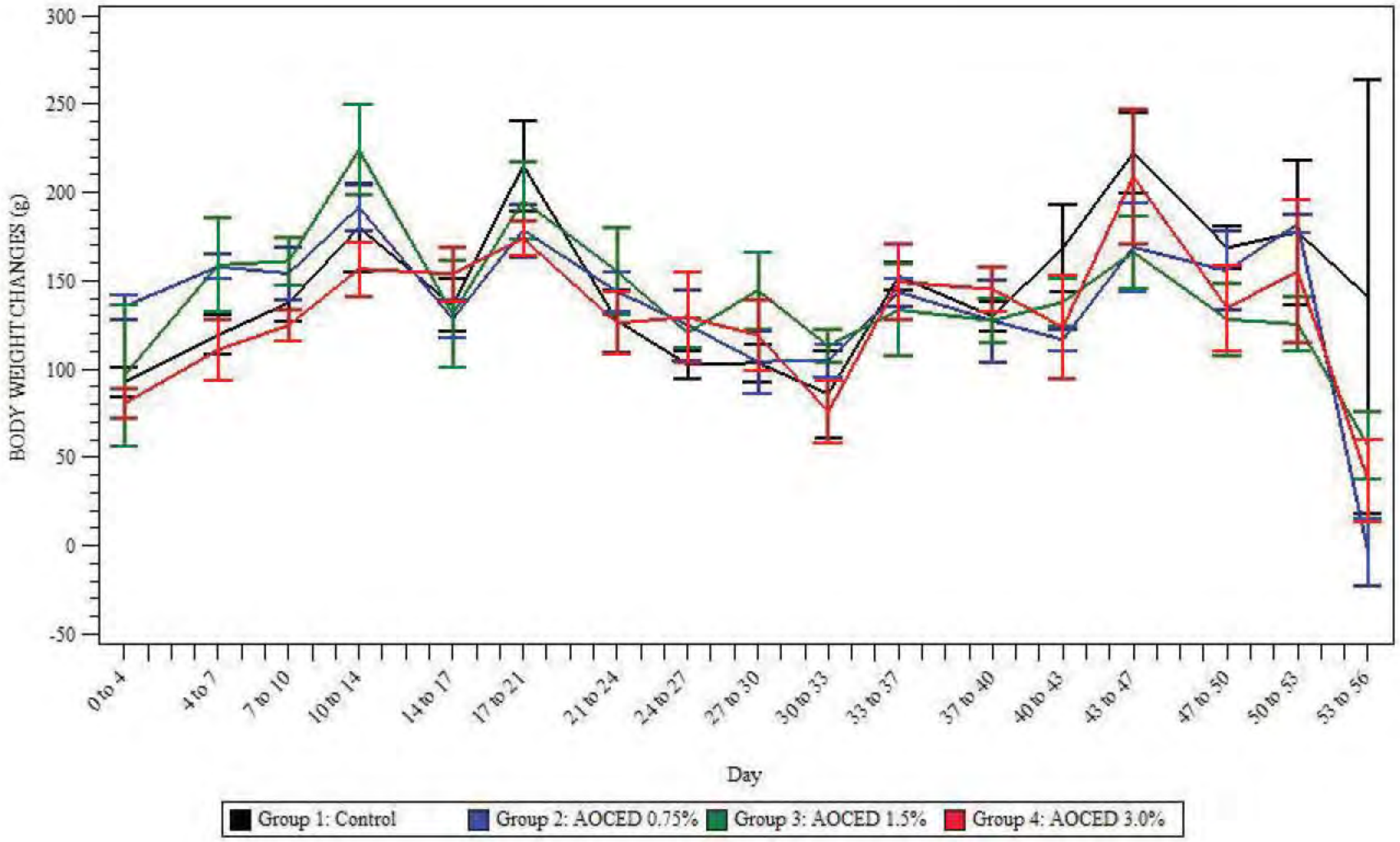


FIGURE NO. 36

(b) (4)

GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Treatment Means based on Litter Means ± SEM

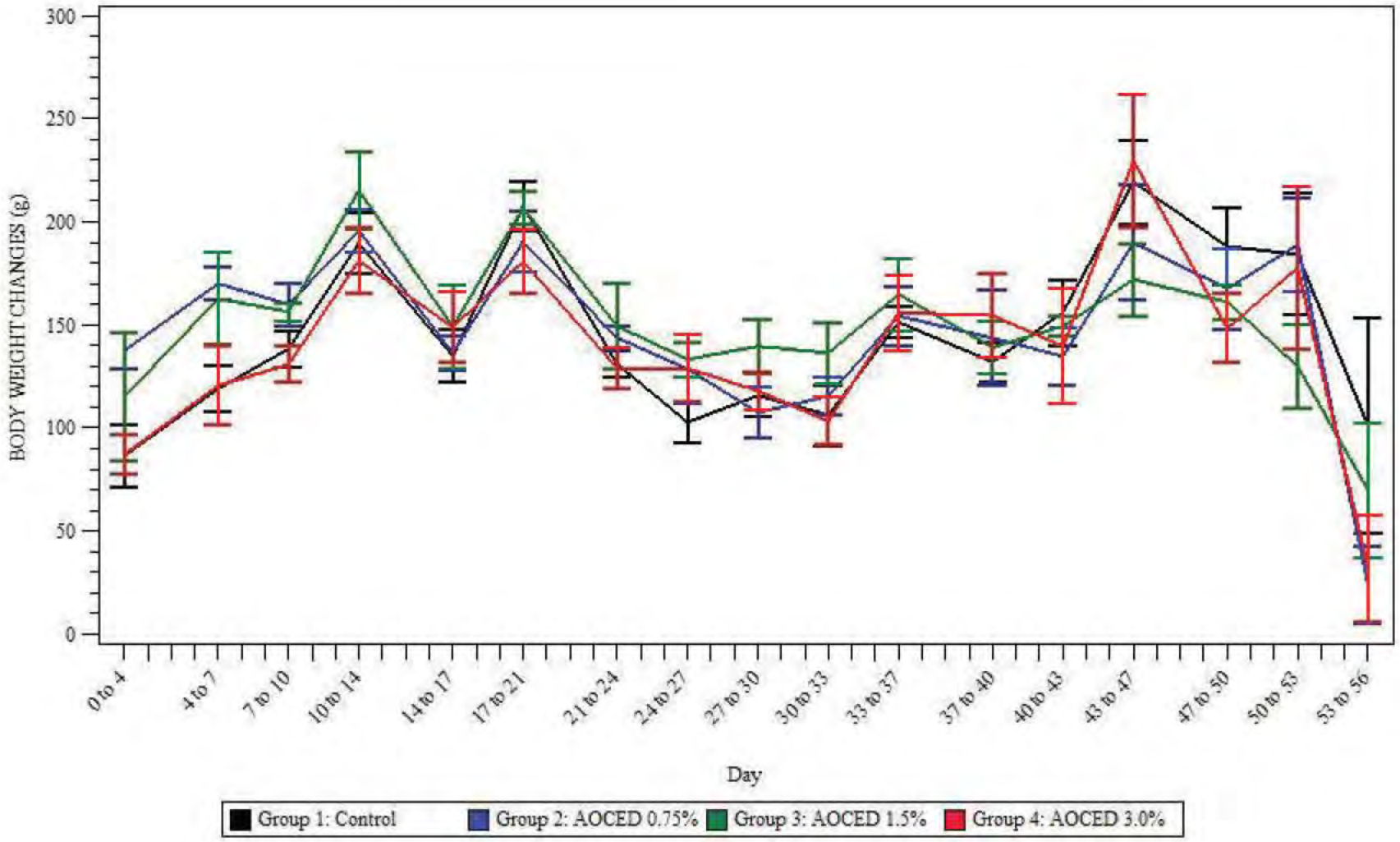
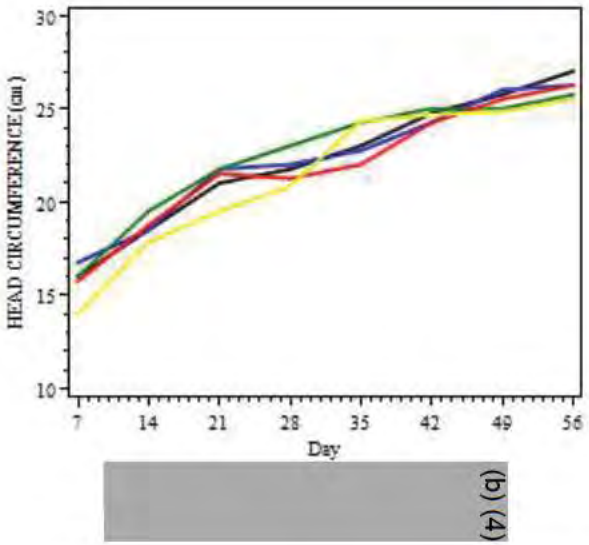
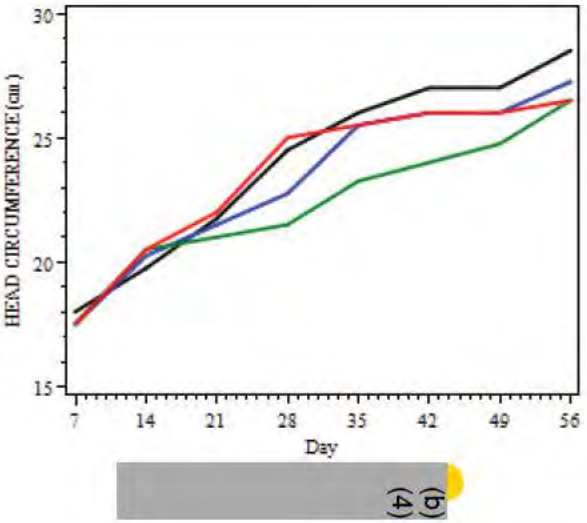
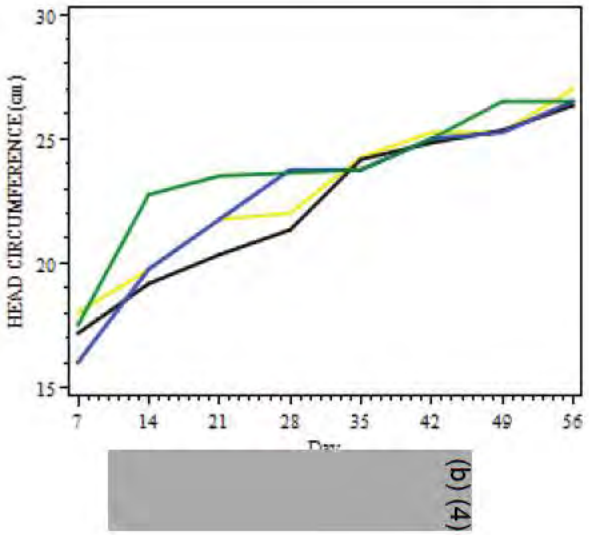


FIGURE NO. 37

GENERATION F1, LACTATION
MALE PUPS
Litter Means







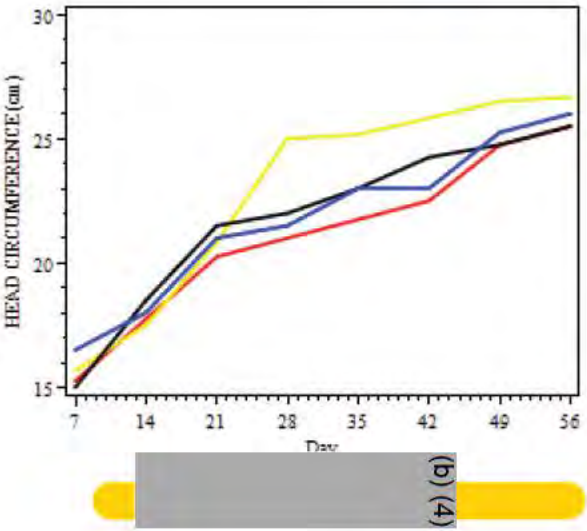
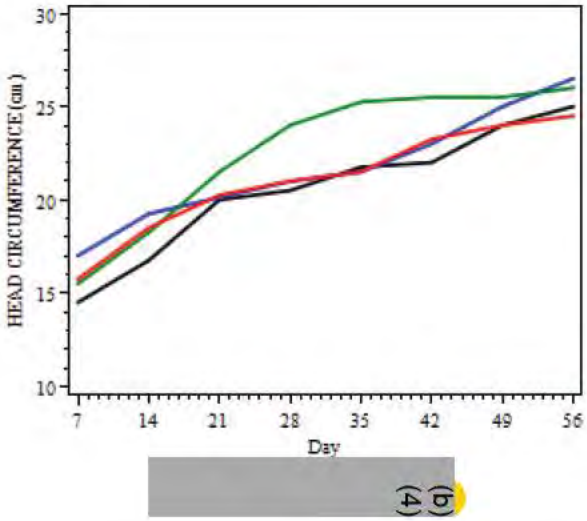


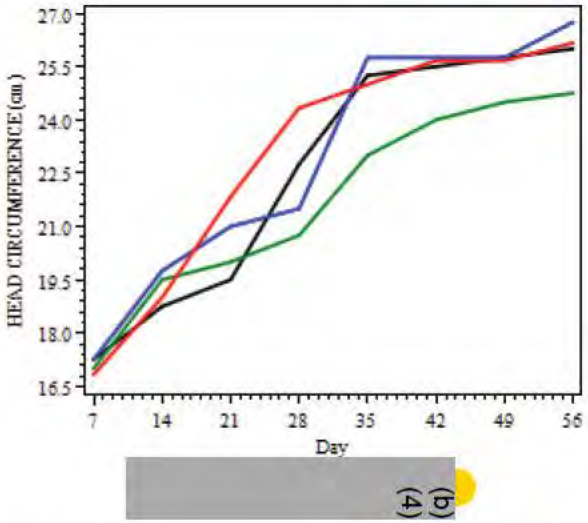
FIGURE NO. 38

[redacted] (b) (4)

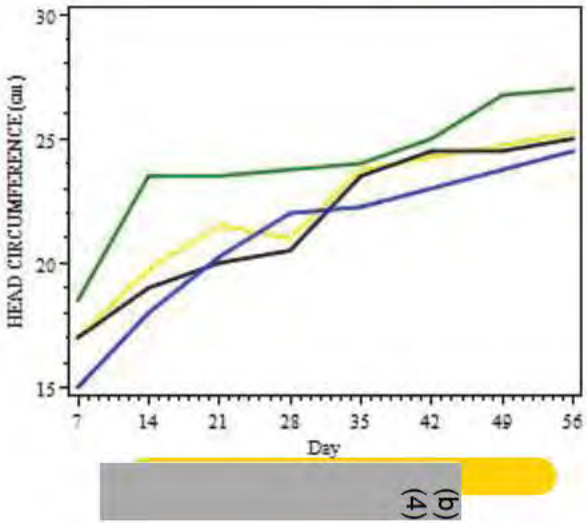
GENERATION F1, LACTATION
FEMALE PUPS
Litter Means



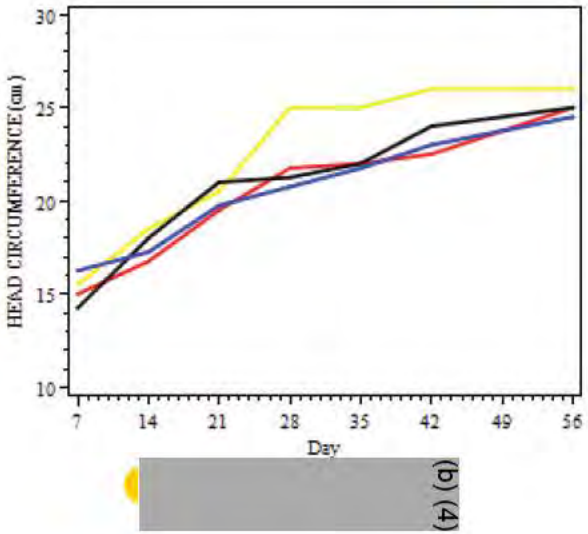
[redacted] (b) (4)



[redacted] (b) (4)



[redacted] (b) (4)

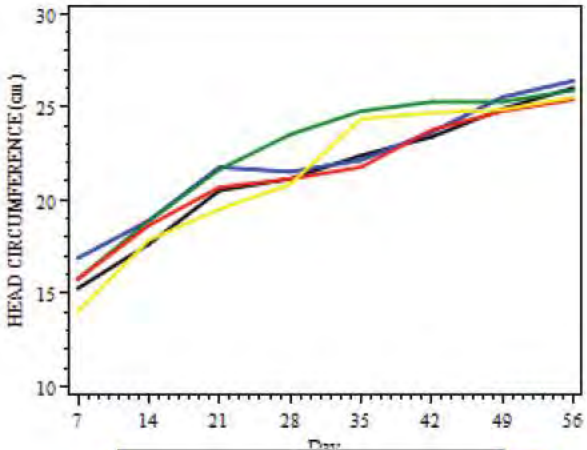


[redacted] (b) (4)

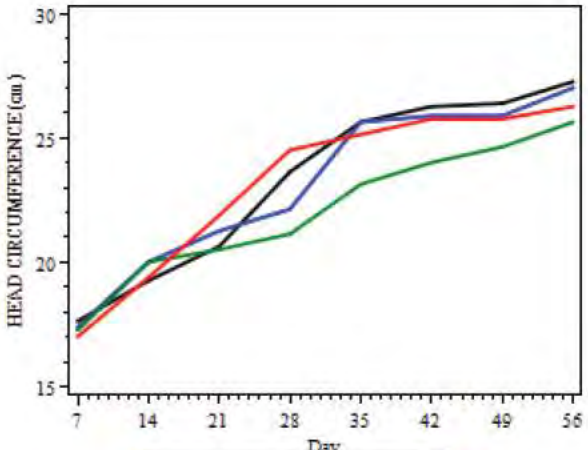
FIGURE NO. 39

(b) (4)

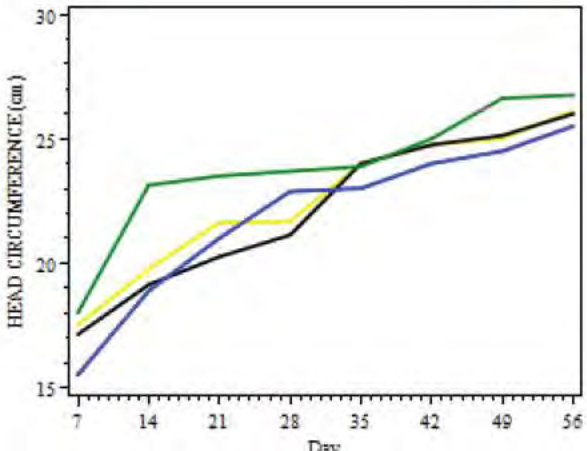
GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Litter Means



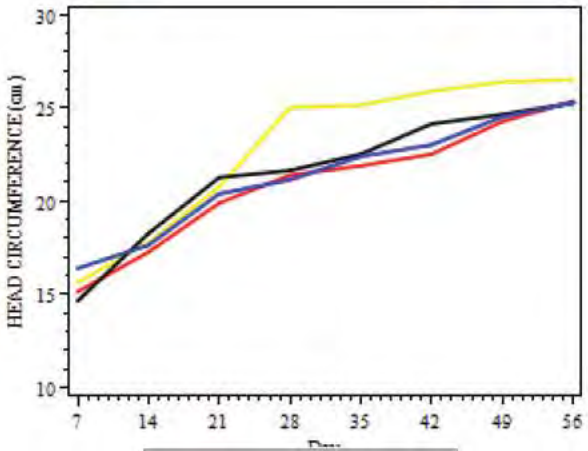
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 40

(b)
(4)

GENERATION F1, LACTATION
MALE PUPS
Treatment Means based on Litter Means ± SEM

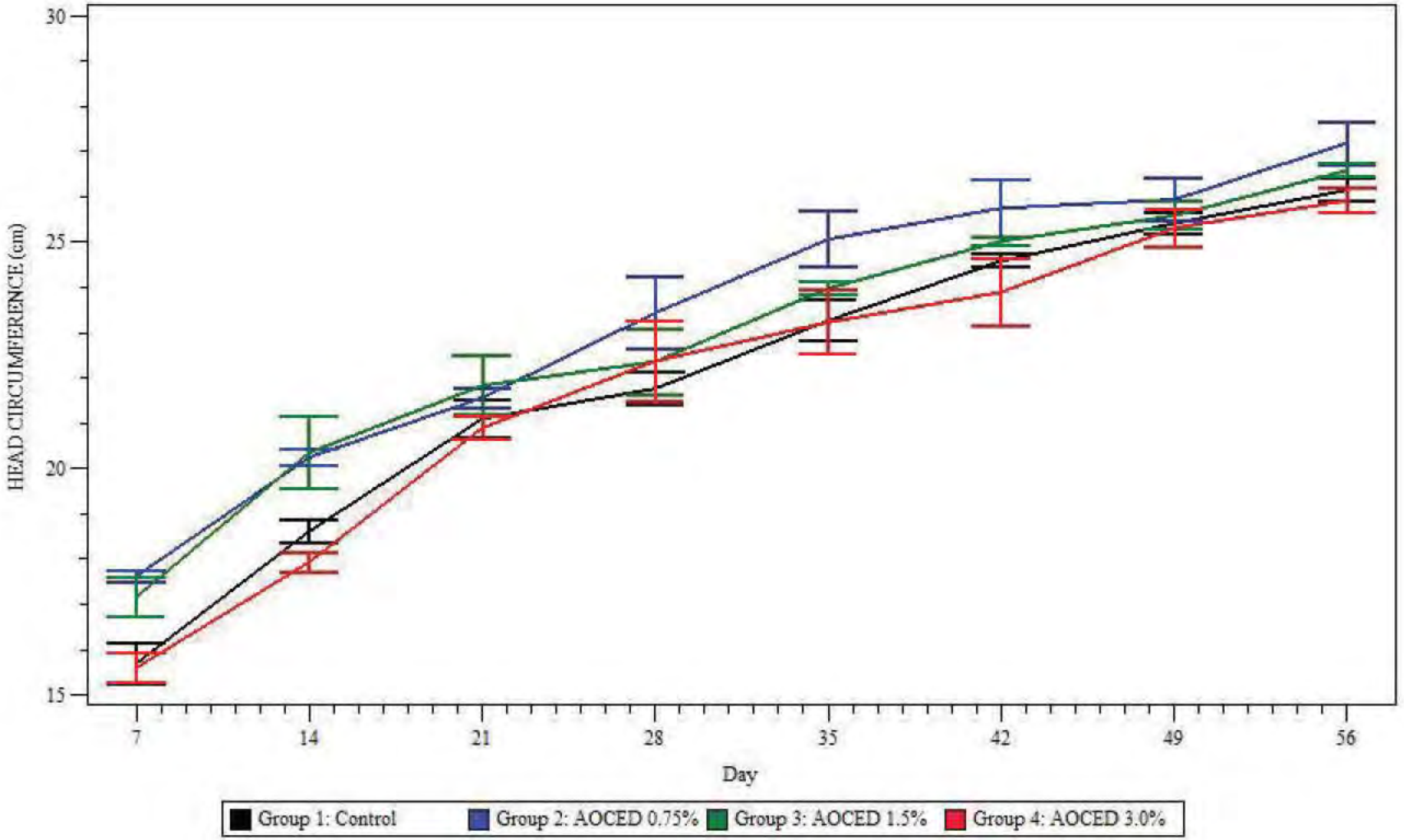


FIGURE NO. 41

(b) (4)

GENERATION F1, LACTATION
FEMALE PUPS
Treatment Means based on Litter Means ± SEM

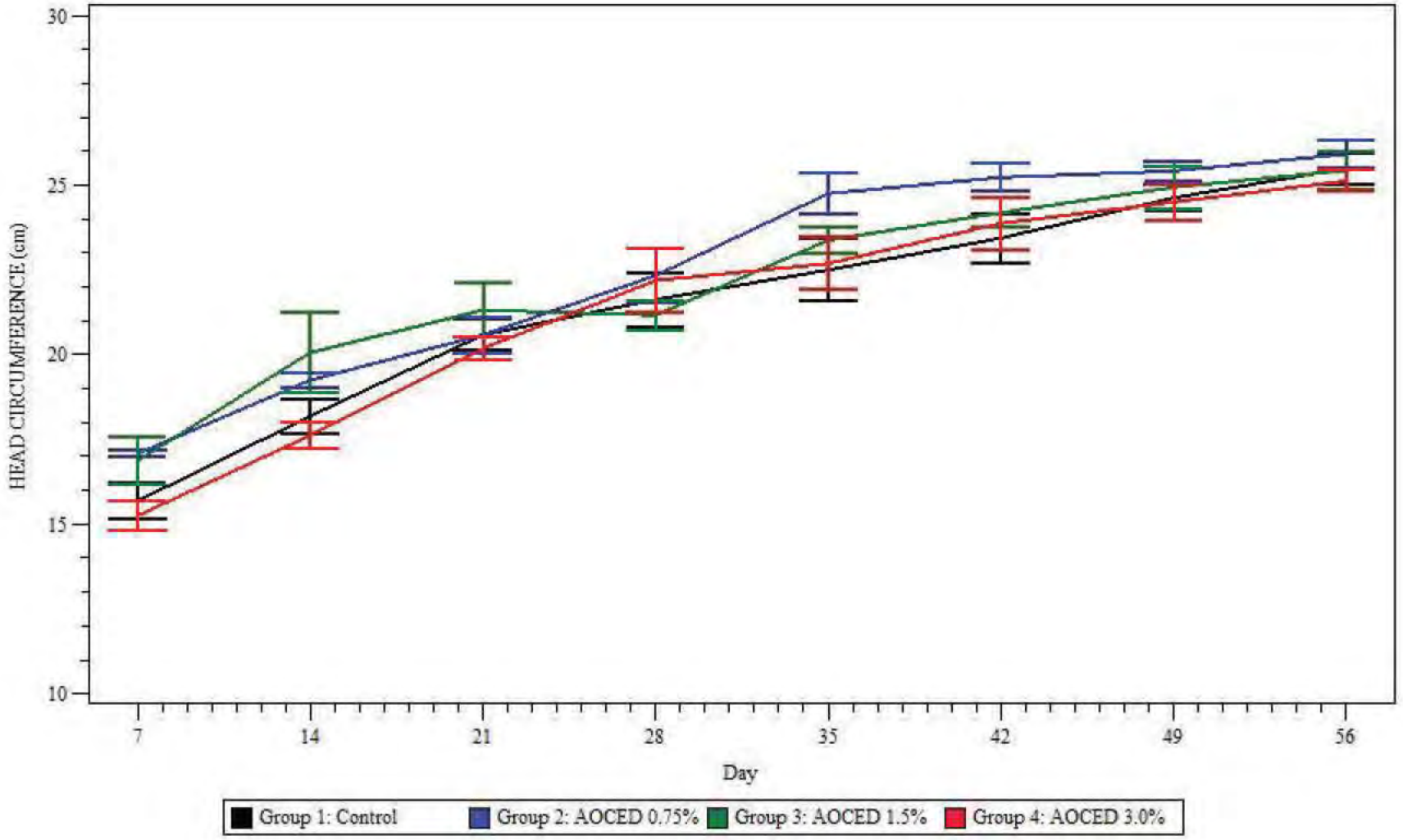


FIGURE NO. 42

(4) (g)

GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Treatment Means based on Litter Means ± SEM

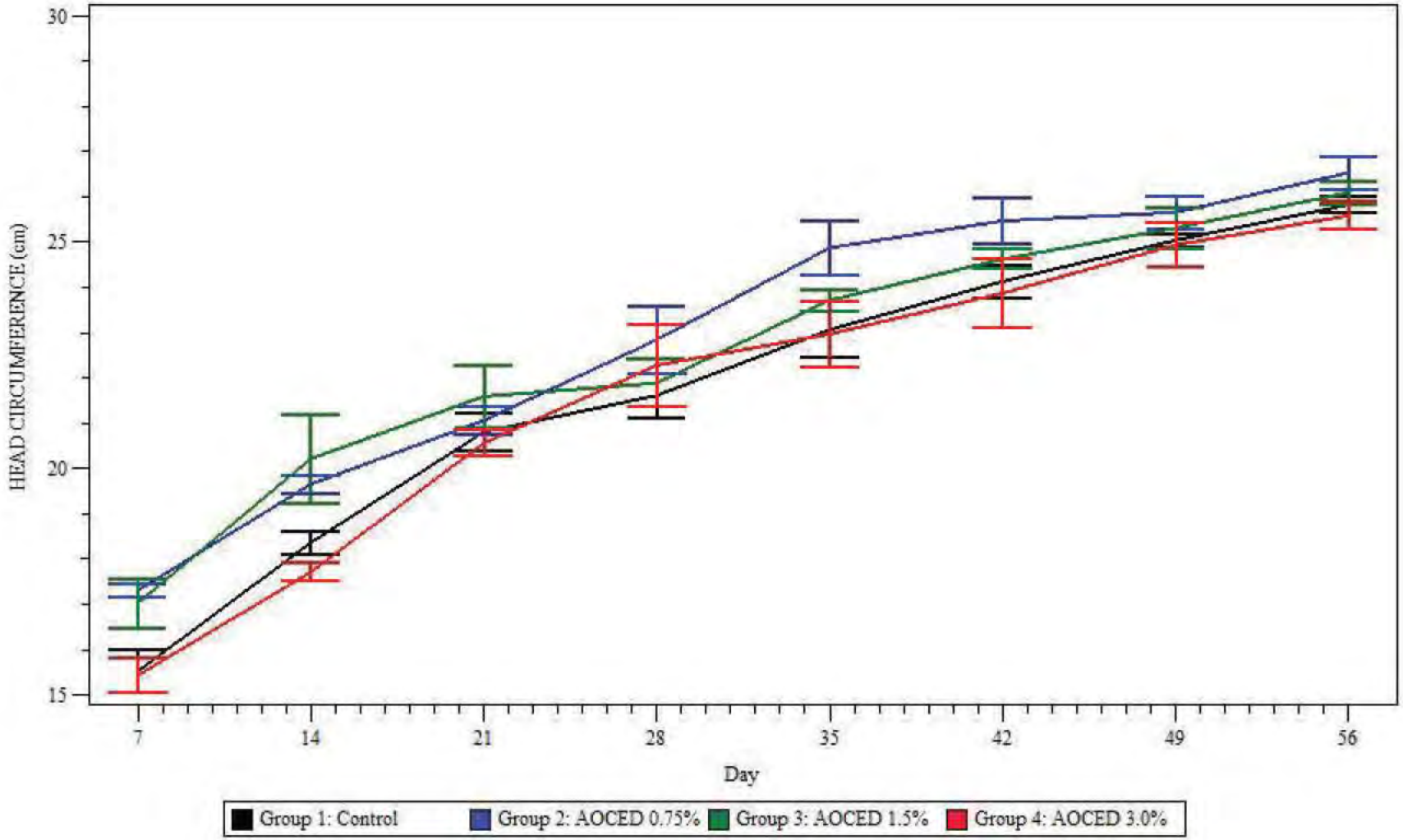
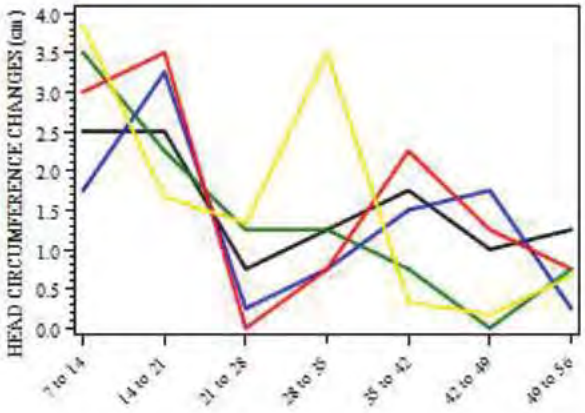
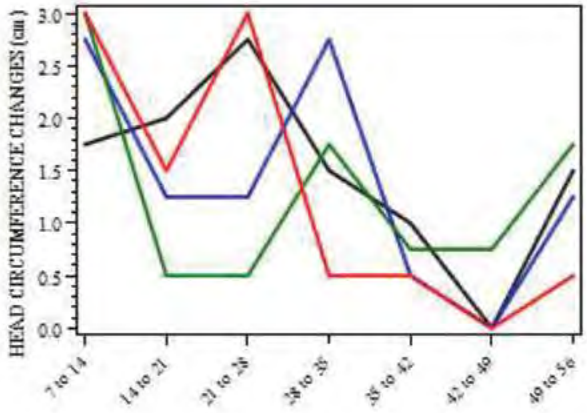


FIGURE NO. 43

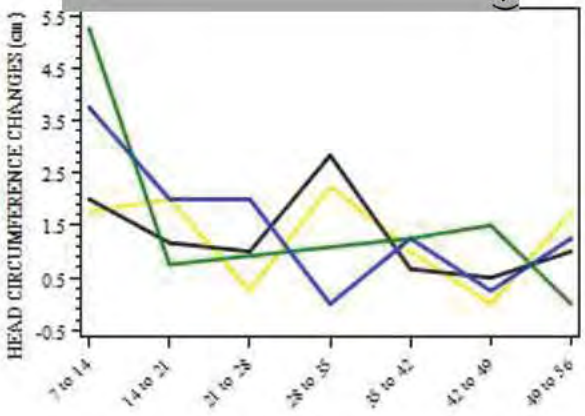
(b) (4)

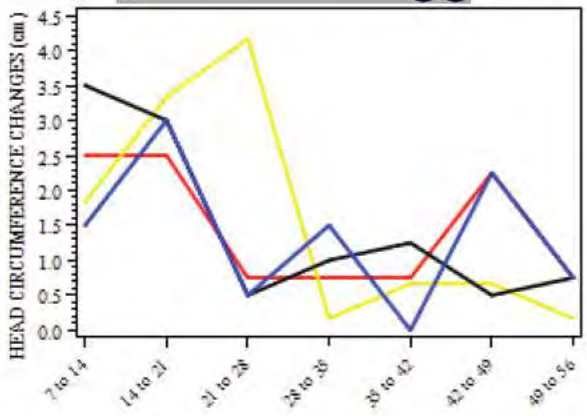
GENERATION F1, LACTATION
MALE PUPS
Litter Means





(b) (4)



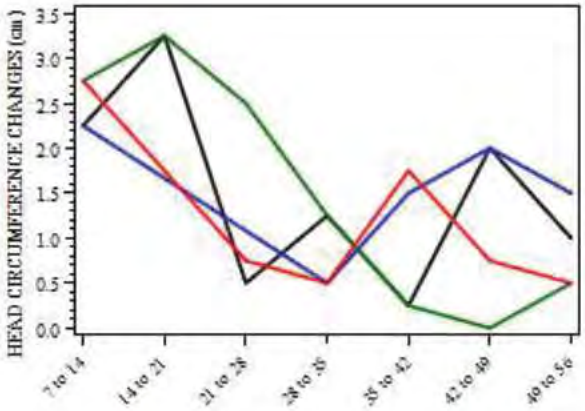


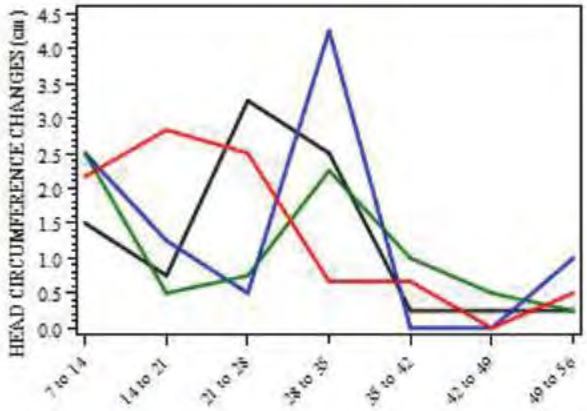
(b) (4)

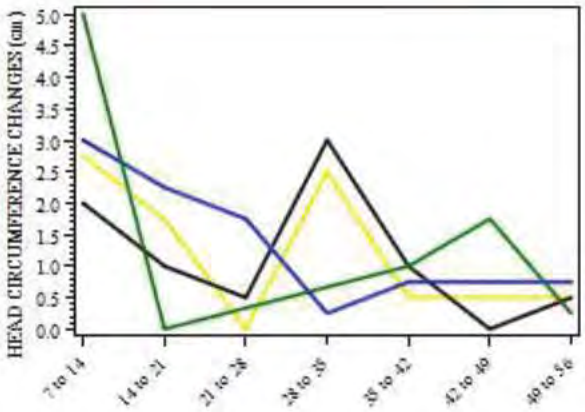
(b) (4)

FIGURE NO. 44

GENERATION F1, LACTATION
FEMALE PUPS
Litter Means







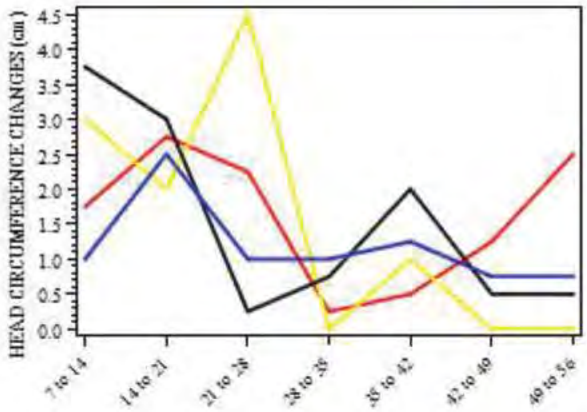
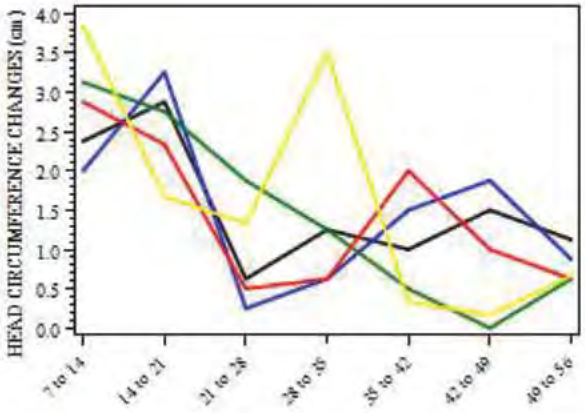


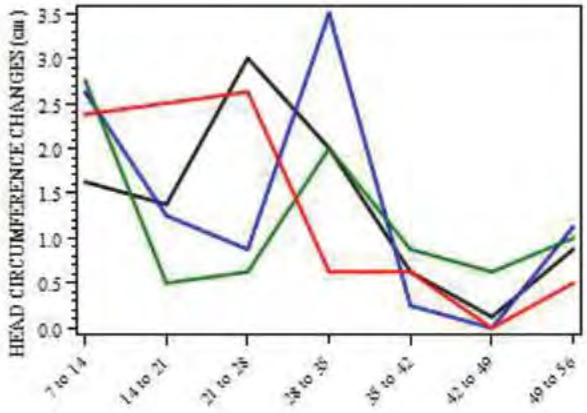
FIGURE NO. 45

(b) (4)

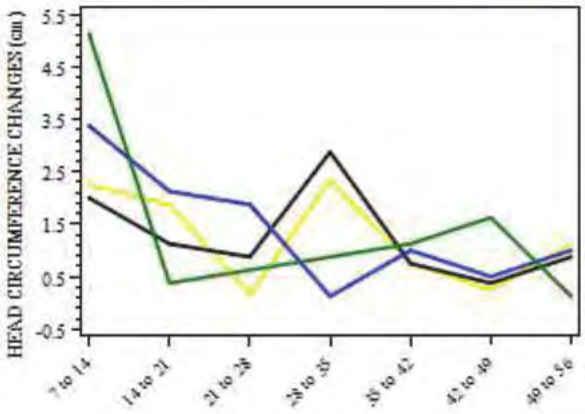
GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Litter Means



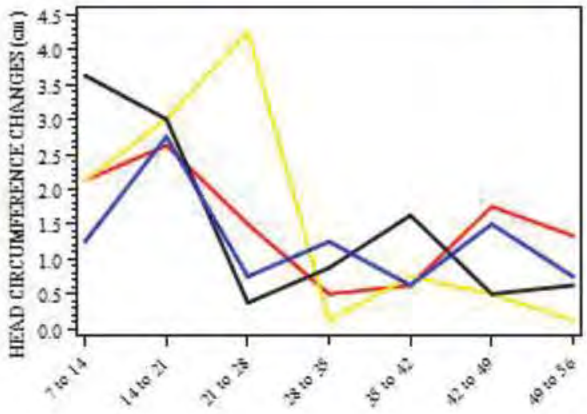
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 46

(b) (4)

GENERATION F1, LACTATION
MALE PUPS
Treatment Means based on Litter Means ± SEM

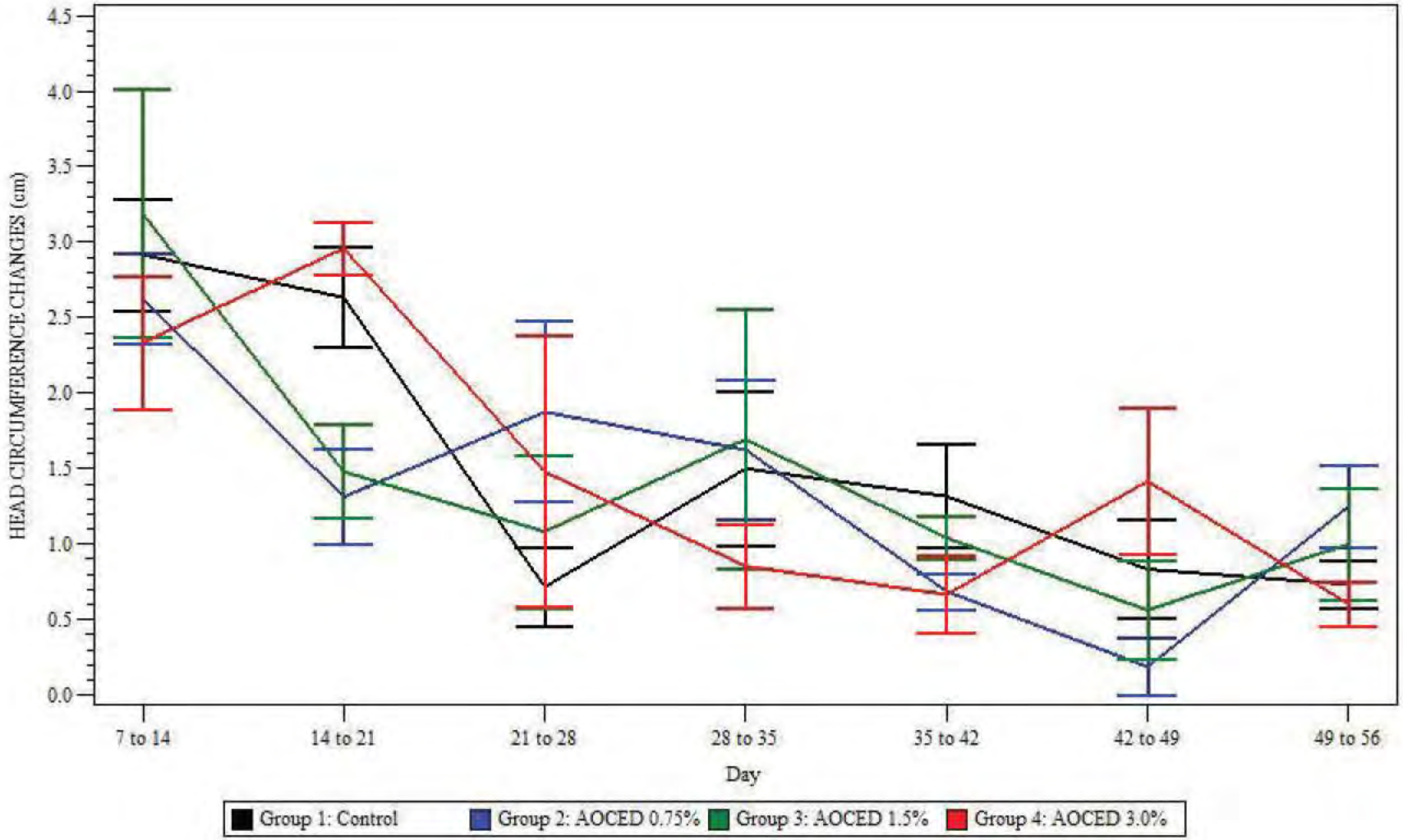


FIGURE NO. 47

(b) (4)

GENERATION F1, LACTATION
FEMALE PUPS
Treatment Means based on Litter Means ± SEM

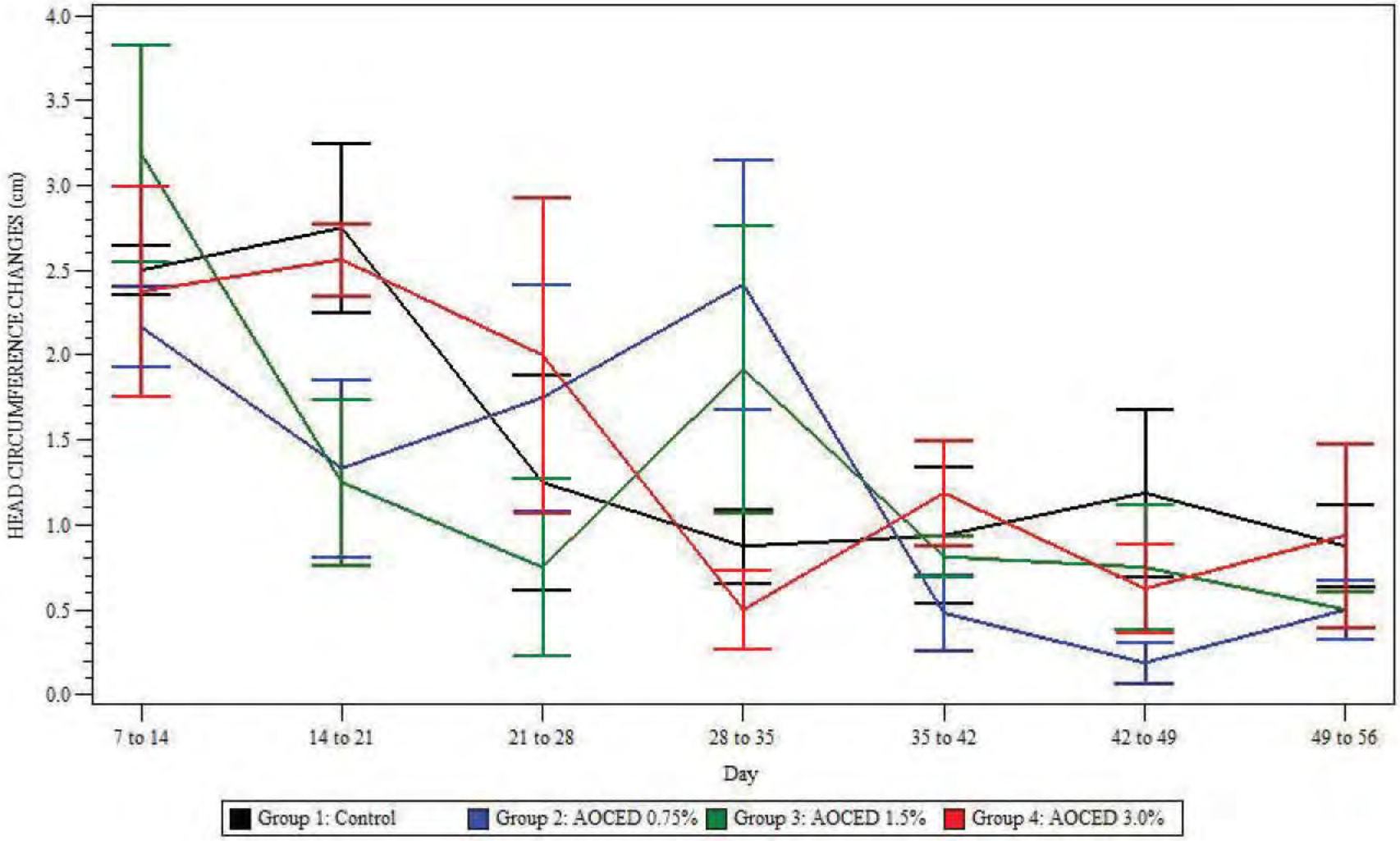


FIGURE NO. 48

(b) (4)

GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Treatment Means based on Litter Means ± SEM

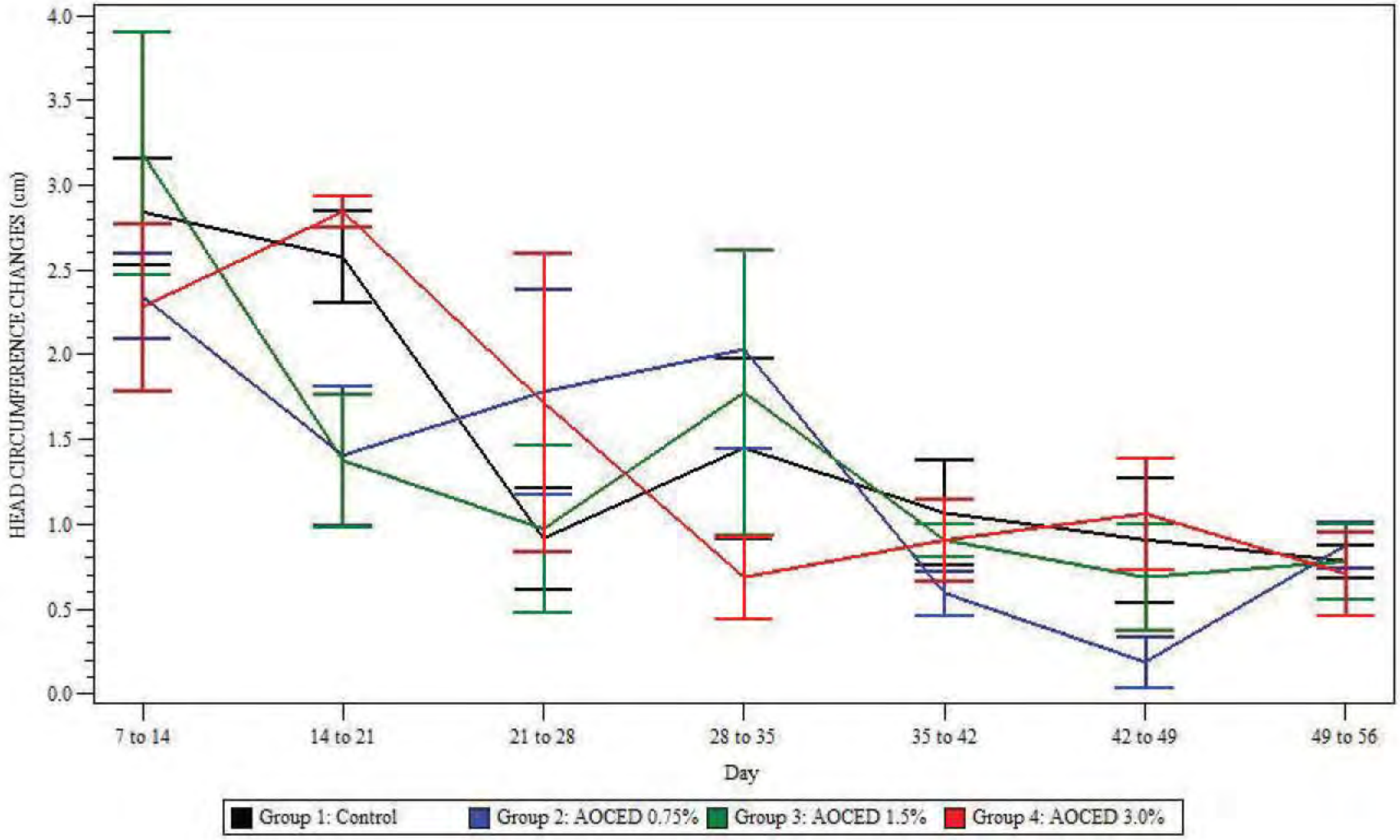


FIGURE NO. 49

(b) (4)

GENERATION F1, LACTATION
MALE PUPS
Litter Means

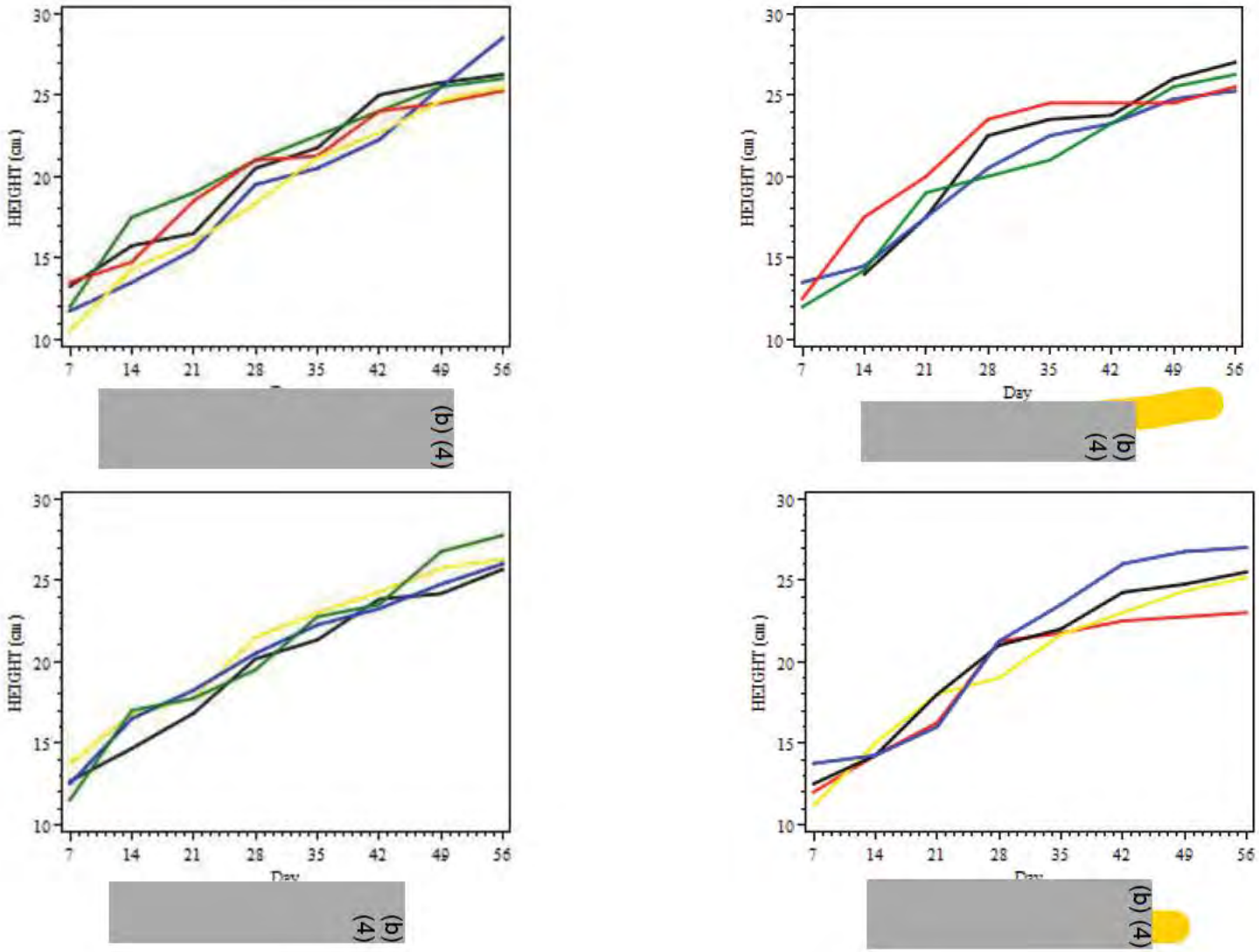


FIGURE NO. 50

(b) (4)

GENERATION F1, LACTATION
FEMALE PUPS
Litter Means

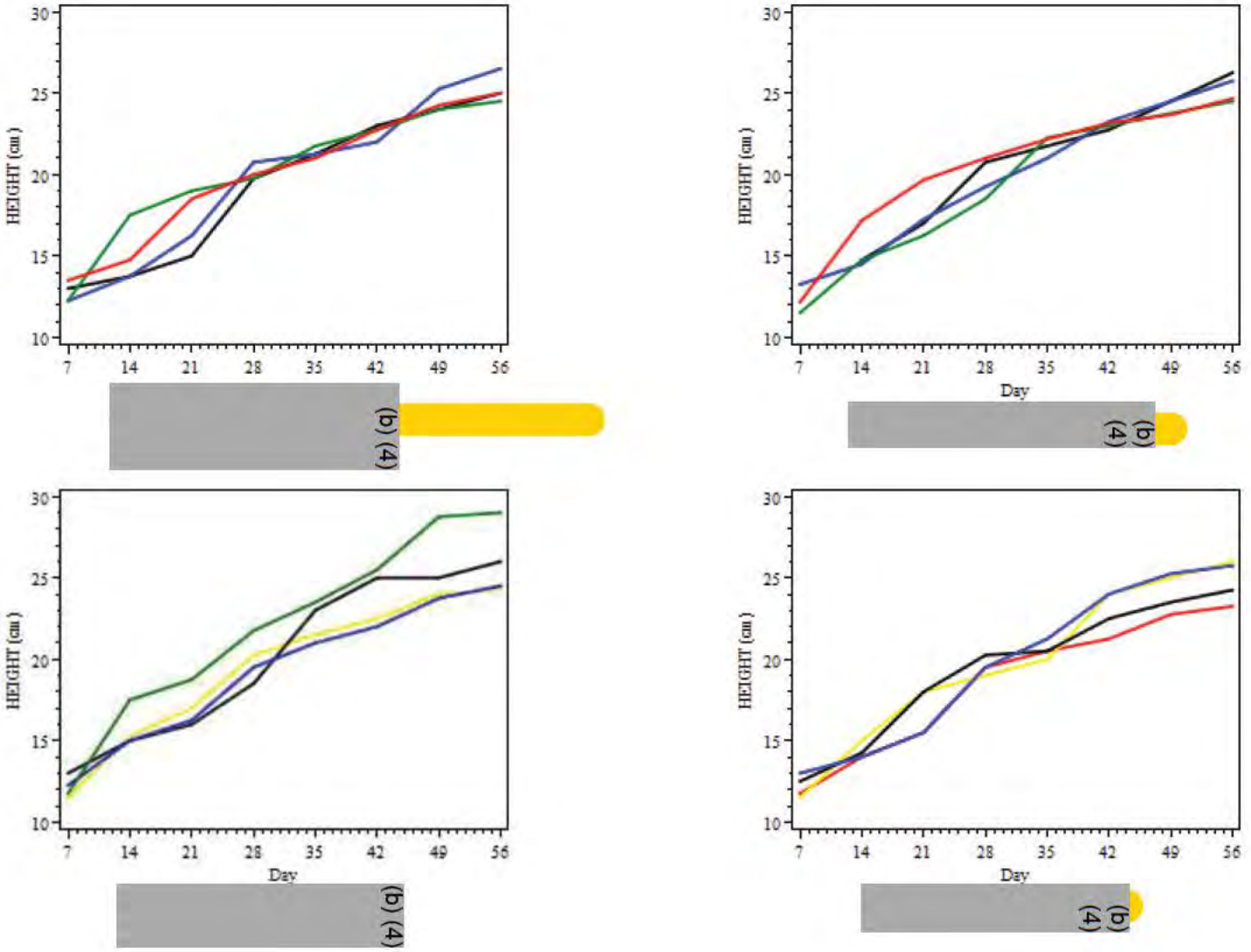
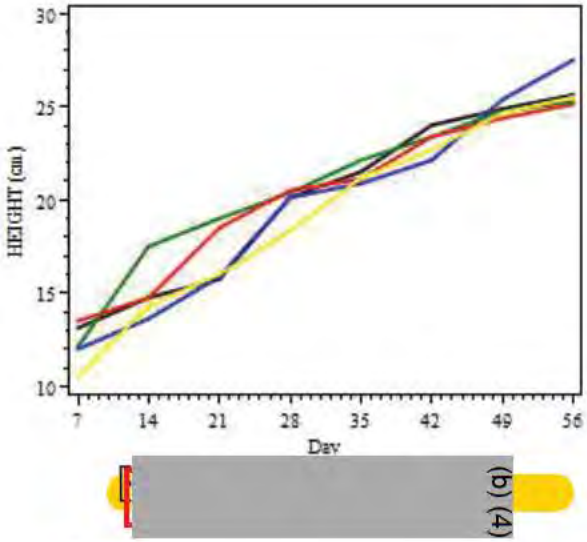
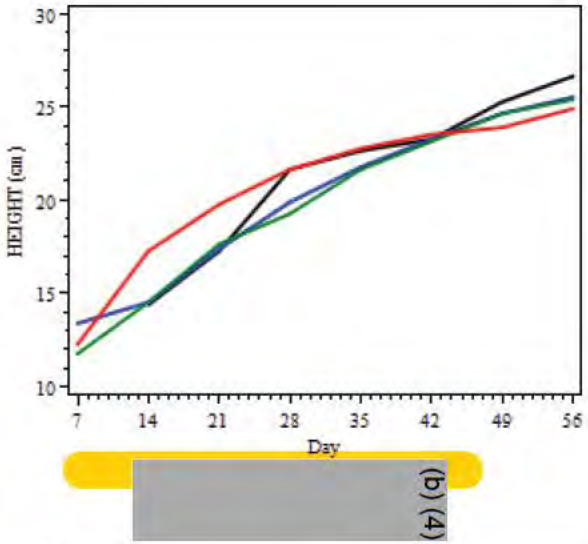
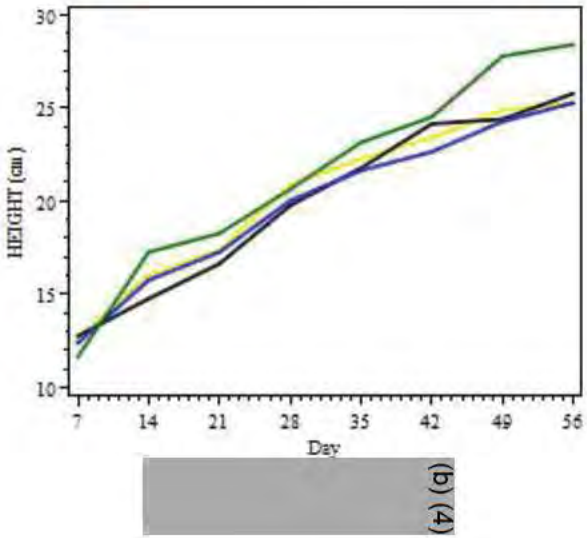


FIGURE NO. 51

GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Litter Means







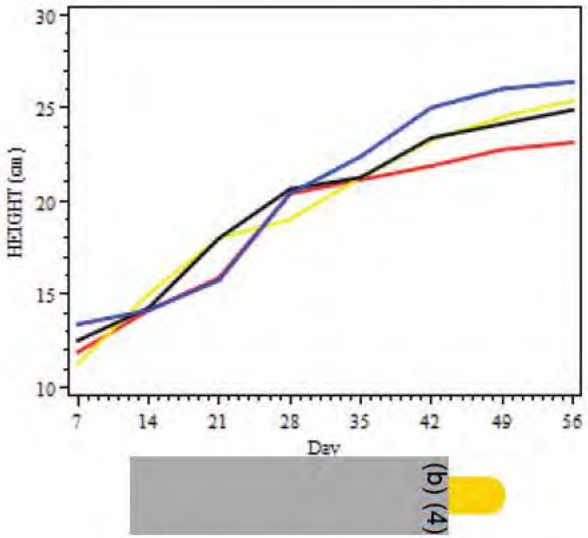


FIGURE NO. 52

(b) (4)

GENERATION F1, LACTATION
MALE PUPS
Treatment Means based on Litter Means ± SEM

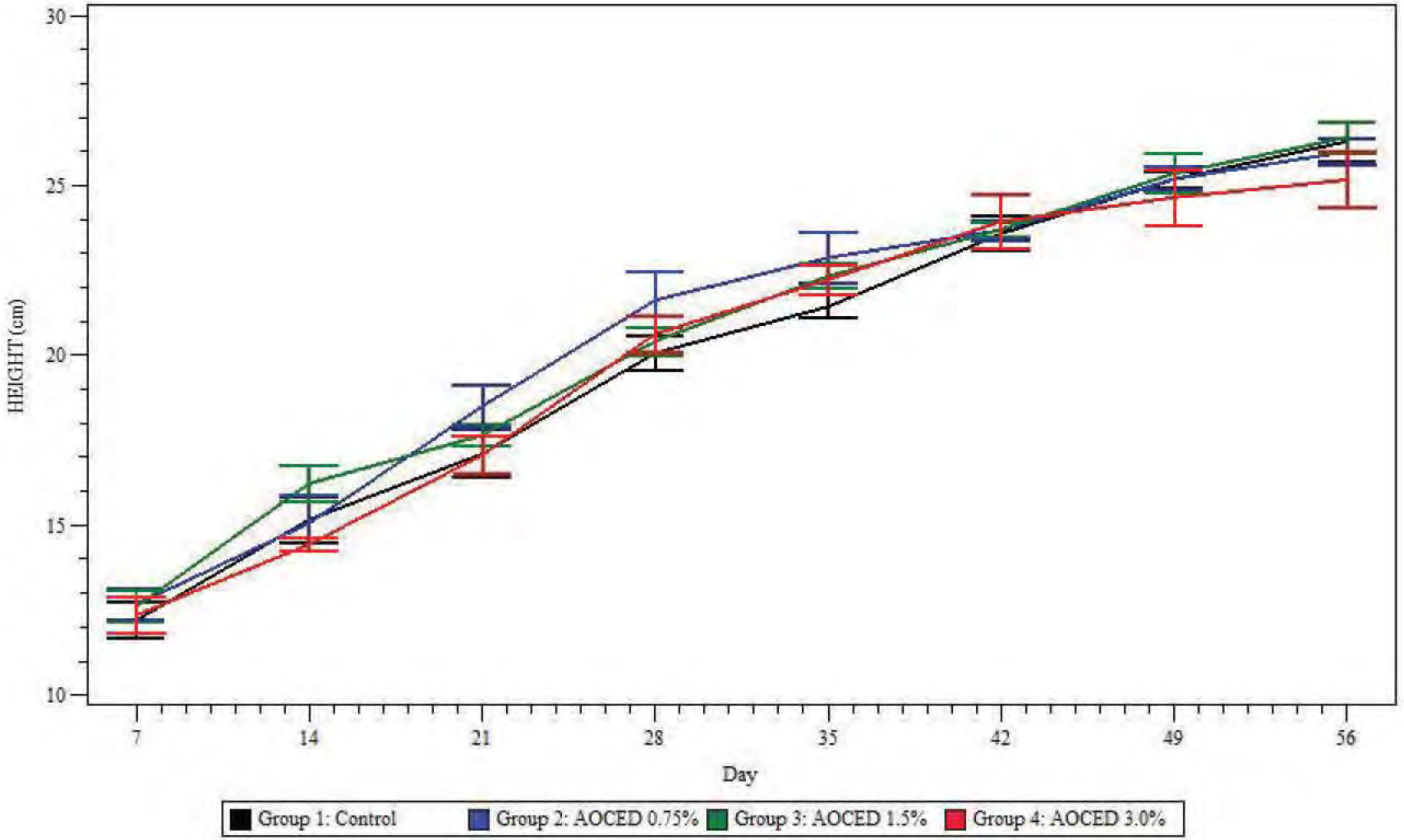


FIGURE NO. 53

(b) (4)

GENERATION F1, LACTATION
FEMALE PUPS
Treatment Means based on Litter Means ± SEM

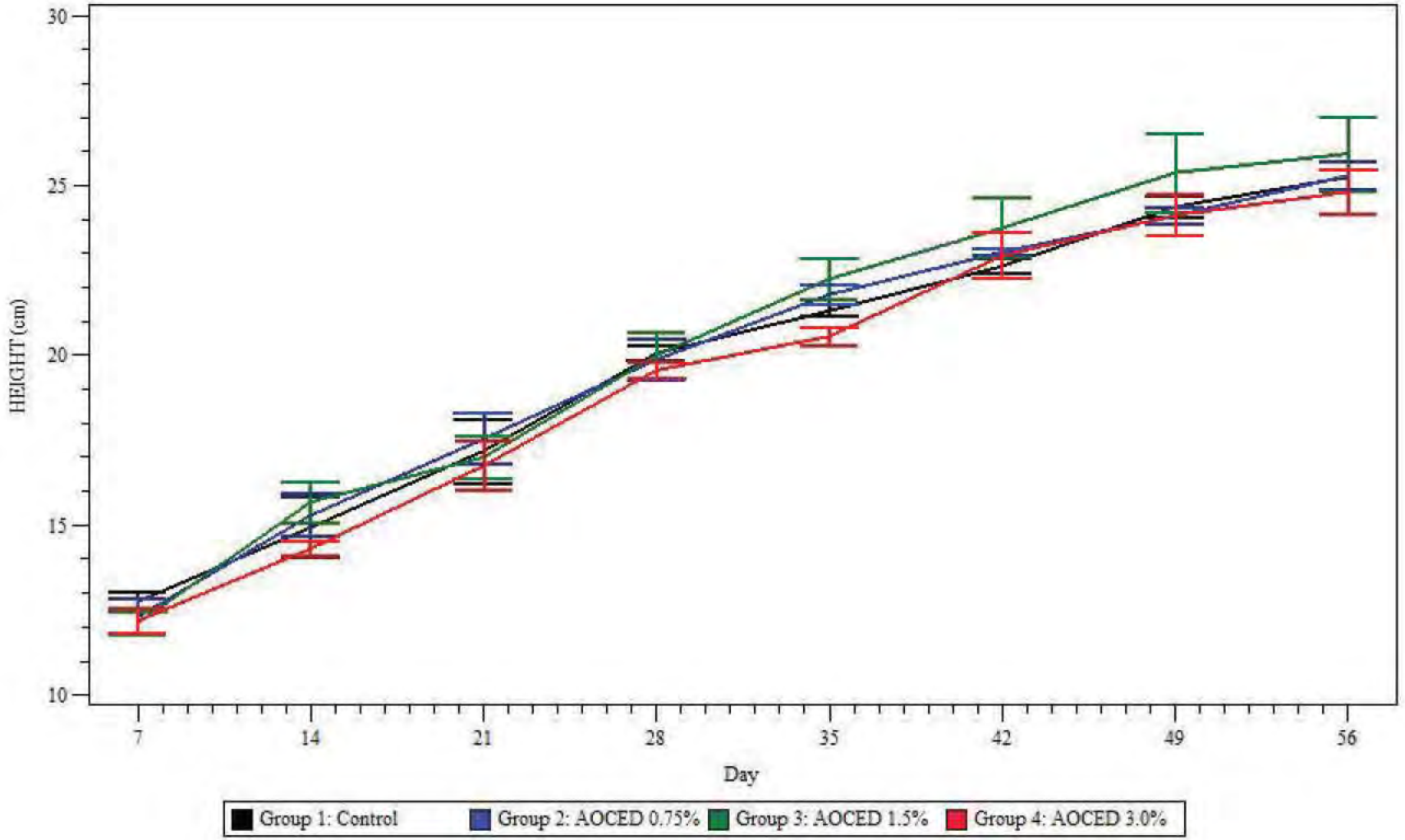


FIGURE NO. 54

(b) (4)

GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Treatment Means based on Litter Means ± SEM

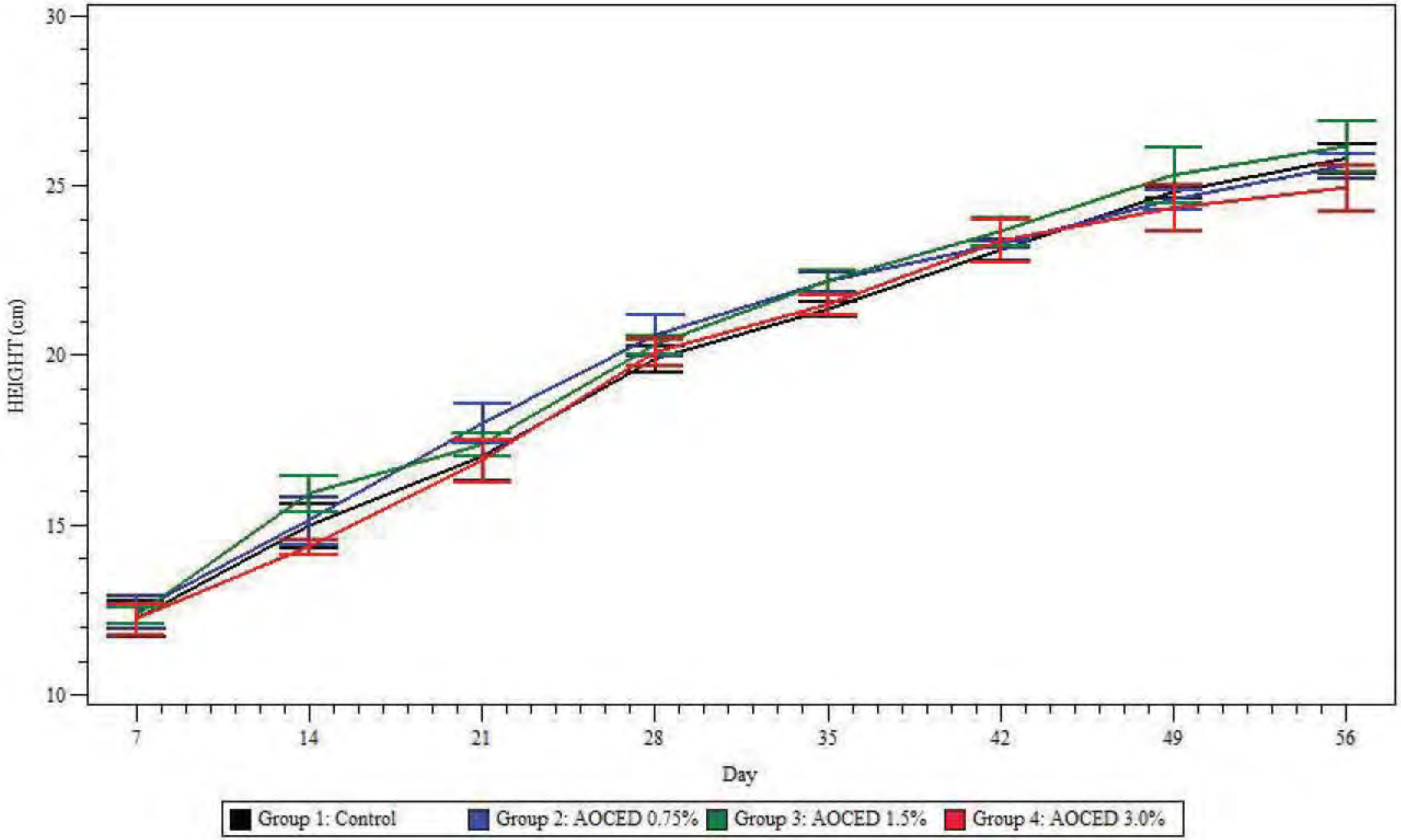
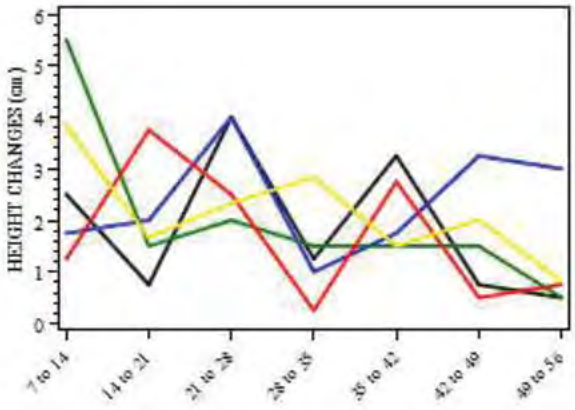


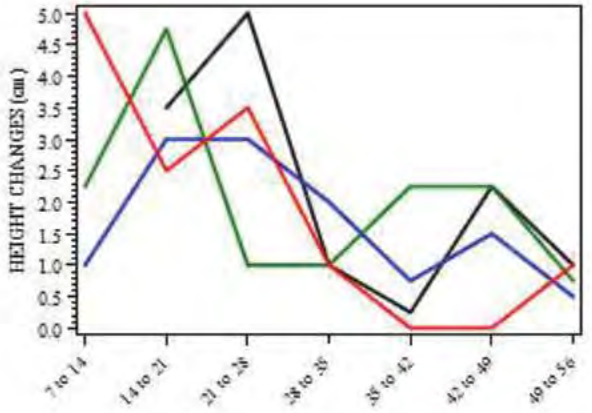
FIGURE NO. 55

[redacted]

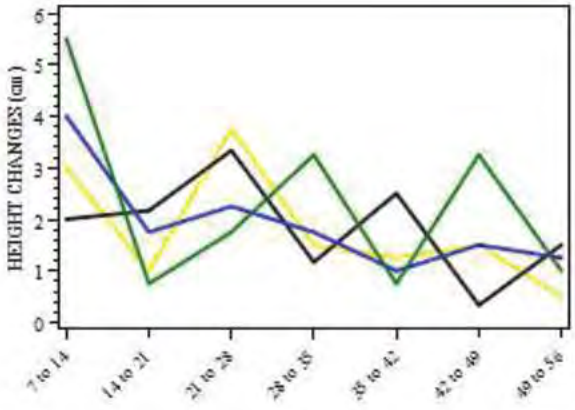
GENERATION F1, LACTATION
MALE PUPS
Litter Means



[redacted]



[redacted]



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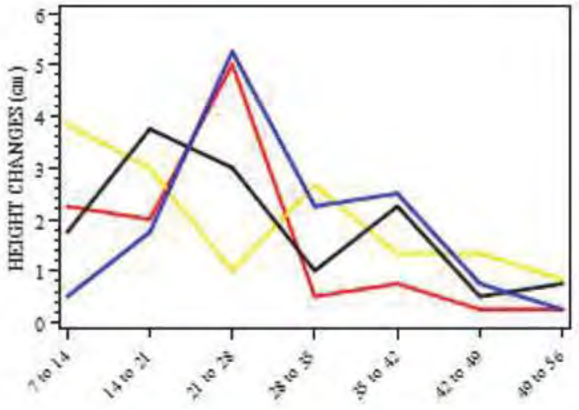
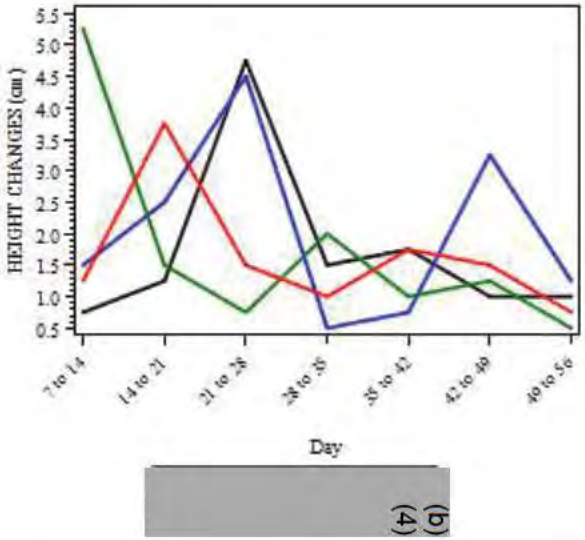


[redacted]

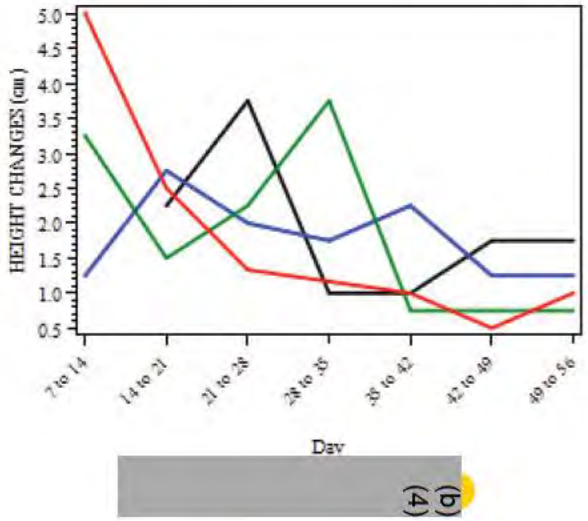
FIGURE NO. 56

[redacted]

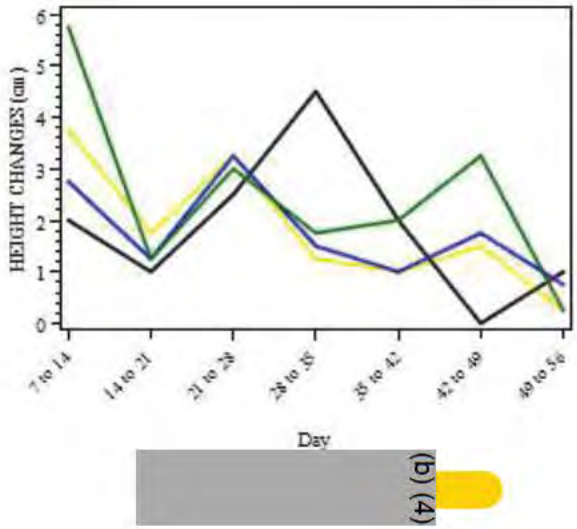
GENERATION F1, LACTATION
FEMALE PUPS
Litter Means



[redacted]



[redacted]



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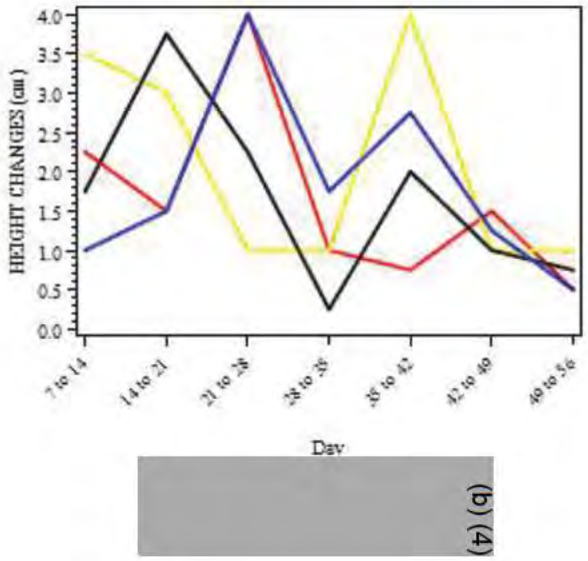
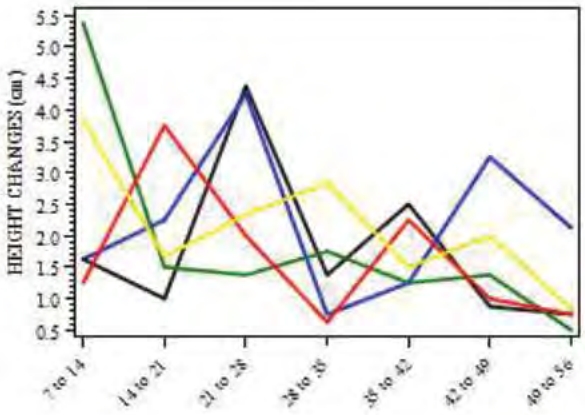


[redacted]

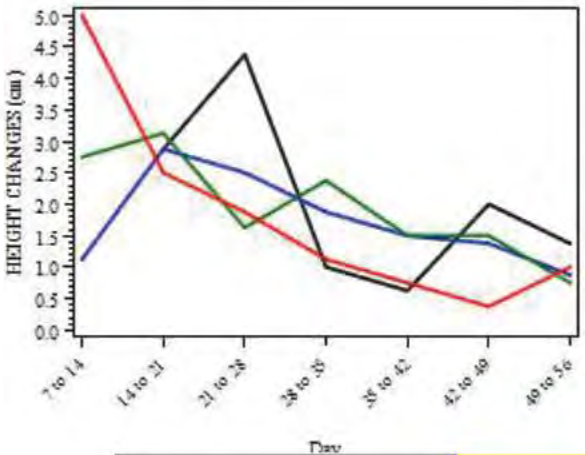
FIGURE NO. 57

(b) (4)

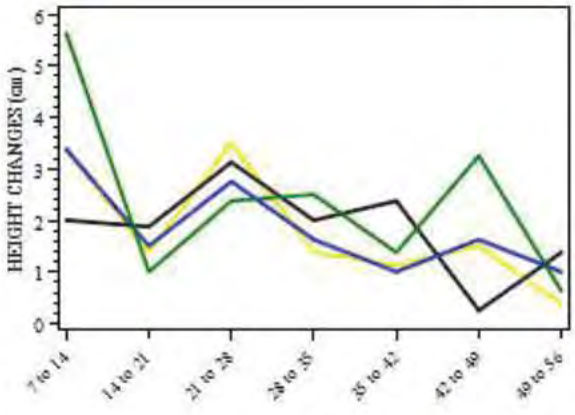
GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Litter Means



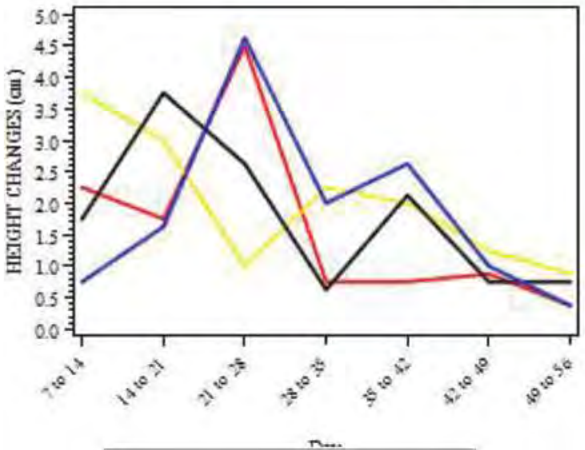
(b) (4)



(b) (4)



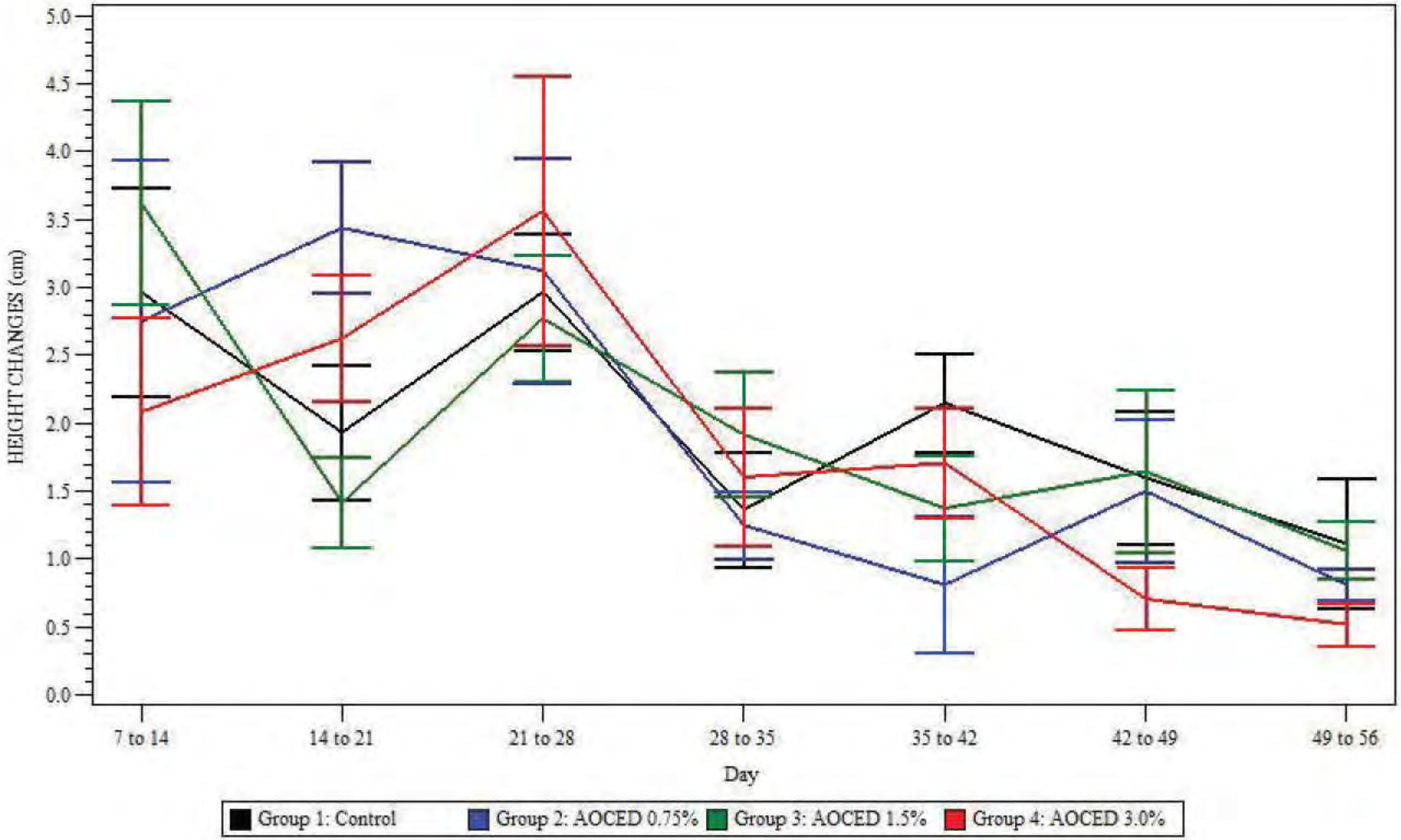
(b) (4)



(b) (4)

FIGURE NO. 58

GENERATION F1, LACTATION
MALE PUPS
Treatment Means based on Litter Means ± SEM



(b)(4)

FIGURE NO. 59

(b) (4)

GENERATION F1, LACTATION
FEMALE PUPS
Treatment Means based on Litter Means ± SEM

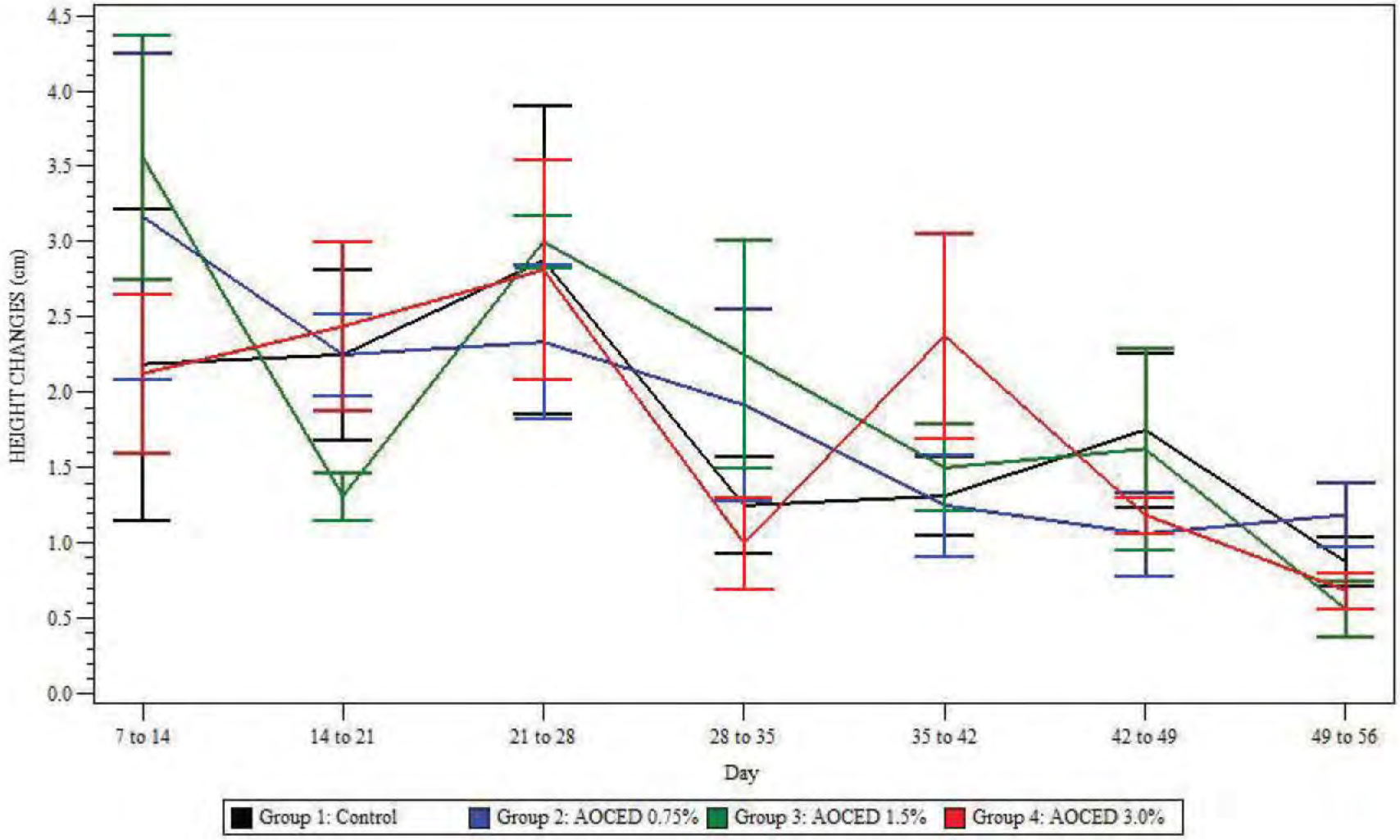
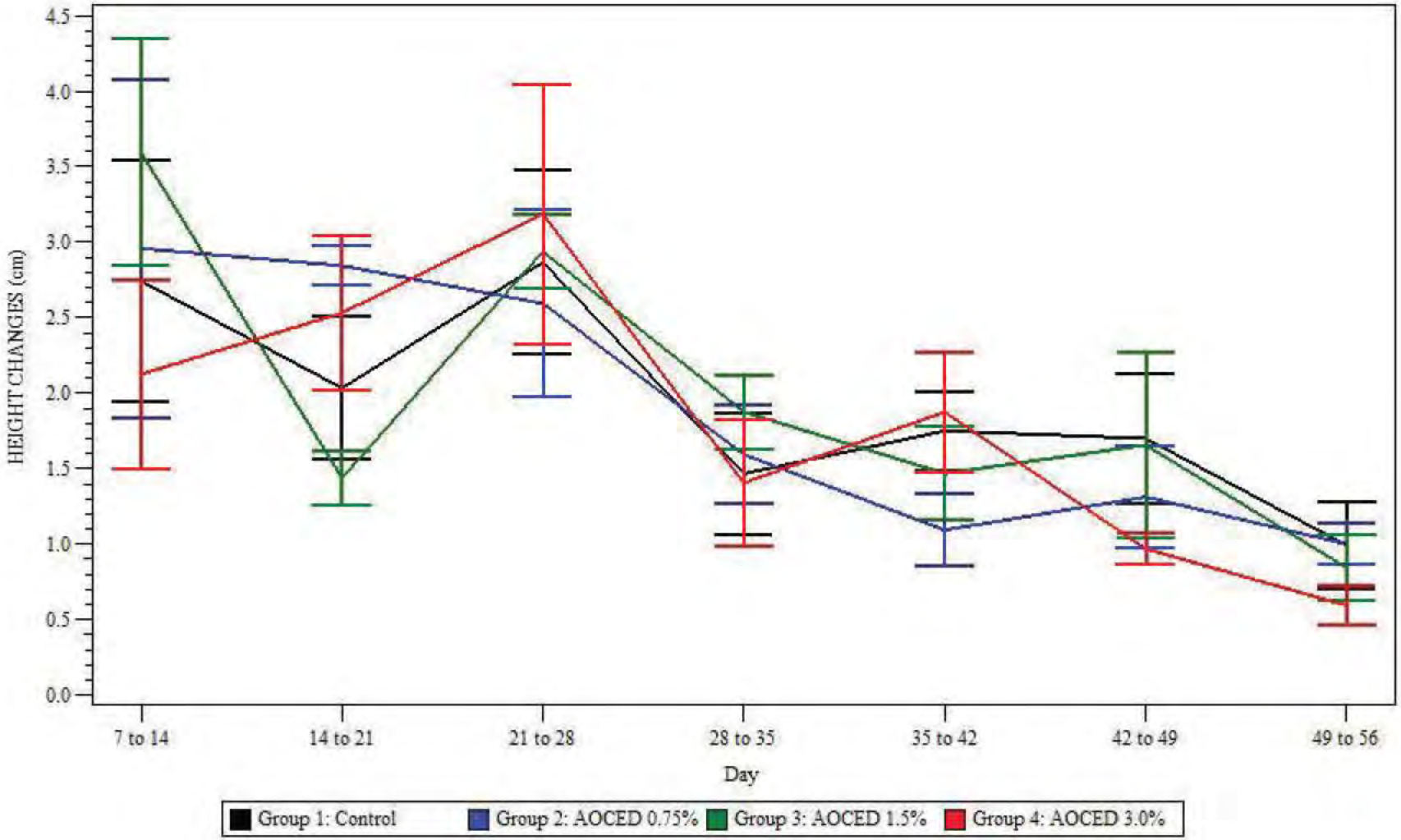


FIGURE NO. 60

(b) (4)

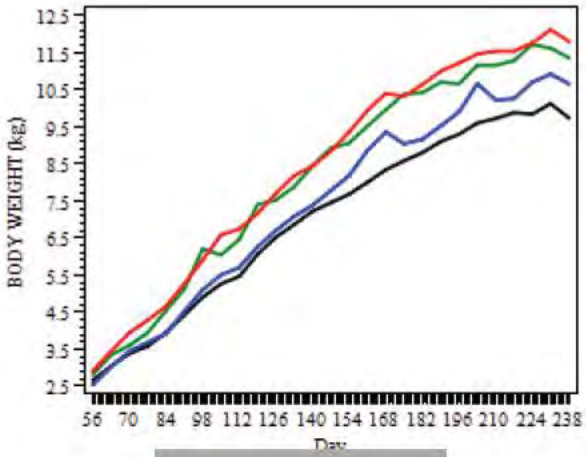
GENERATION F1, LACTATION
MALE AND FEMALE PUPS COMBINED
Treatment Means based on Litter Means ± SEM



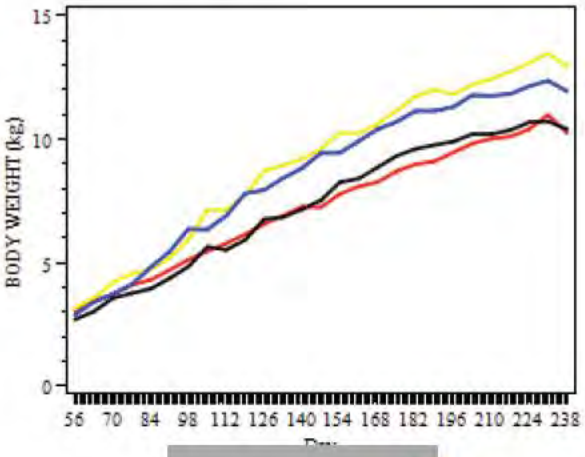
FIGURES
F1 PUPPIES POST-WEANING

FIGURE NO. 61

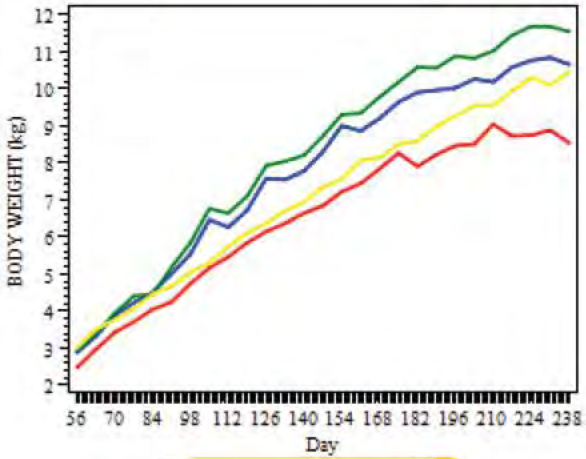
GENERATION F1, POST WEANING - PUPPIES
MALES



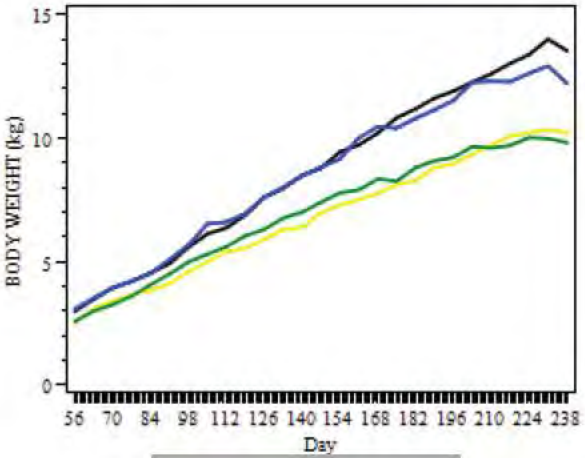
(b) (4)



(b) (4)



(b) (4)

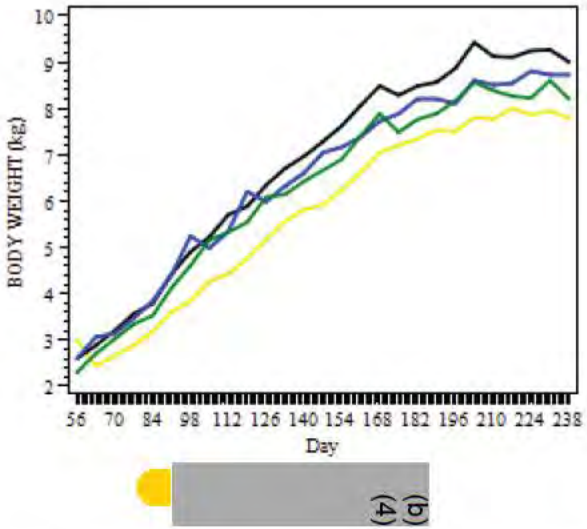


(b) (4)

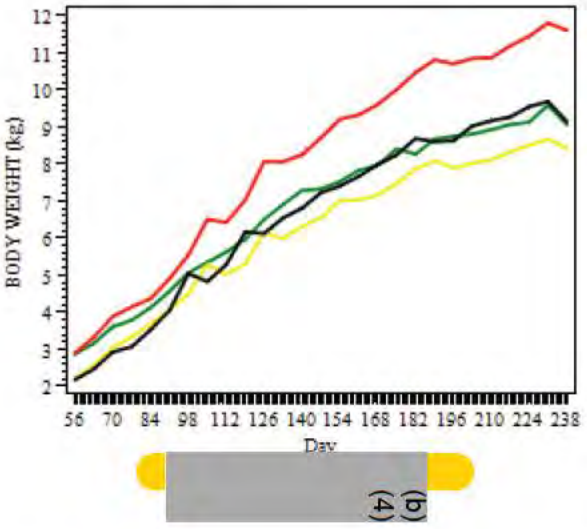
FIGURE NO. 62

(b) (4)

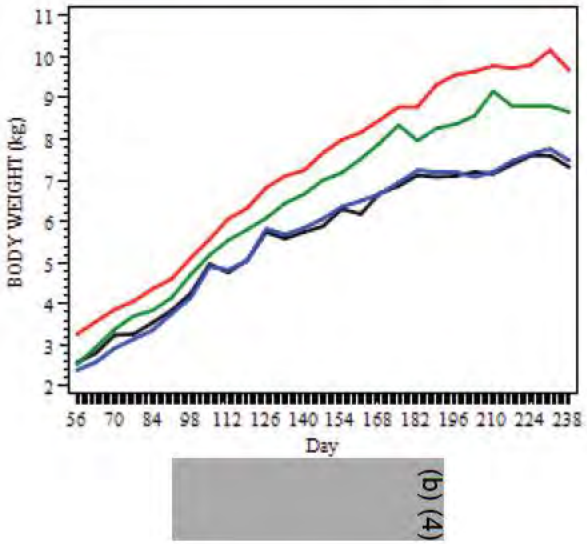
GENERATION F1, POST WEANING - PUPPIES
FEMALES



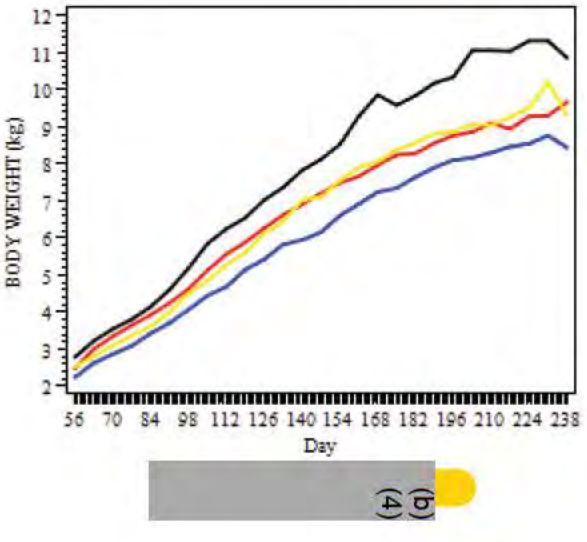
(b) (4)



(b) (4)



(b) (4)



(b) (4)

131 of 1567

FIGURE NO. 63

[redacted] (b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

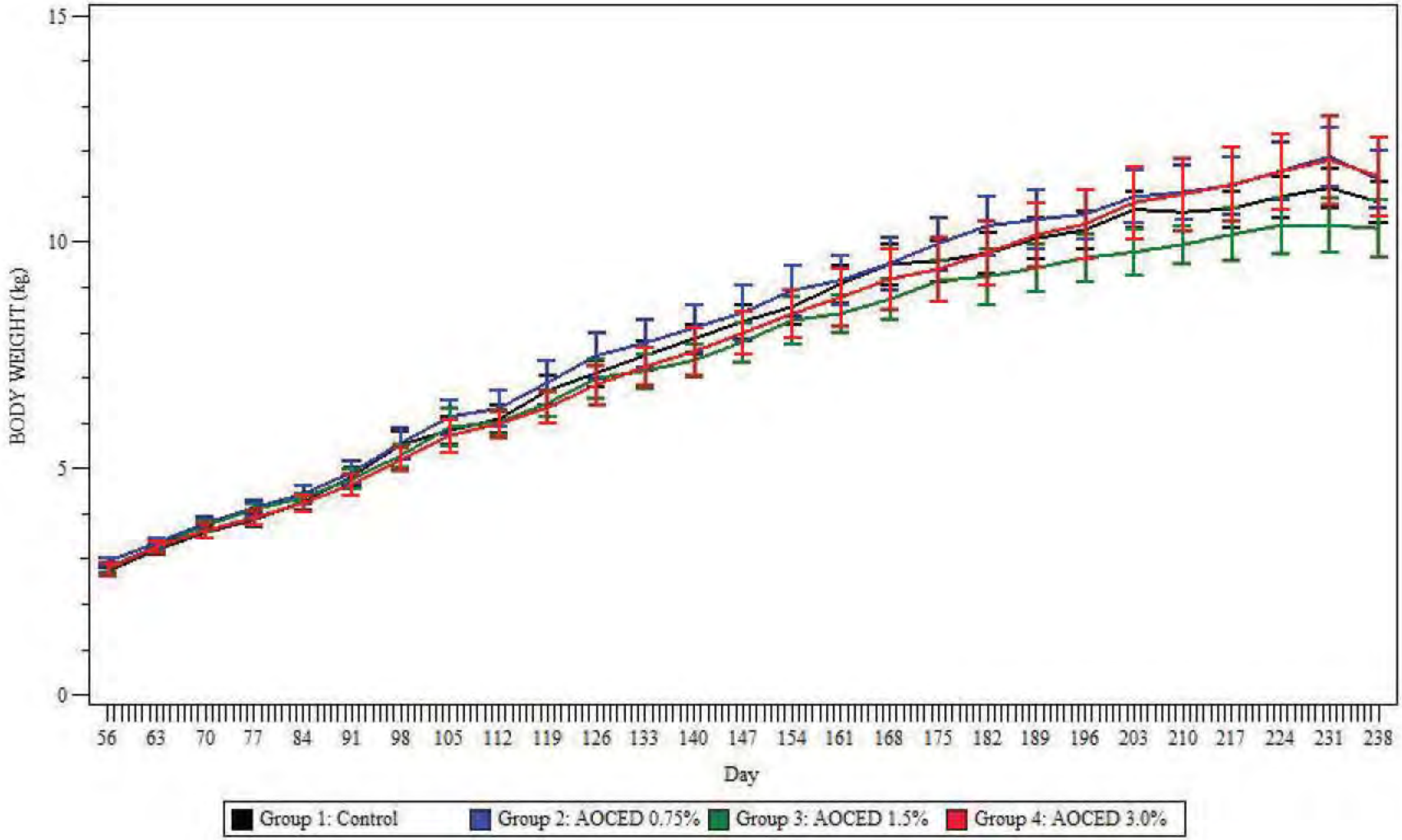


FIGURE NO. 64

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

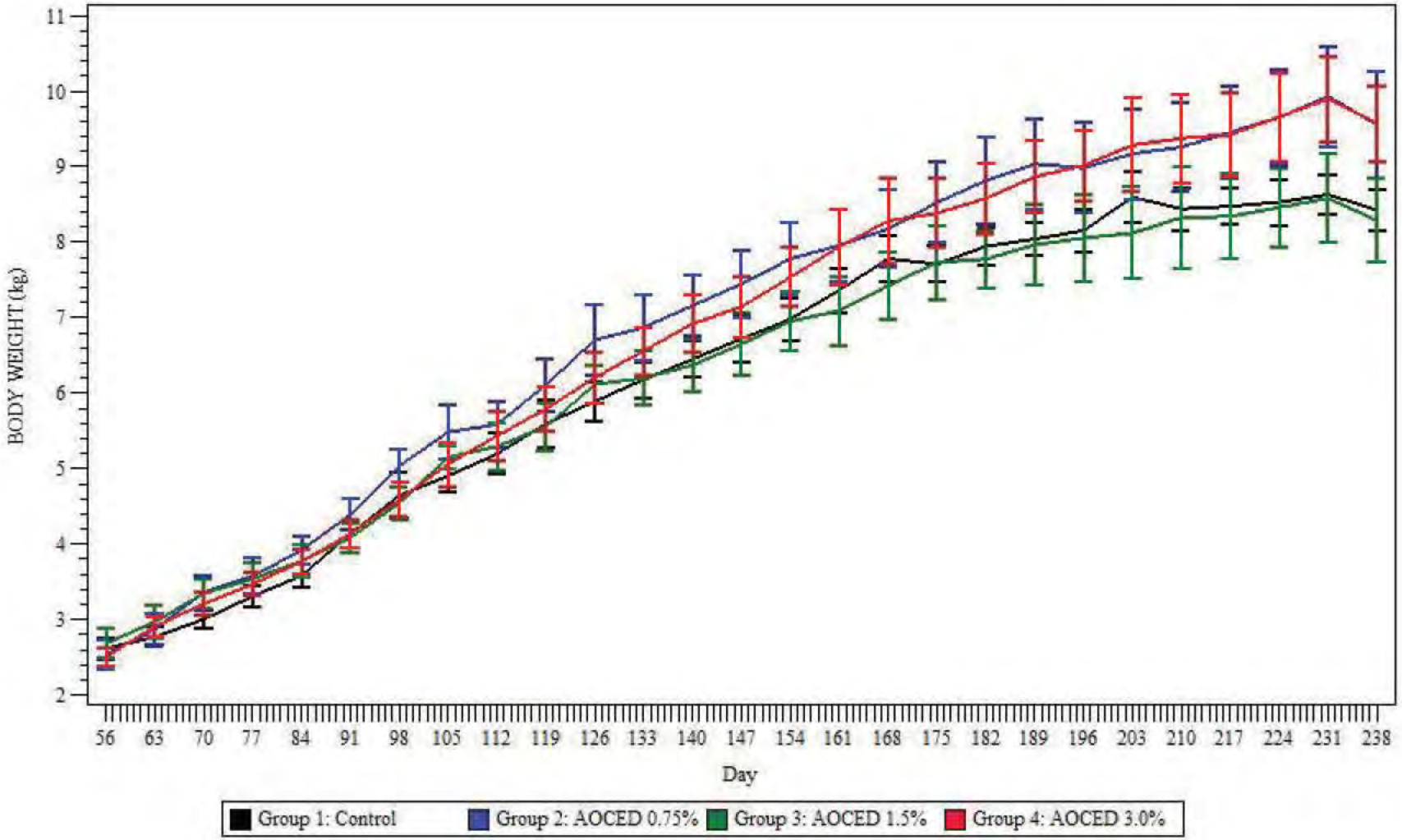
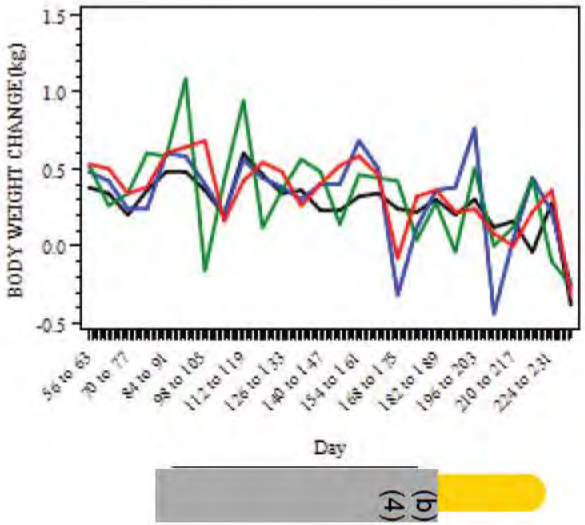


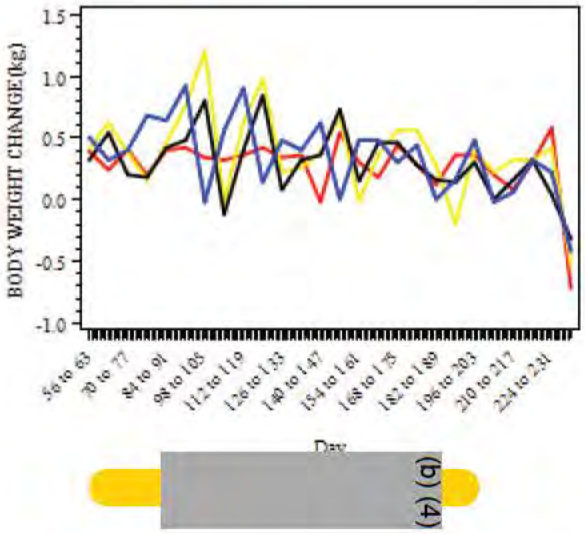
FIGURE NO. 65

(b) (4)

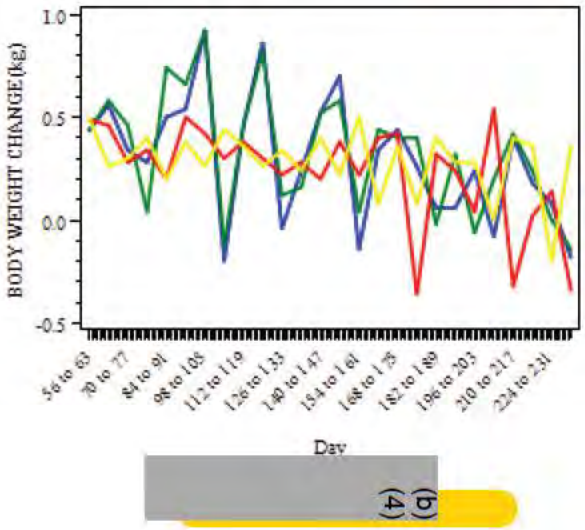
GENERATION F1, POST WEANING - PUPPIES
MALES



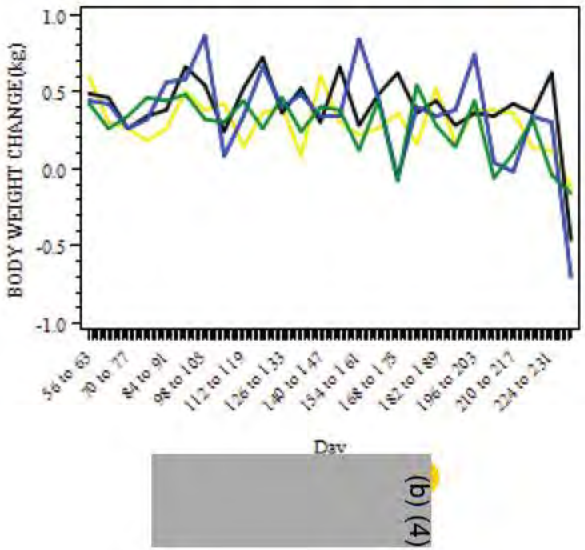
(b) (4)



(b) (4)



(b) (4)

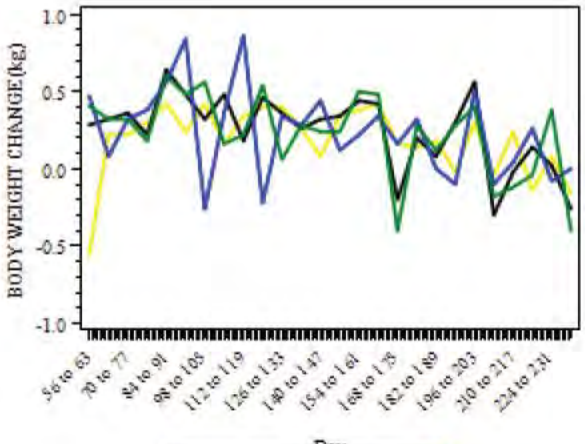


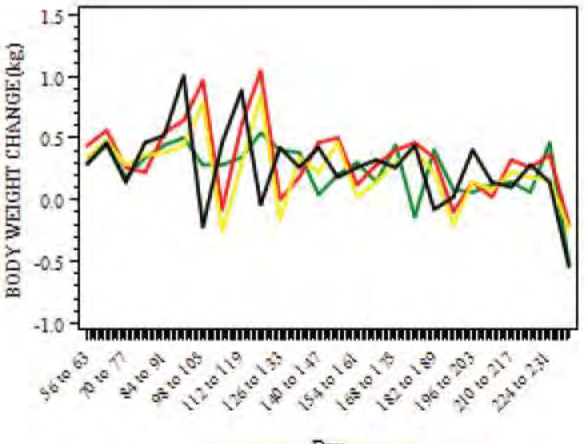
(b) (4)

FIGURE NO.66

(b) (4)

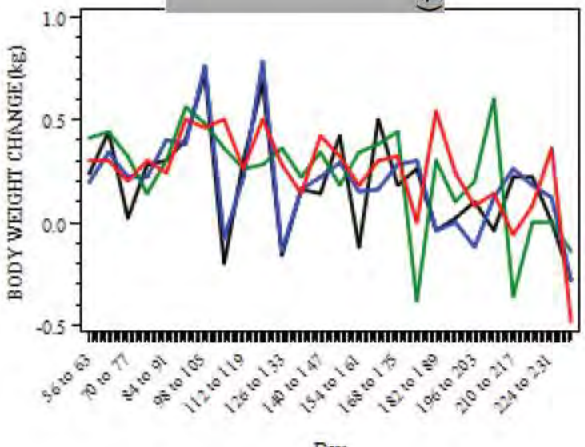
GENERATION F1, POST WEANING - PUPPIES
FEMALES

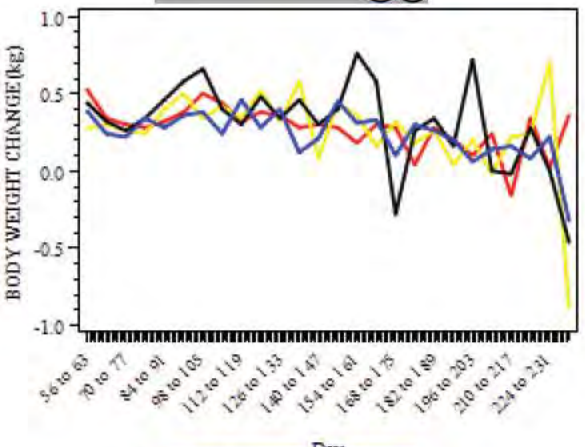




(b) (4)

(b) (4)





(b) (4)

(b) (4)

FIGURE NO. 67

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

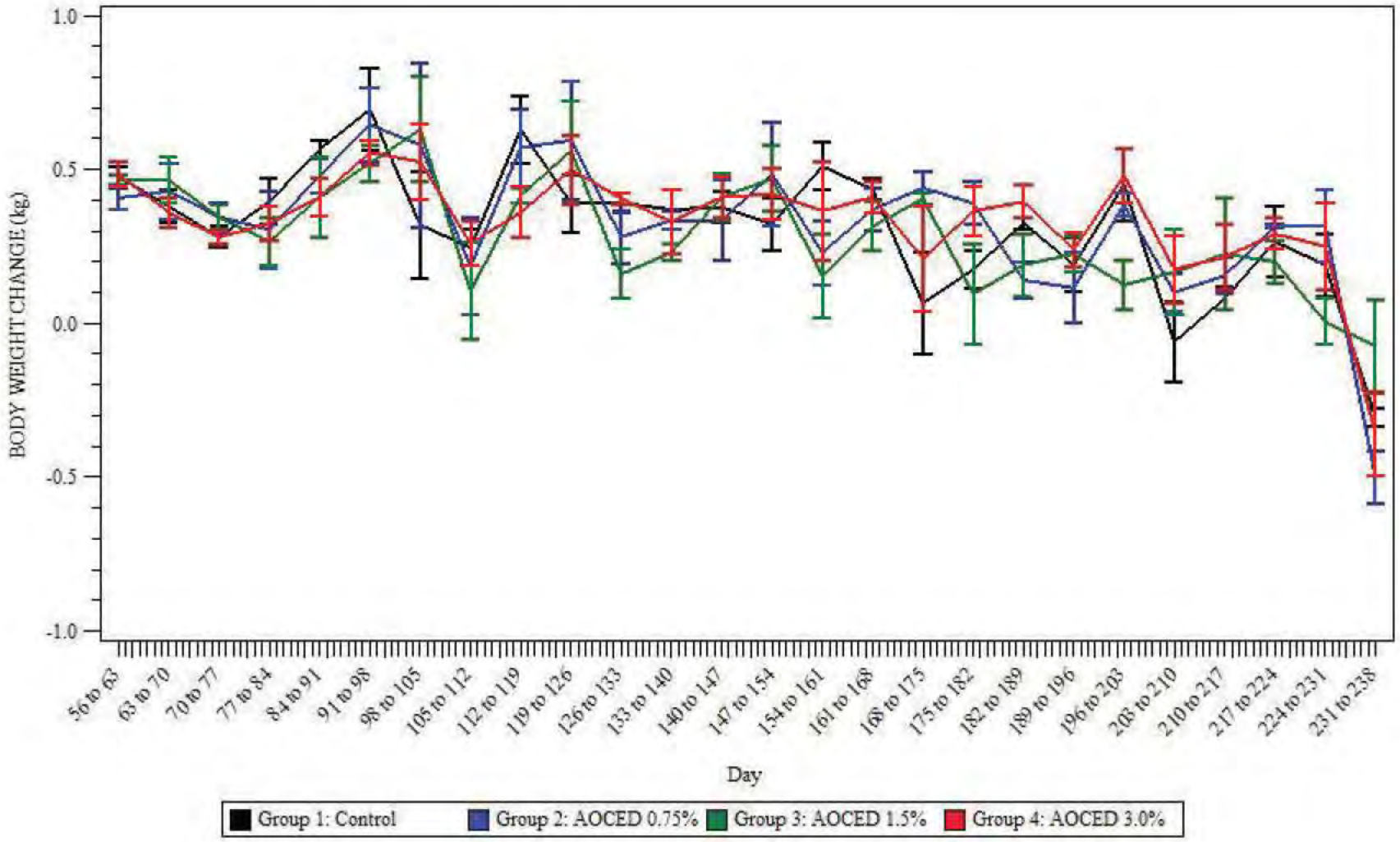


FIGURE NO. 68

(b) (4)

GENERATION F1, POST WEANING
FEMALES
Treatment Means ± SEM

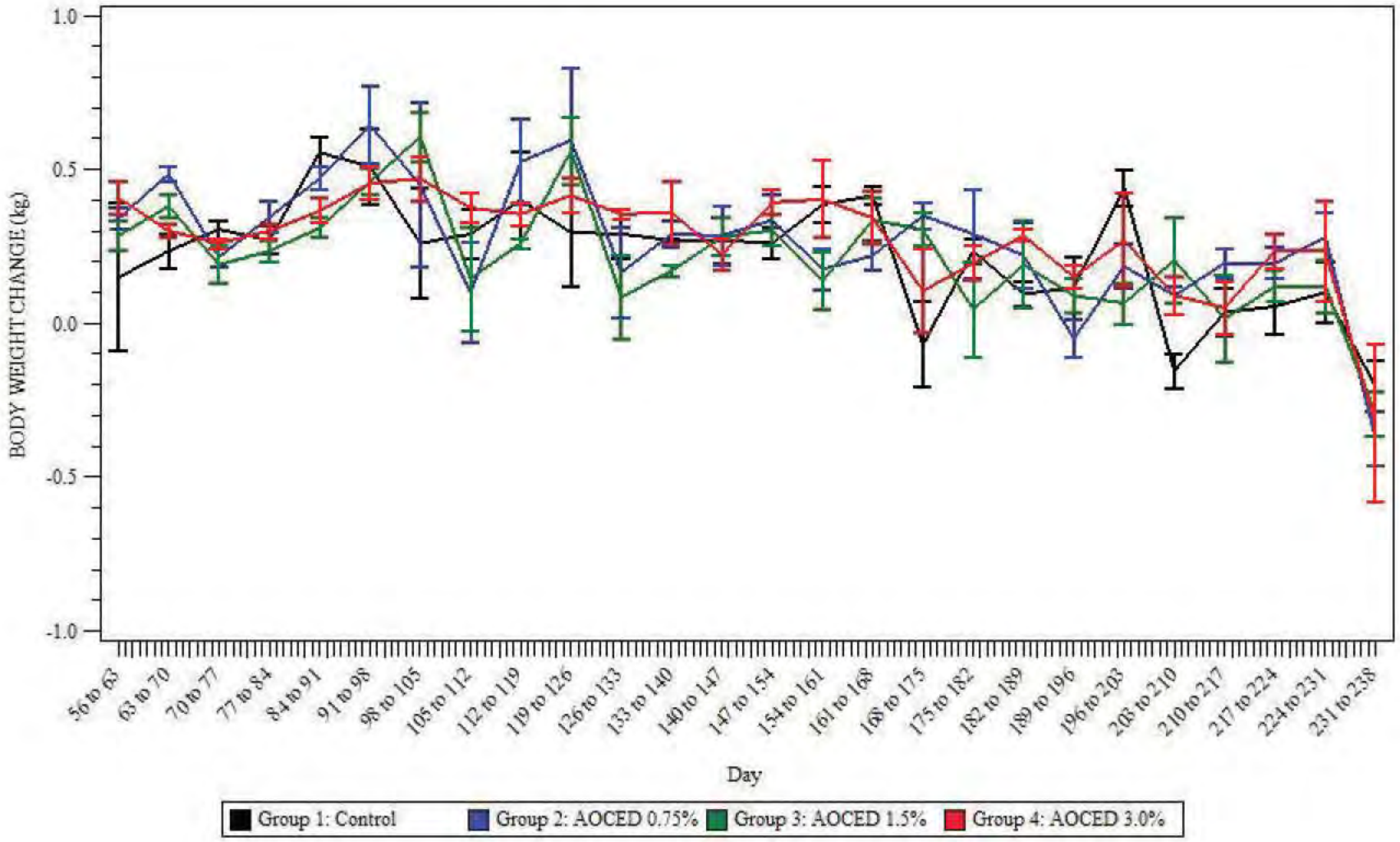
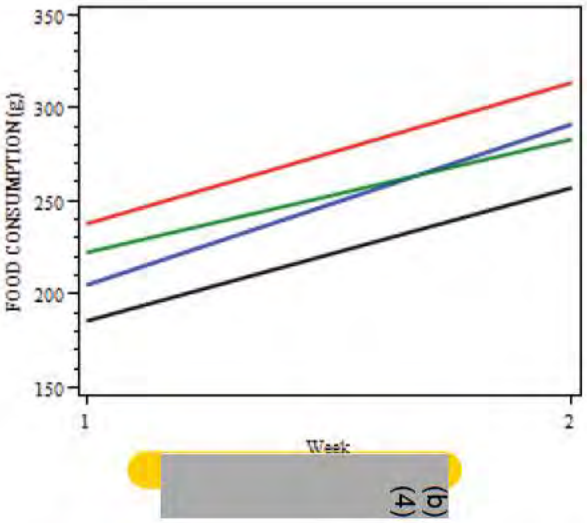


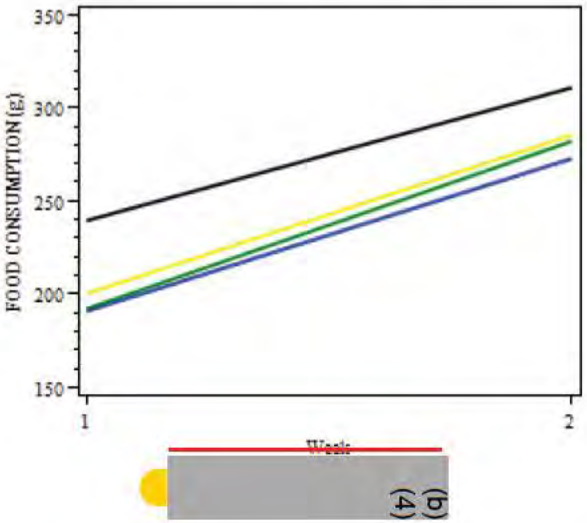
FIGURE NO. 69

[redacted]

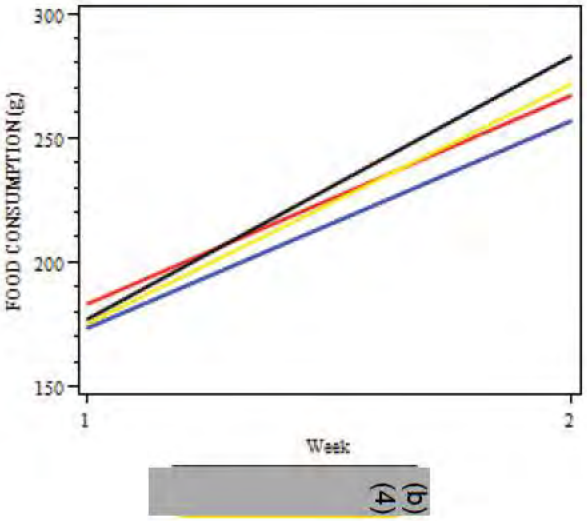
GENERATION F1, FIRST 2 WEEKS POST WEANING - PUPPIES
CAGES (MALES AND FEMALES)



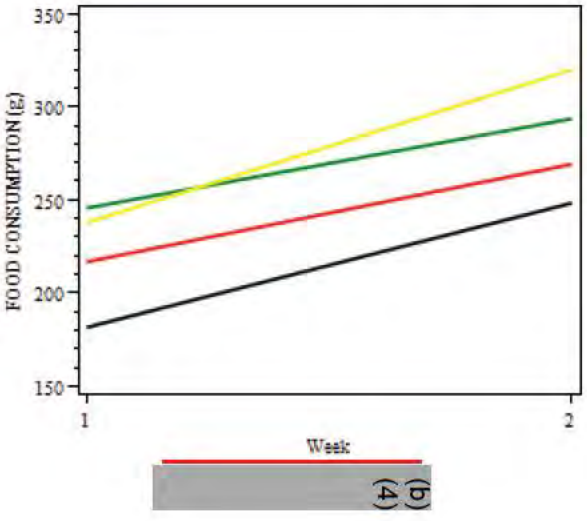
[redacted]



[redacted]



[redacted]



[redacted]

FIGURE NO. 70

(b) (4)

GENERATION F1, FIRST 2 WEEKS POST WEANING - PUPPIES
CAGES (MALES AND FEMALES)
Treatment Means ± SEM

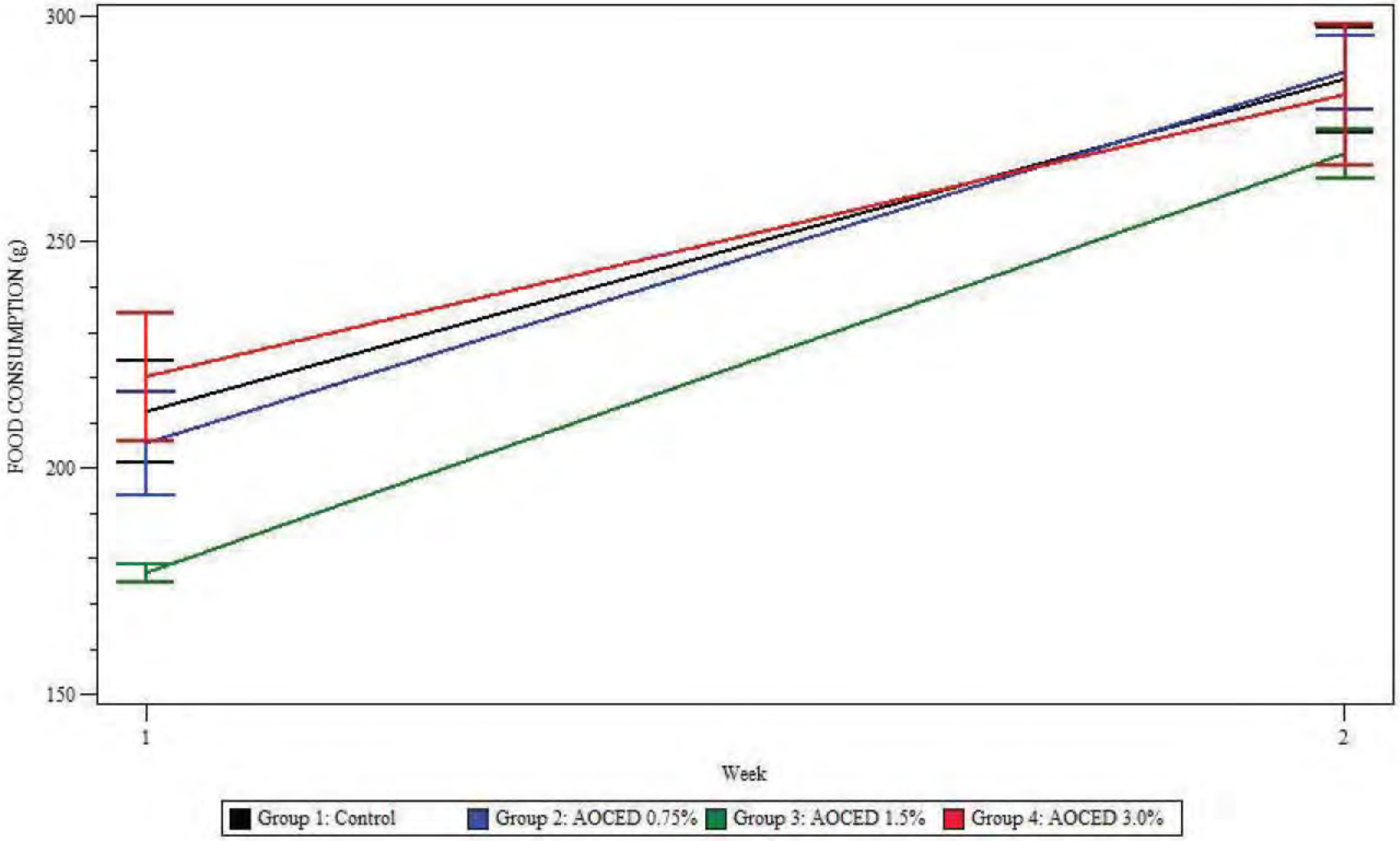
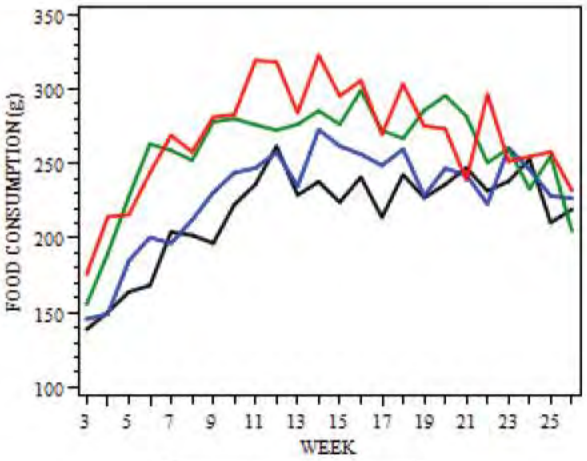


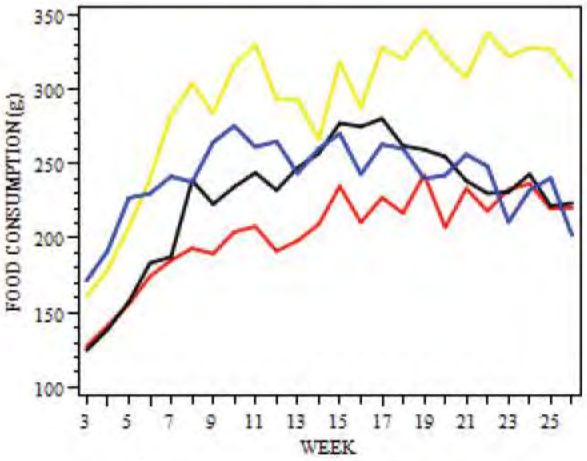
FIGURE NO. 71

(b) (4)

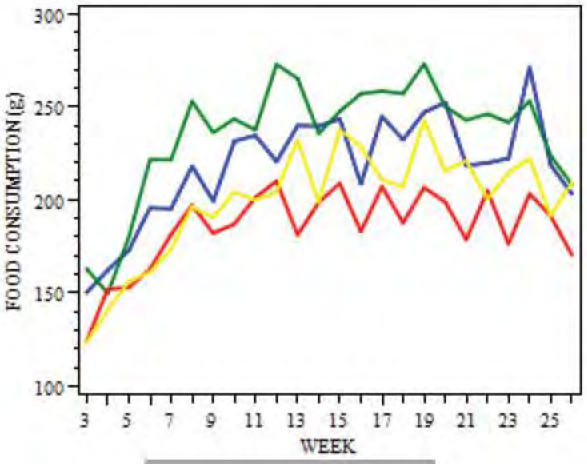
GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
MALES



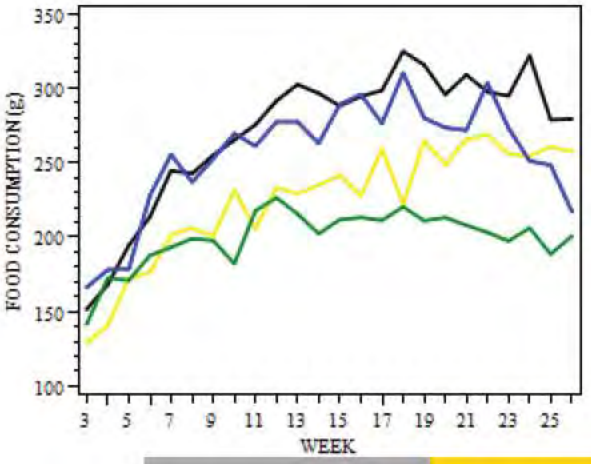
(b) (4)



(b) (4)



(b) (4)

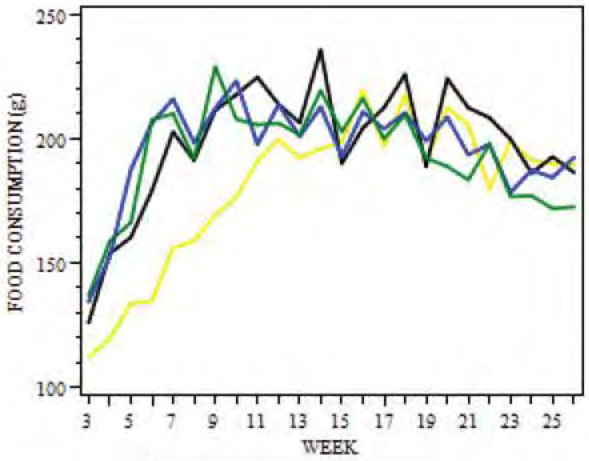


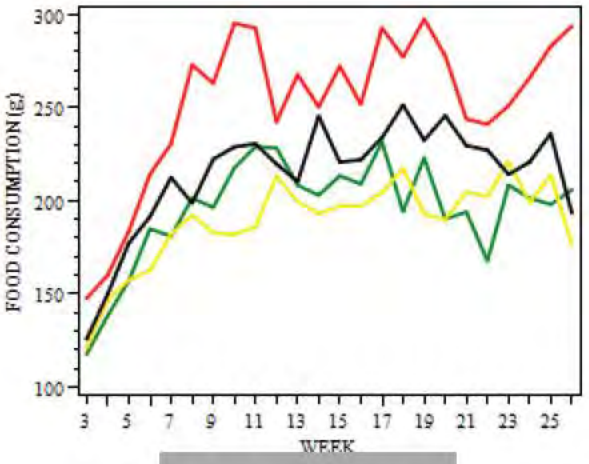
(b) (4)

FIGURE NO. 72

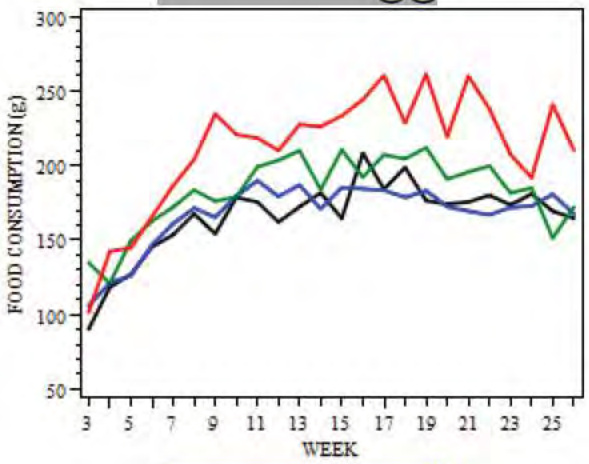
[redacted] (b) (4)

GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
FEMALES

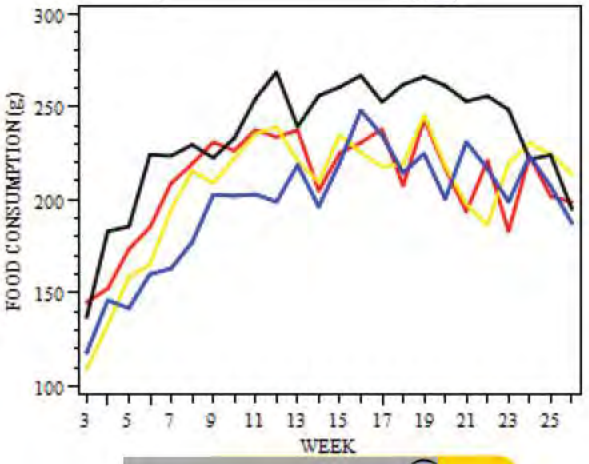




[redacted] (b) (4)



[redacted] (b) (4)



[redacted] (b) (4)

FIGURE NO. 73

(b) (4)

GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

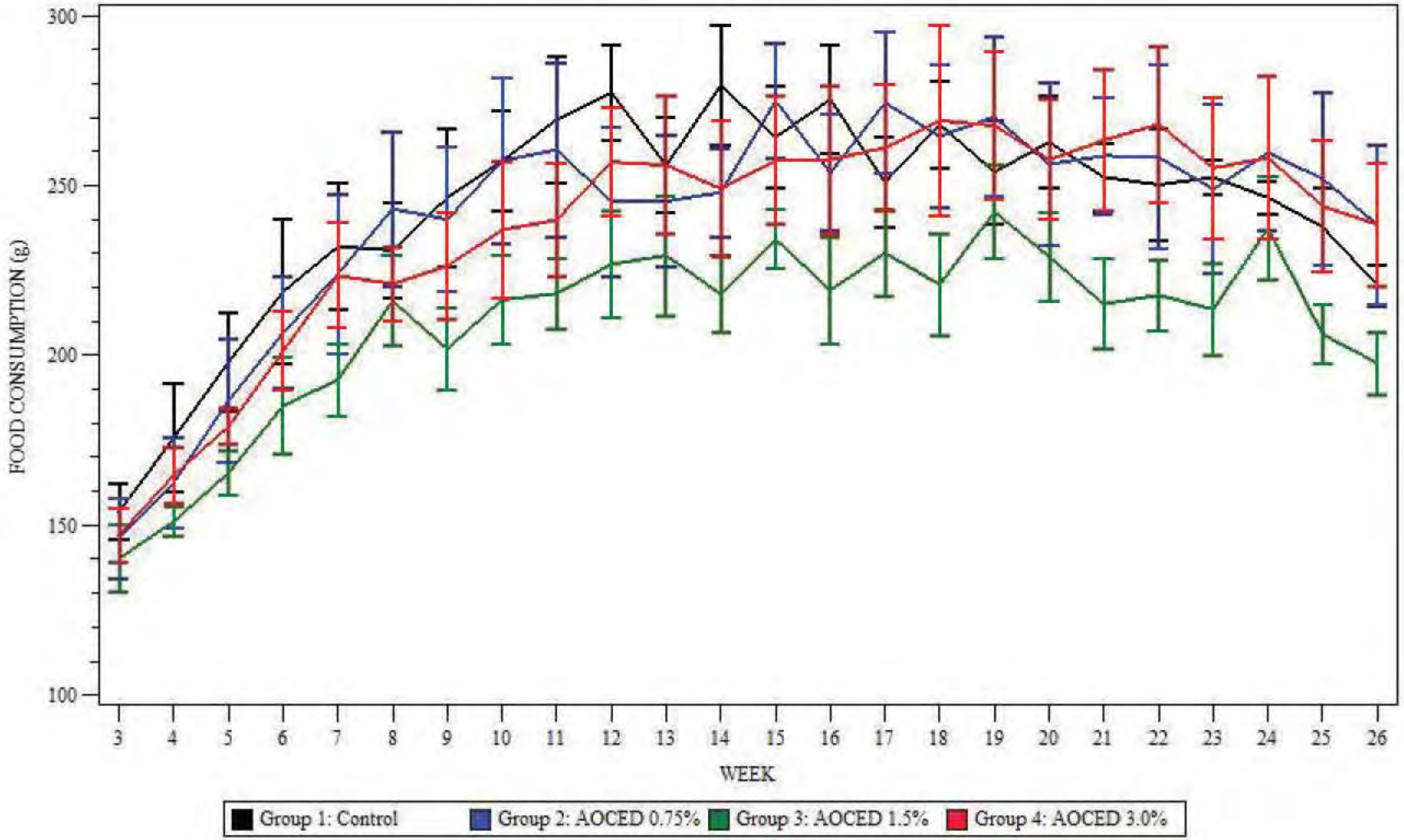


FIGURE NO. 74

(b) (4)

GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

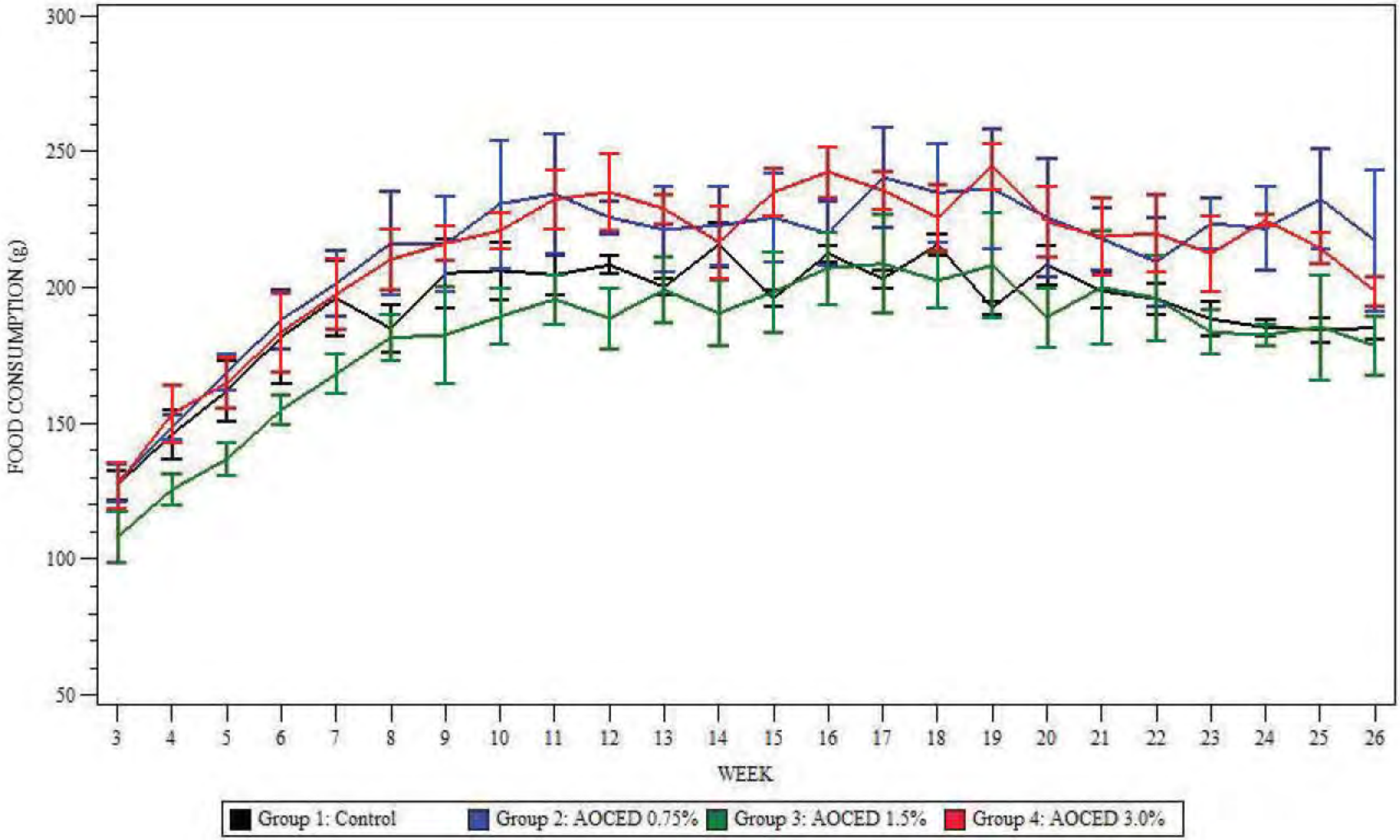
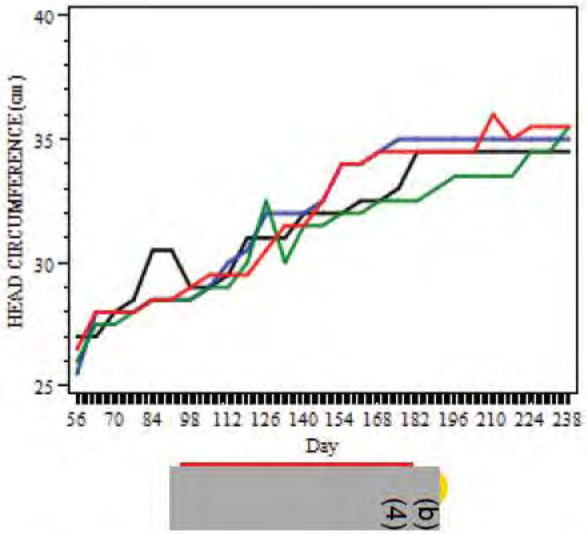


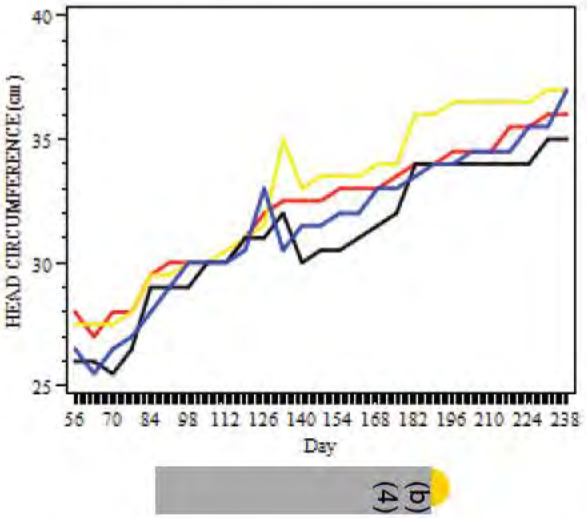
FIGURE NO. 75

(b) (4)

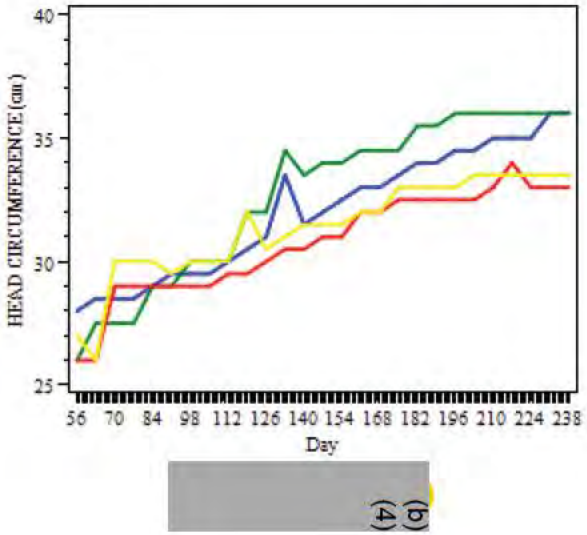
GENERATION F1, POST WEANING - PUPPIES
MALES



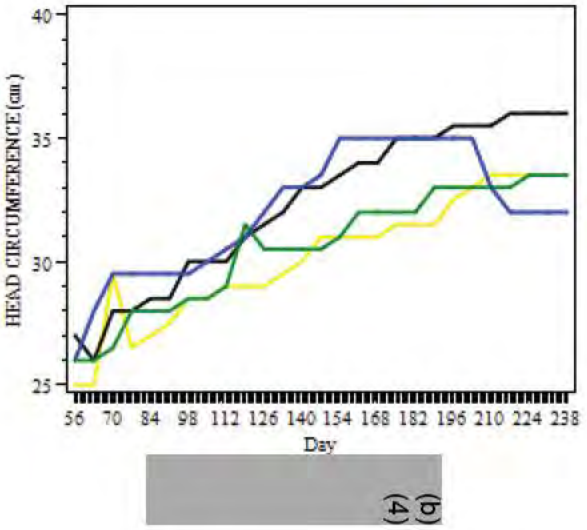
(b) (4)



(b) (4)



(b) (4)

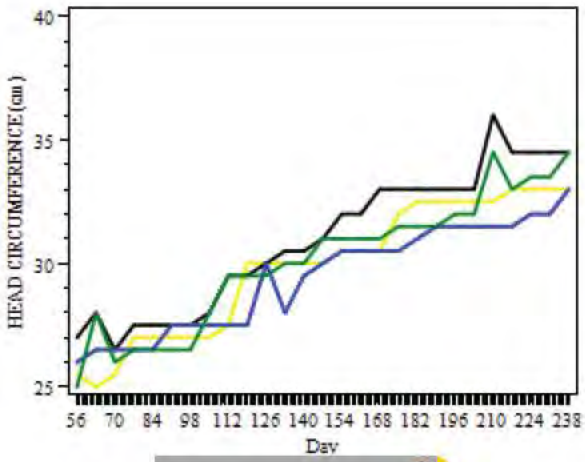


(b) (4)

FIGURE NO. 76

[redacted]

GENERATION F1, POST WEANING - PUPPIES
FEMALES



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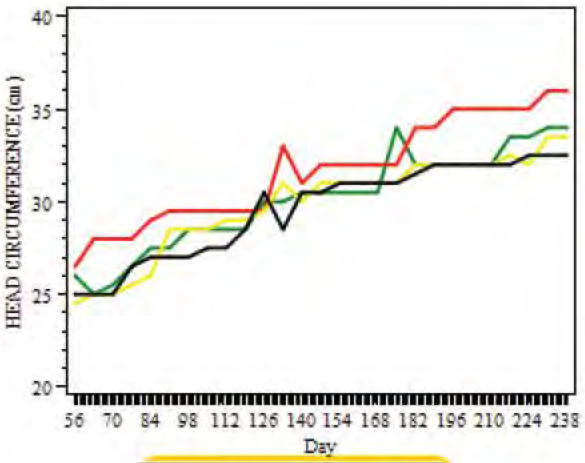
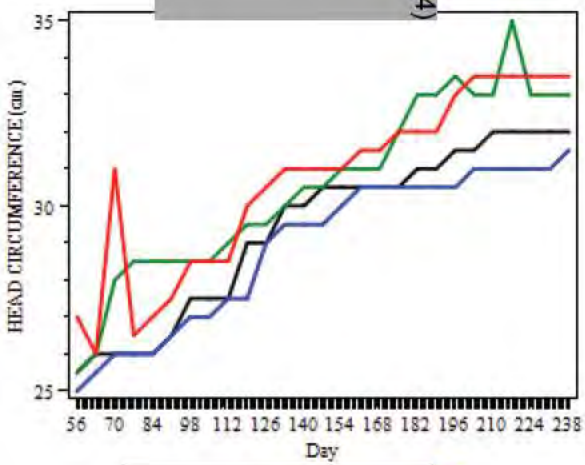
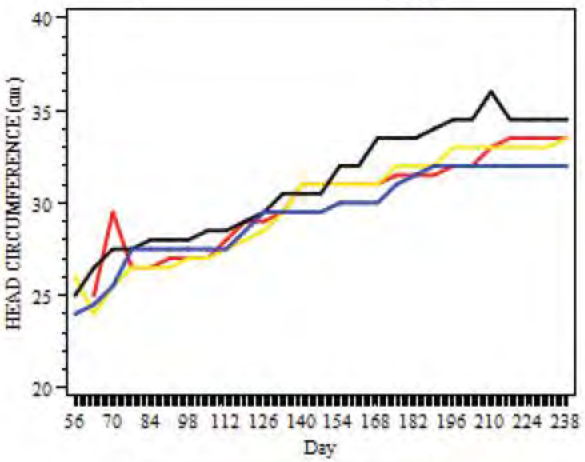


[redacted]



[redacted]



[redacted]

FIGURE NO. 77

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

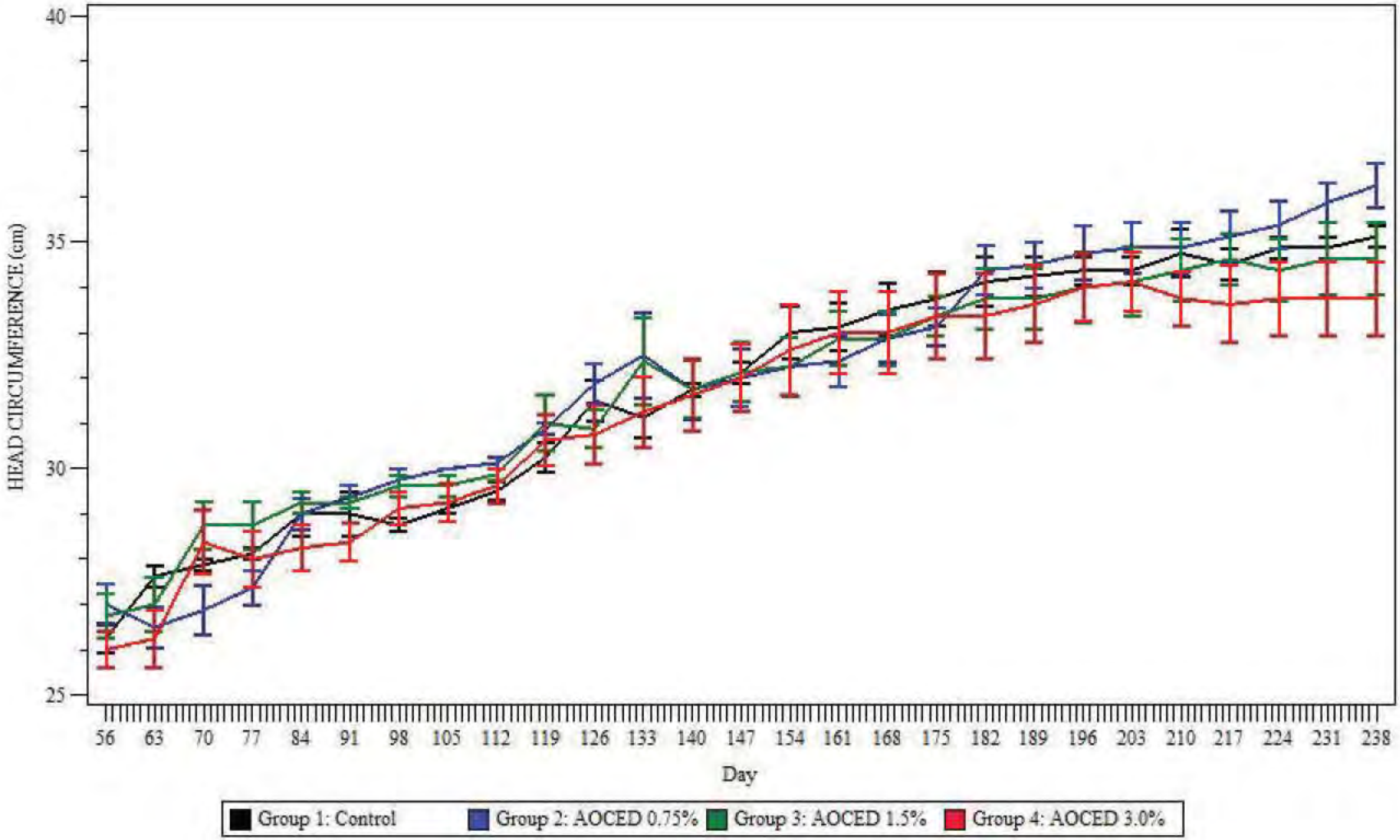


FIGURE NO. 78

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

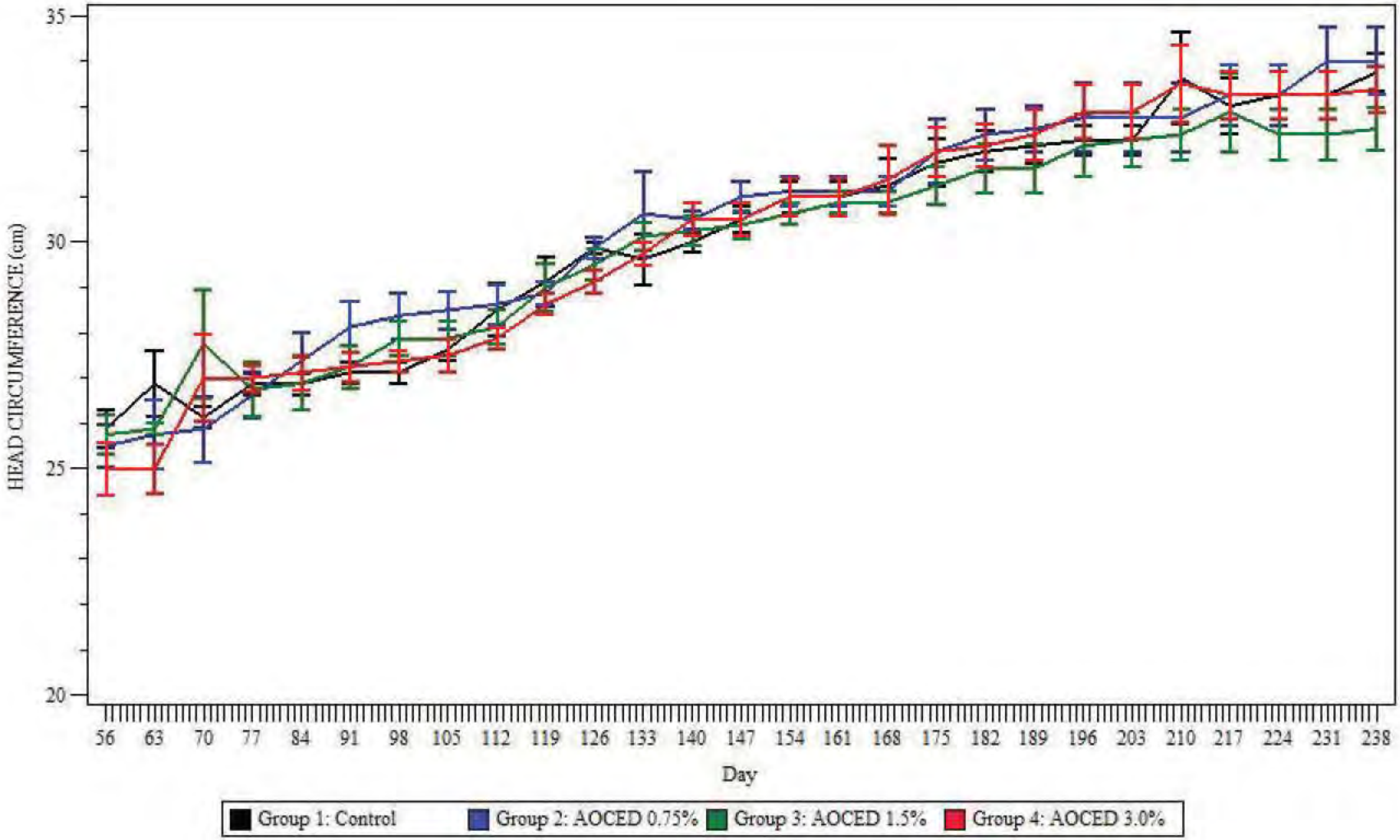
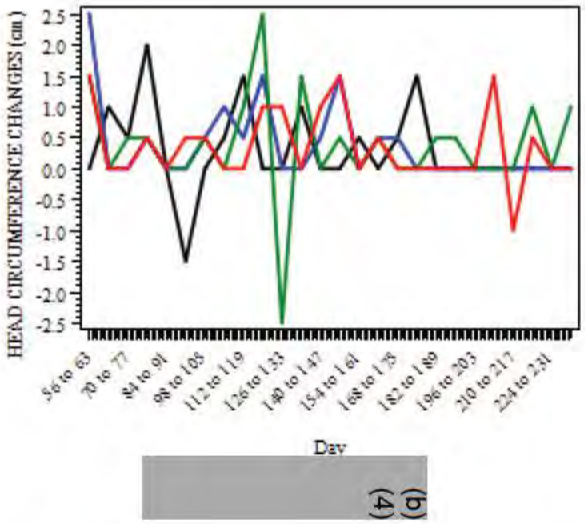


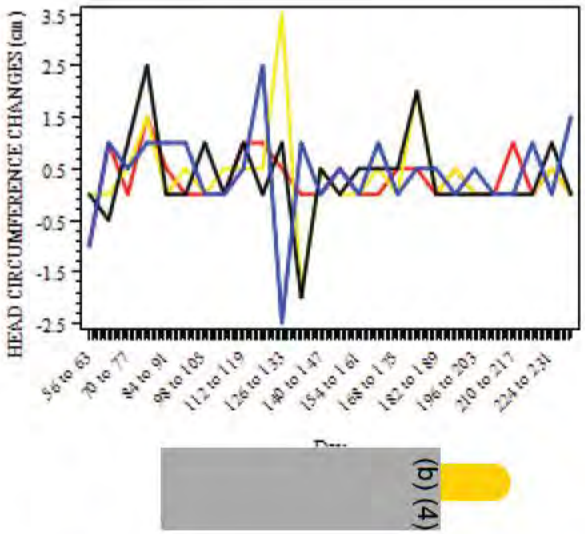
FIGURE NO. 79

(b) (4)

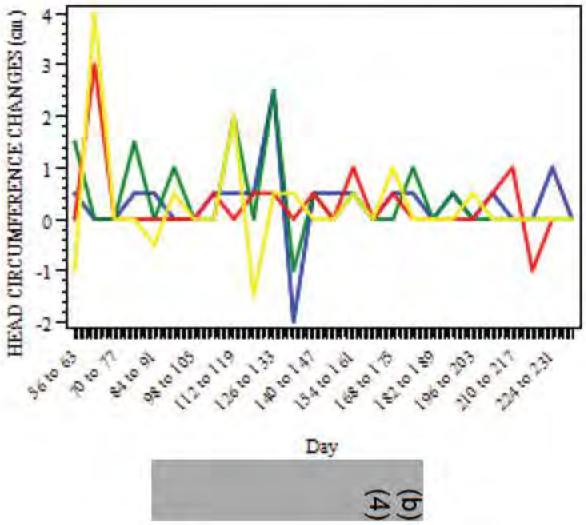
GENERATION F1, POST WEANING - PUPPIES
MALES



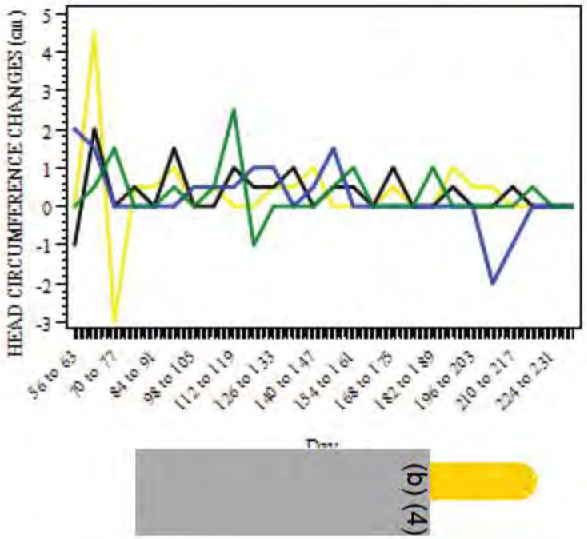
(b) (4)



(b) (4)



(b) (4)

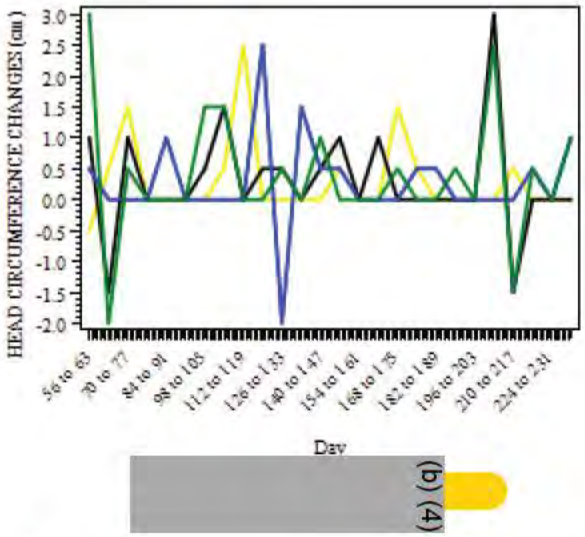


(b) (4)

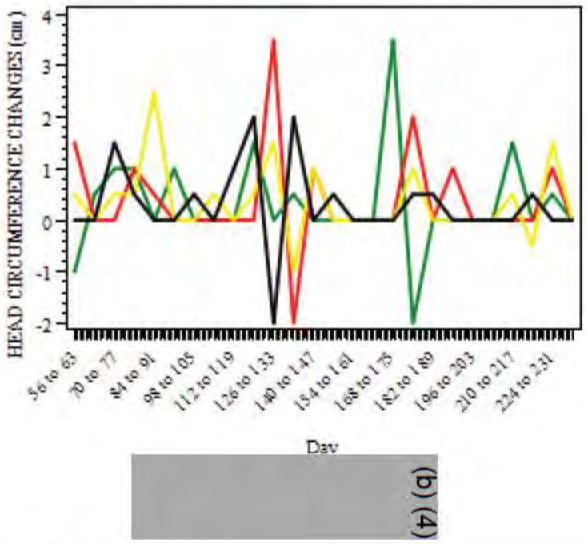
FIGURE NO. 80

(b) (4)

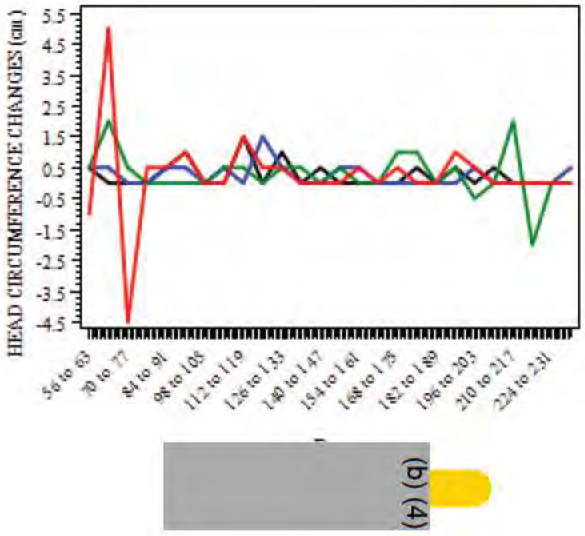
GENERATION F1, POST WEANING - PUPPIES
FEMALES



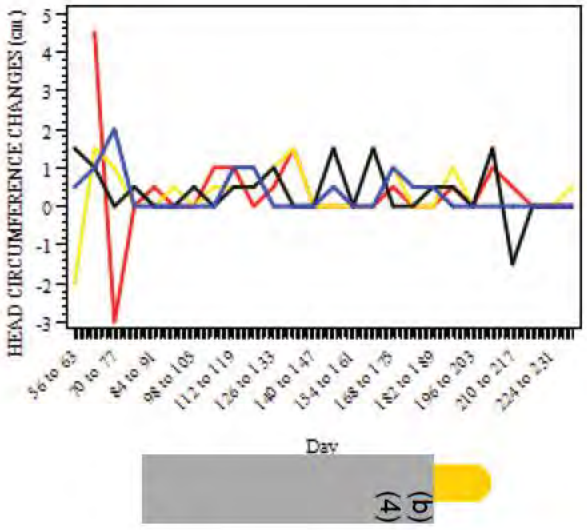
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 81

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

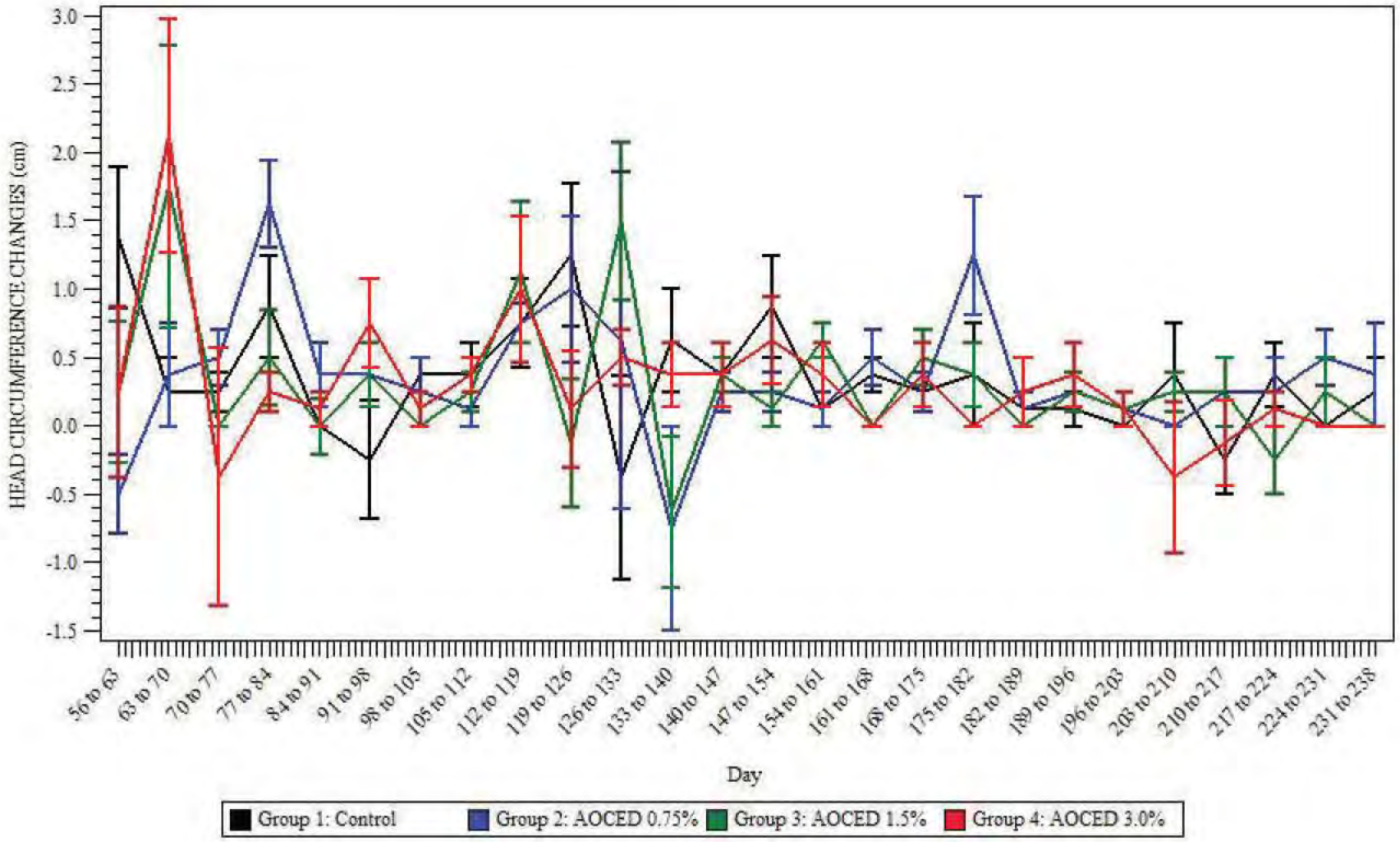


FIGURE NO. 82

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

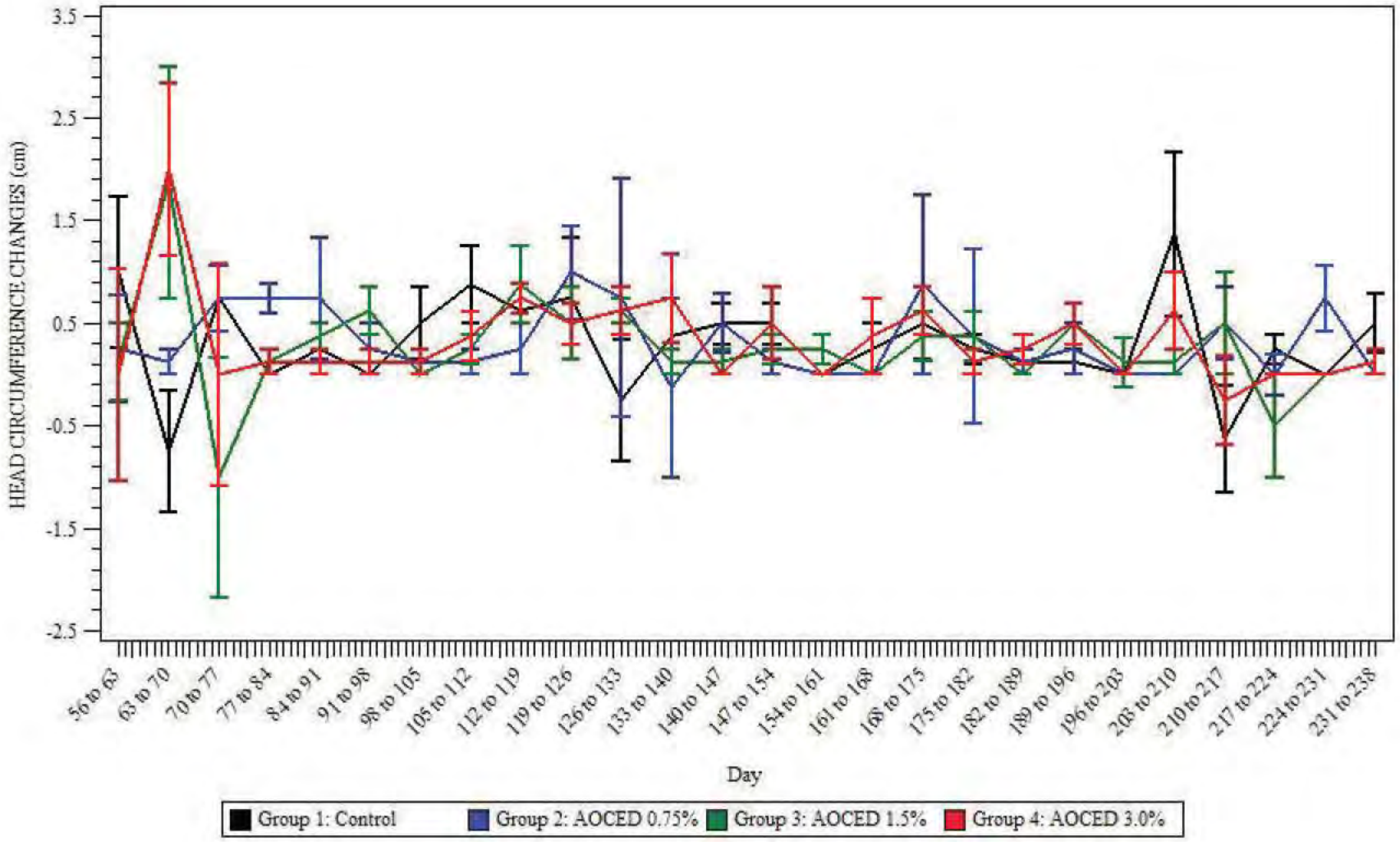
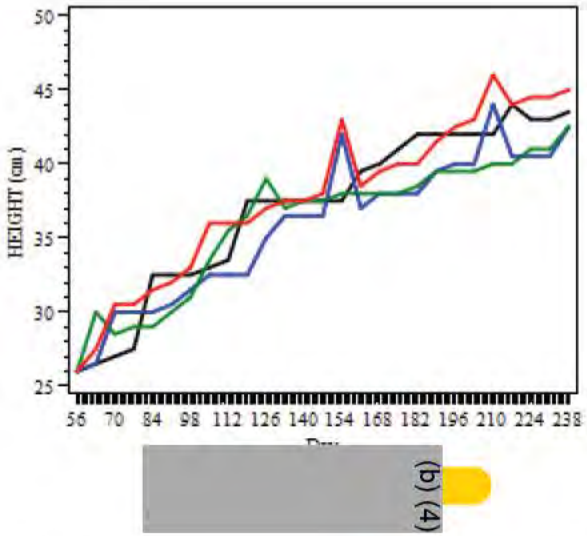


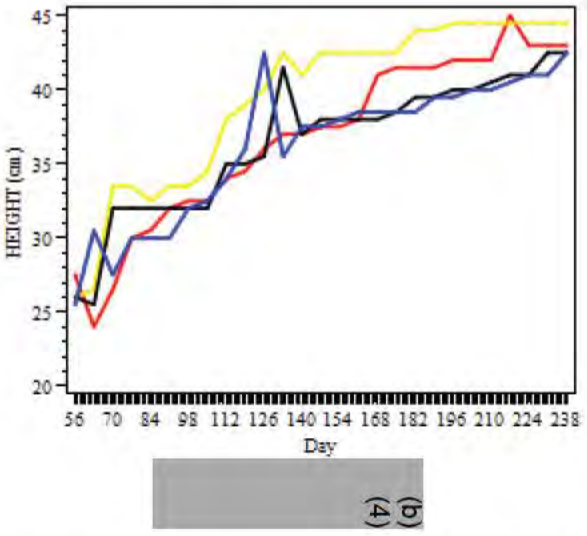
FIGURE NO. 83

(b) (4)

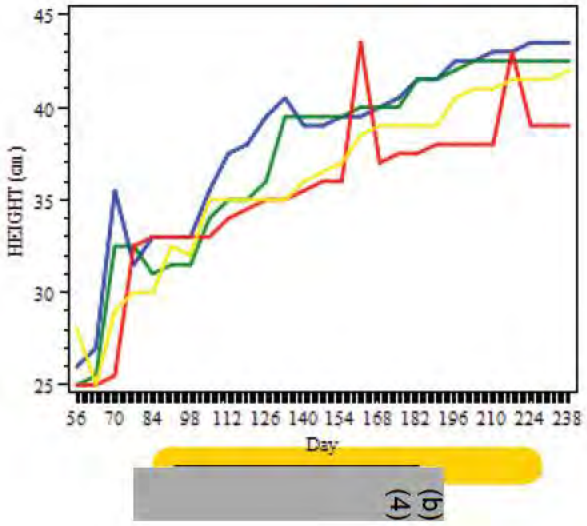
GENERATION F1, POST WEANING - PUPPIES
MALES



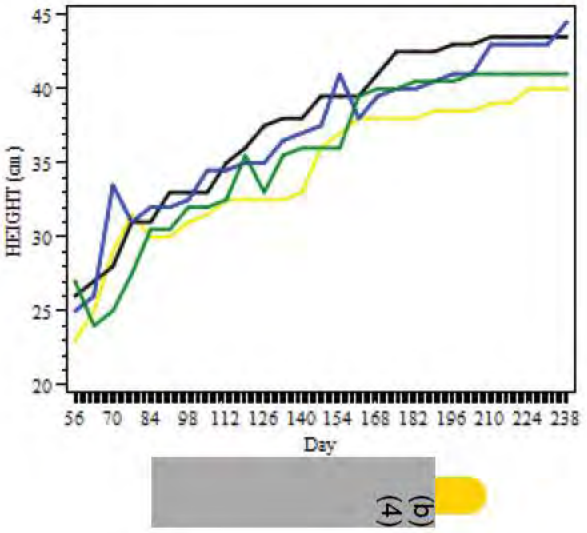
(b) (4)



(b) (4)



(b) (4)

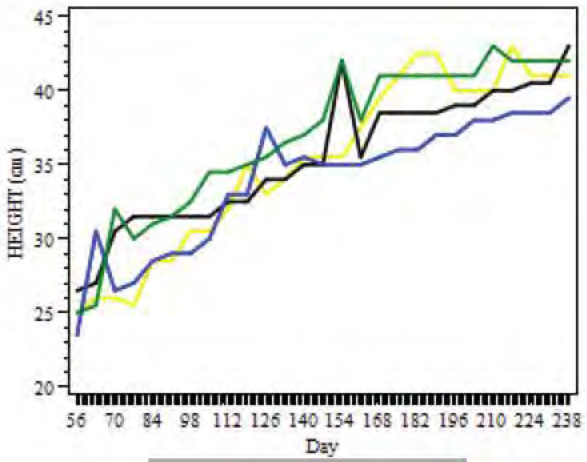


(b) (4)

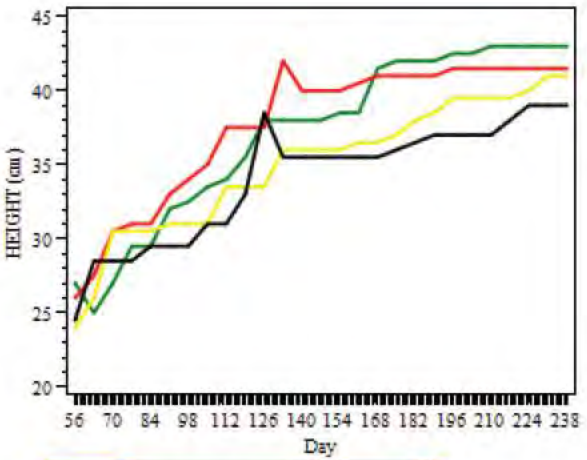
FIGURE NO. 84

(b) (4)

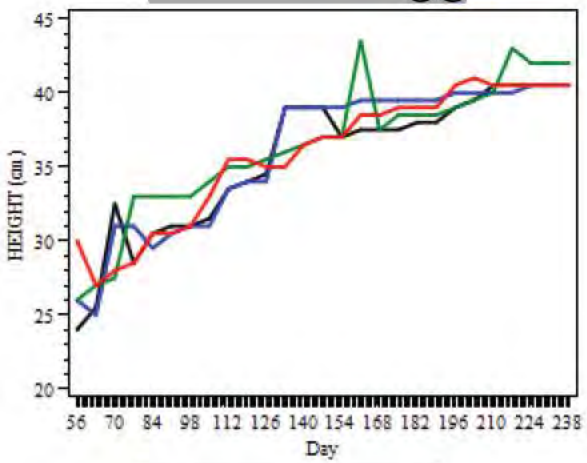
GENERATION F1, POST WEANING - PUPPIES
FEMALES



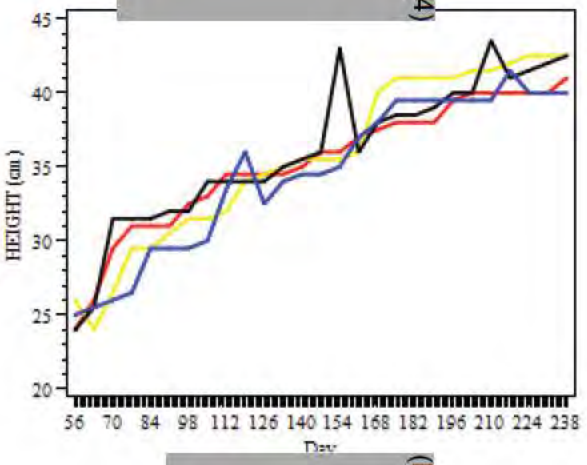
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO.85

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

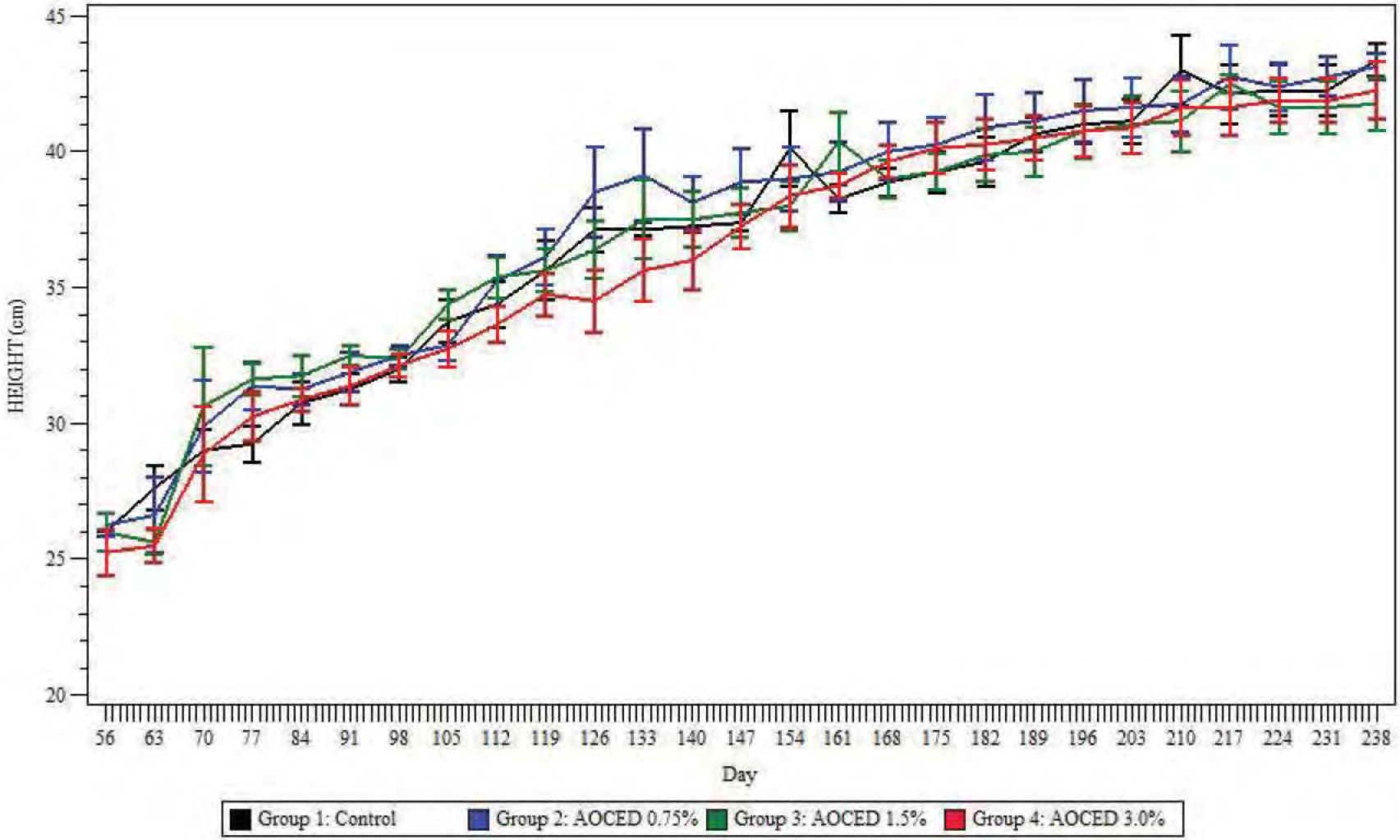


FIGURE NO. 86

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

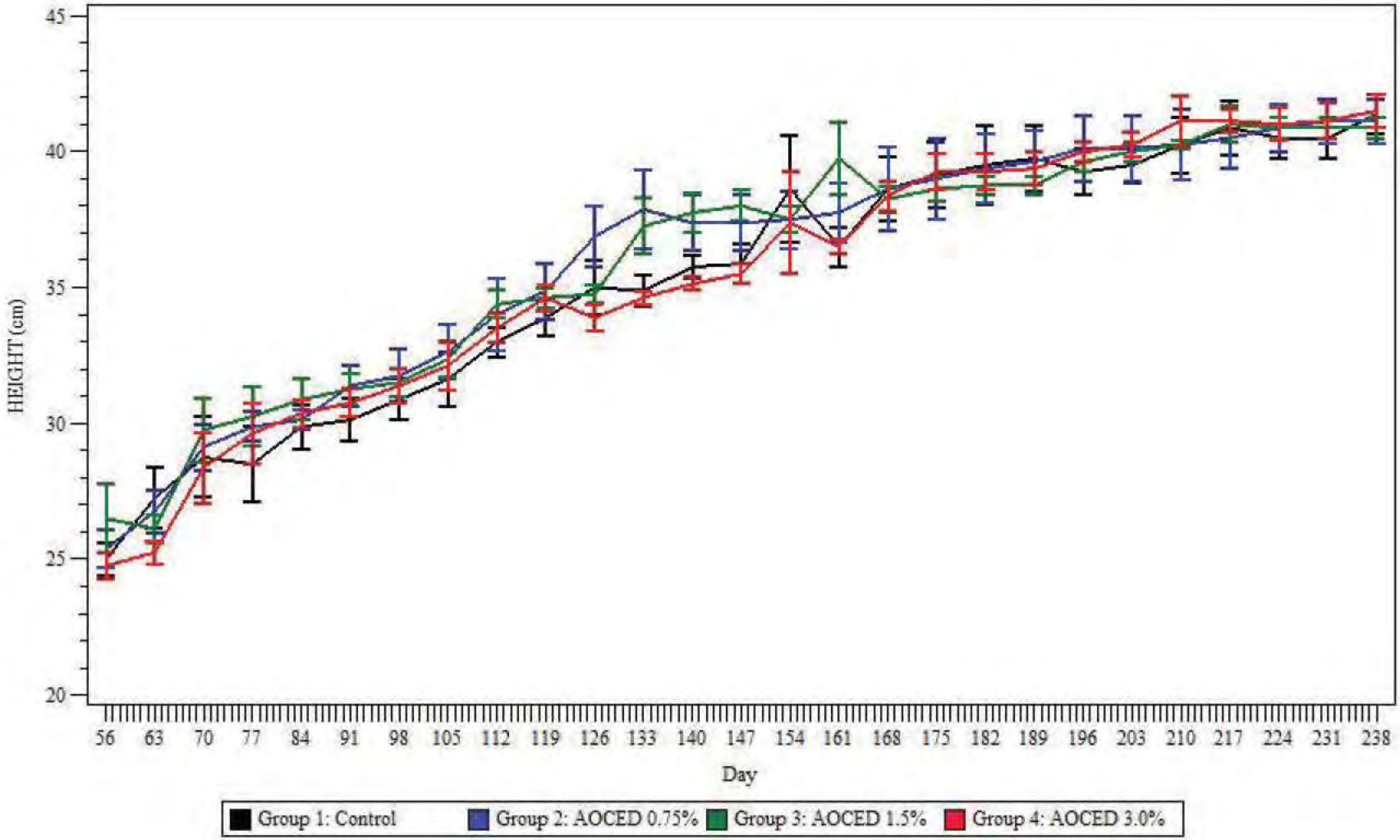
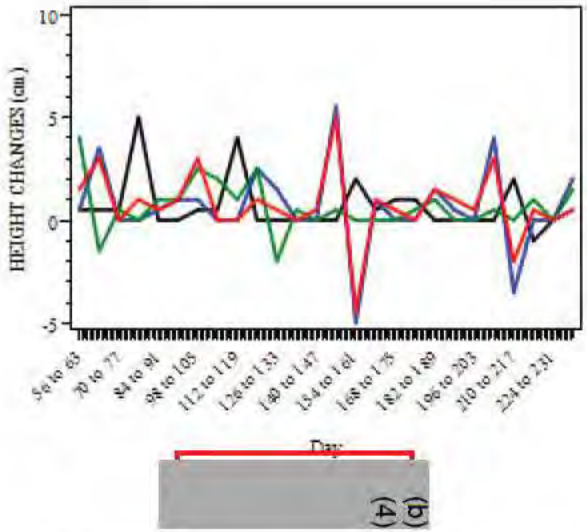
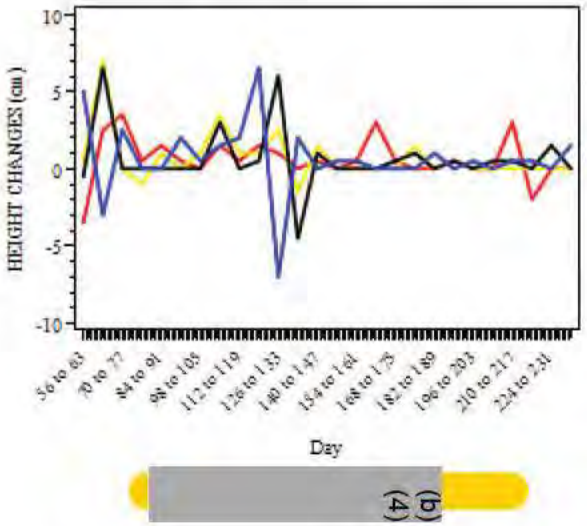


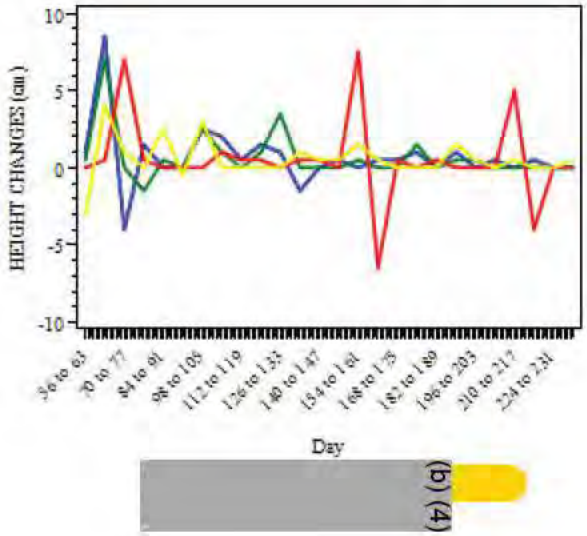
FIGURE NO. 87

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES







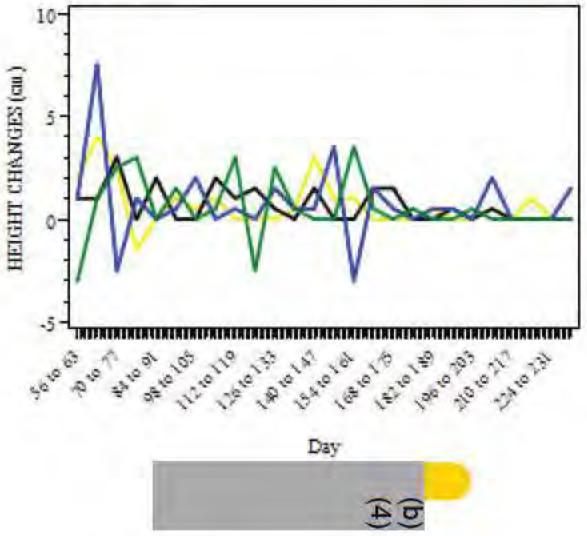
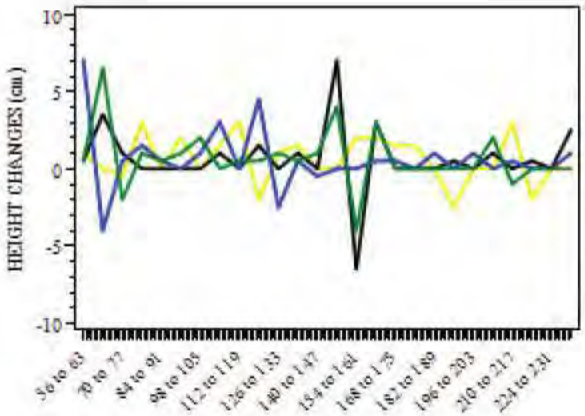
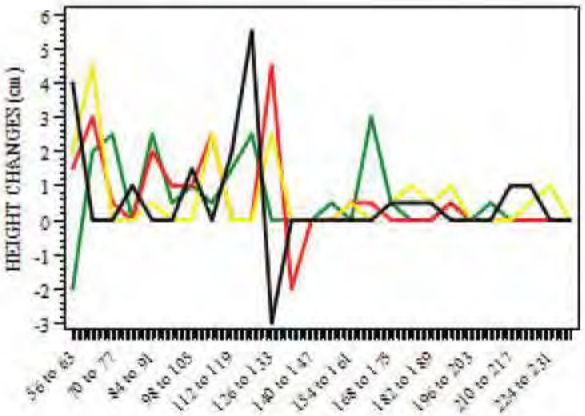
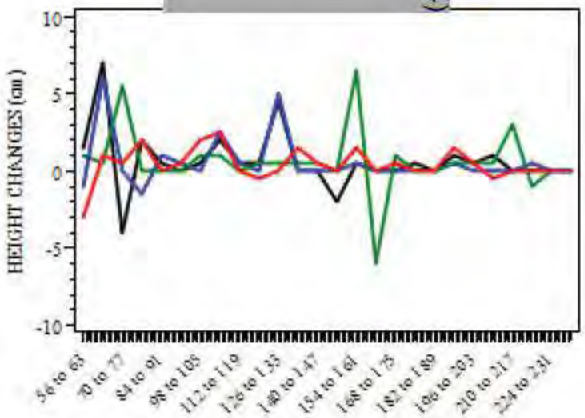


FIGURE NO. 88

GENERATION F1, POST WEANING - PUPPIES
FEMALES







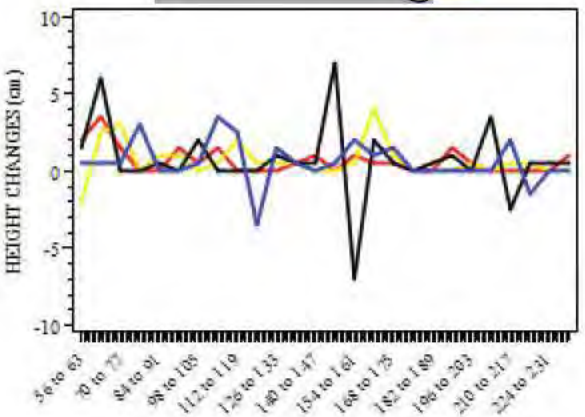


FIGURE NO. 89

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

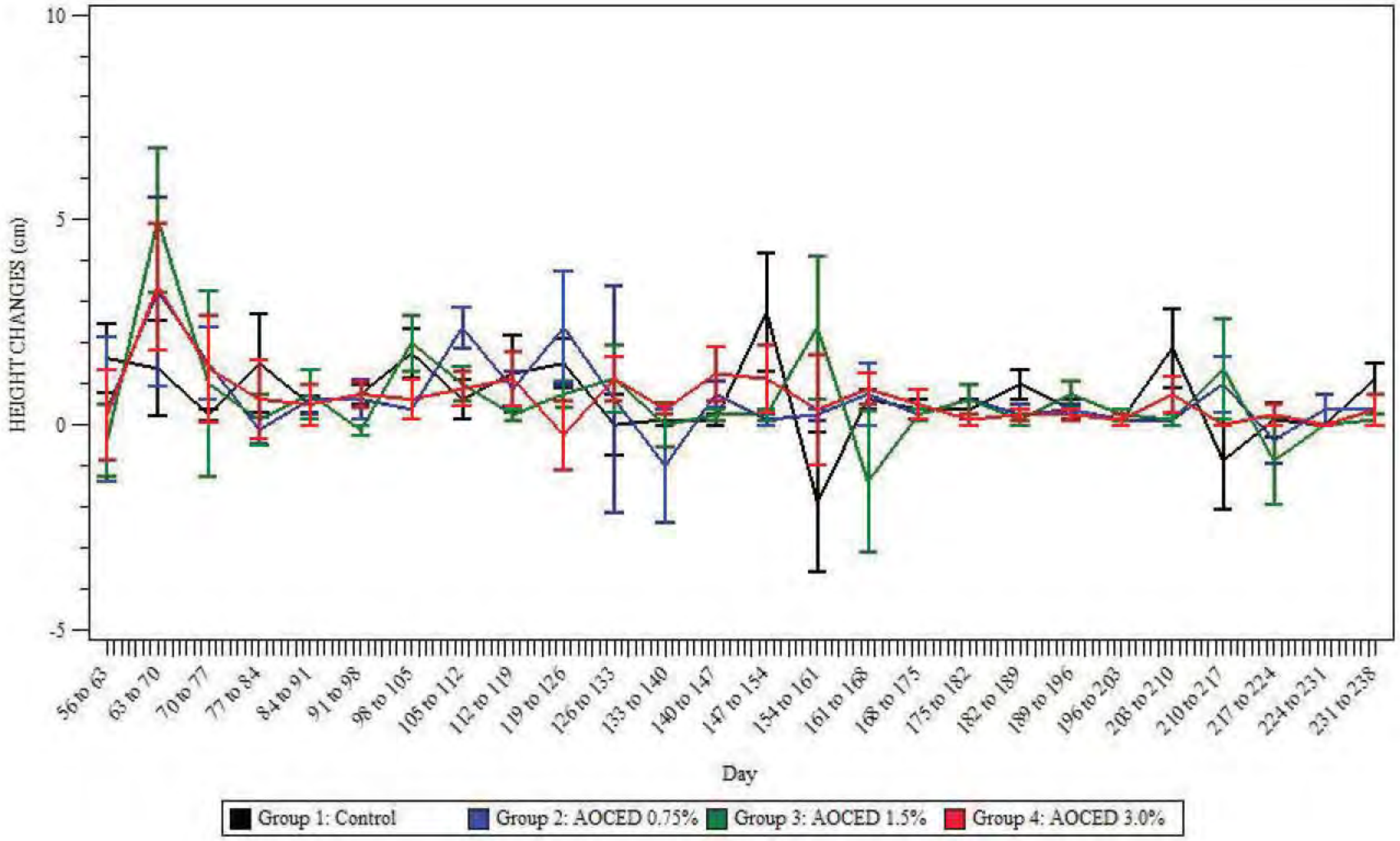


FIGURE NO. 90

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

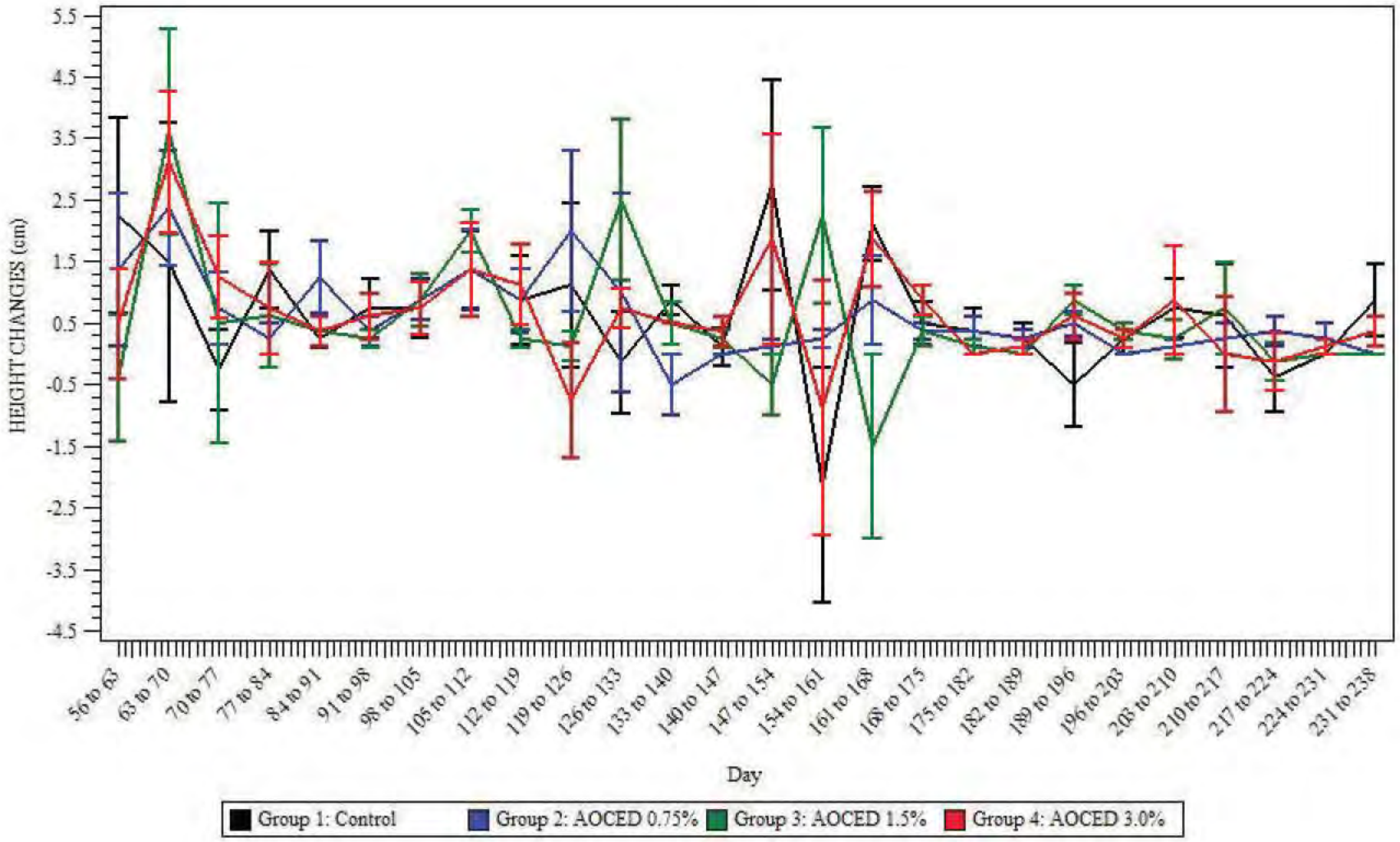
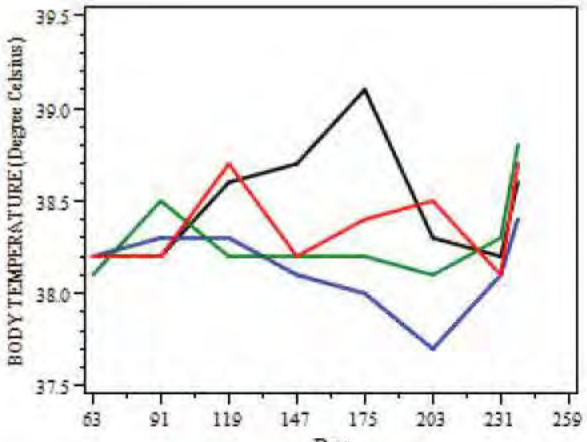


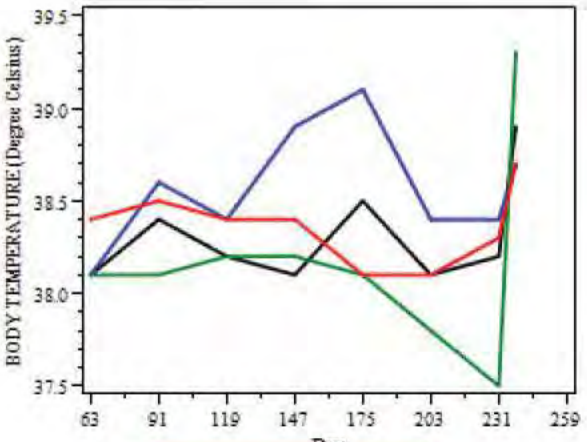
FIGURE NO. 91

(b) (4)

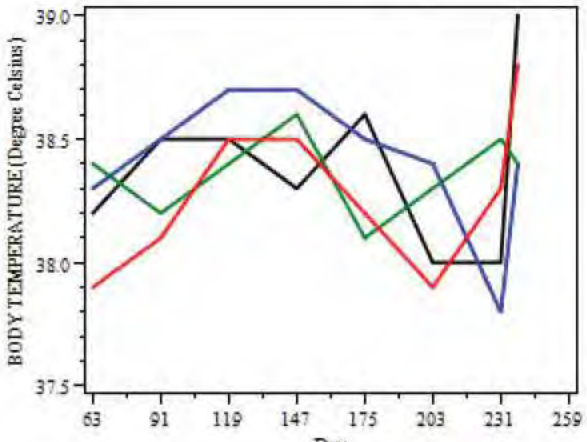
GENERATION F1, POST WEANING - PUPPIES
MALES



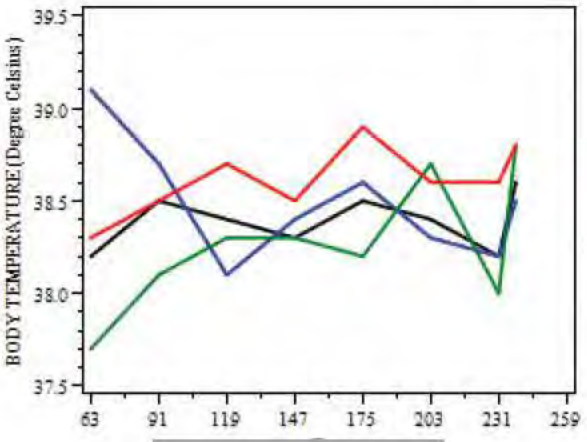
(b) (4)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 92

[redacted]

GENERATION F1, POST WEANING - PUPPIES
FEMALES

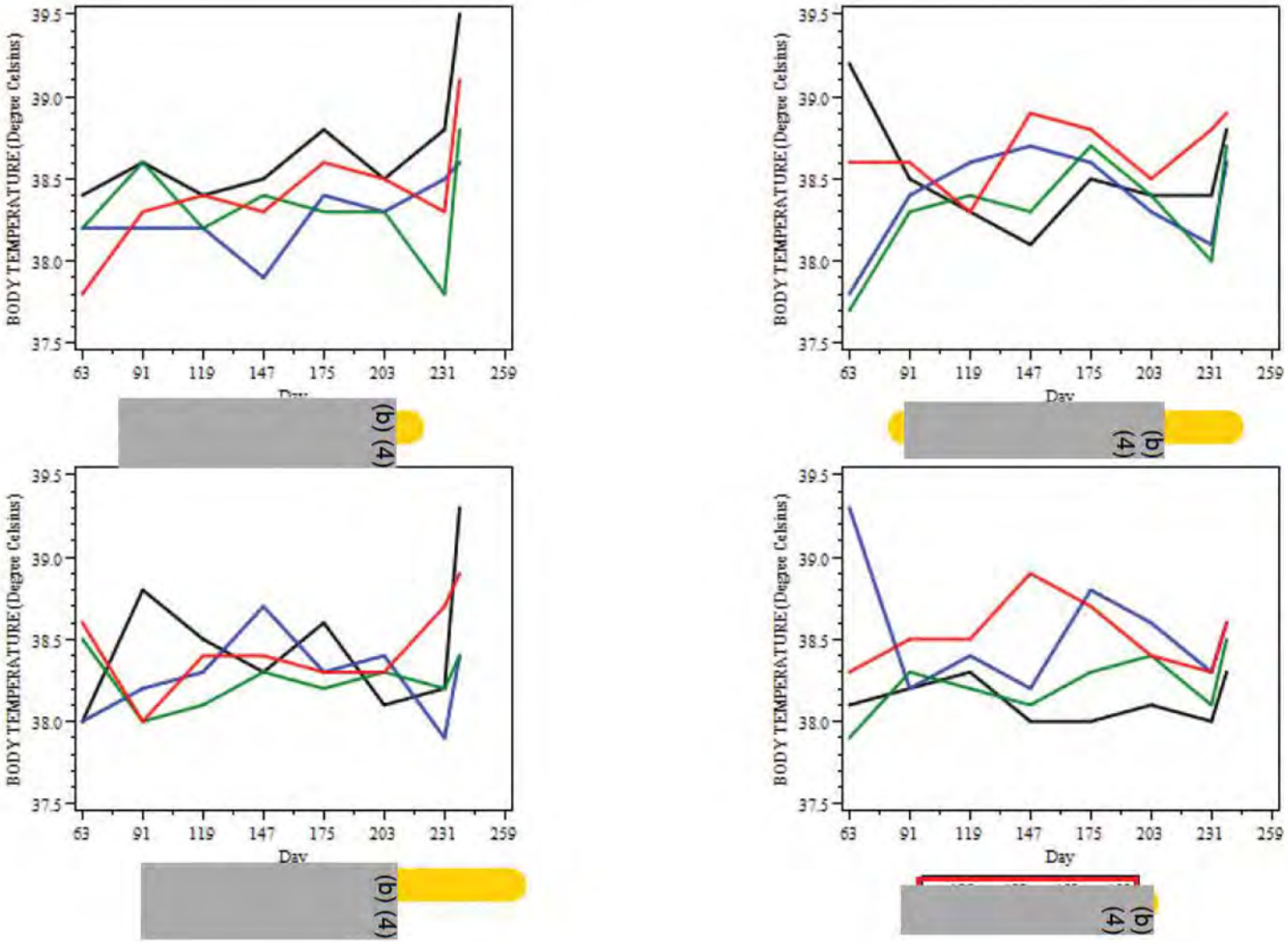


FIGURE NO. 93

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

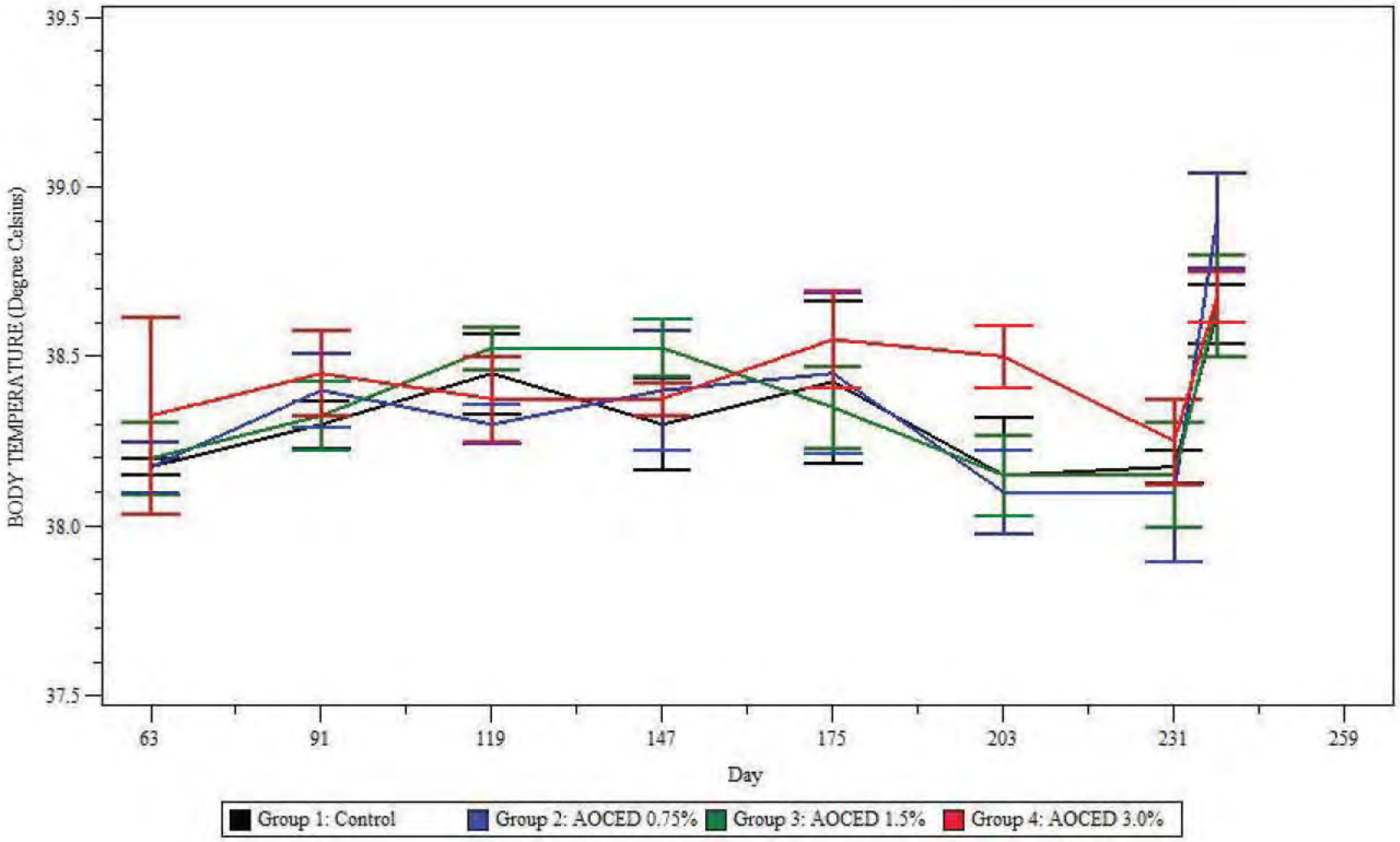


FIGURE NO. 94

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

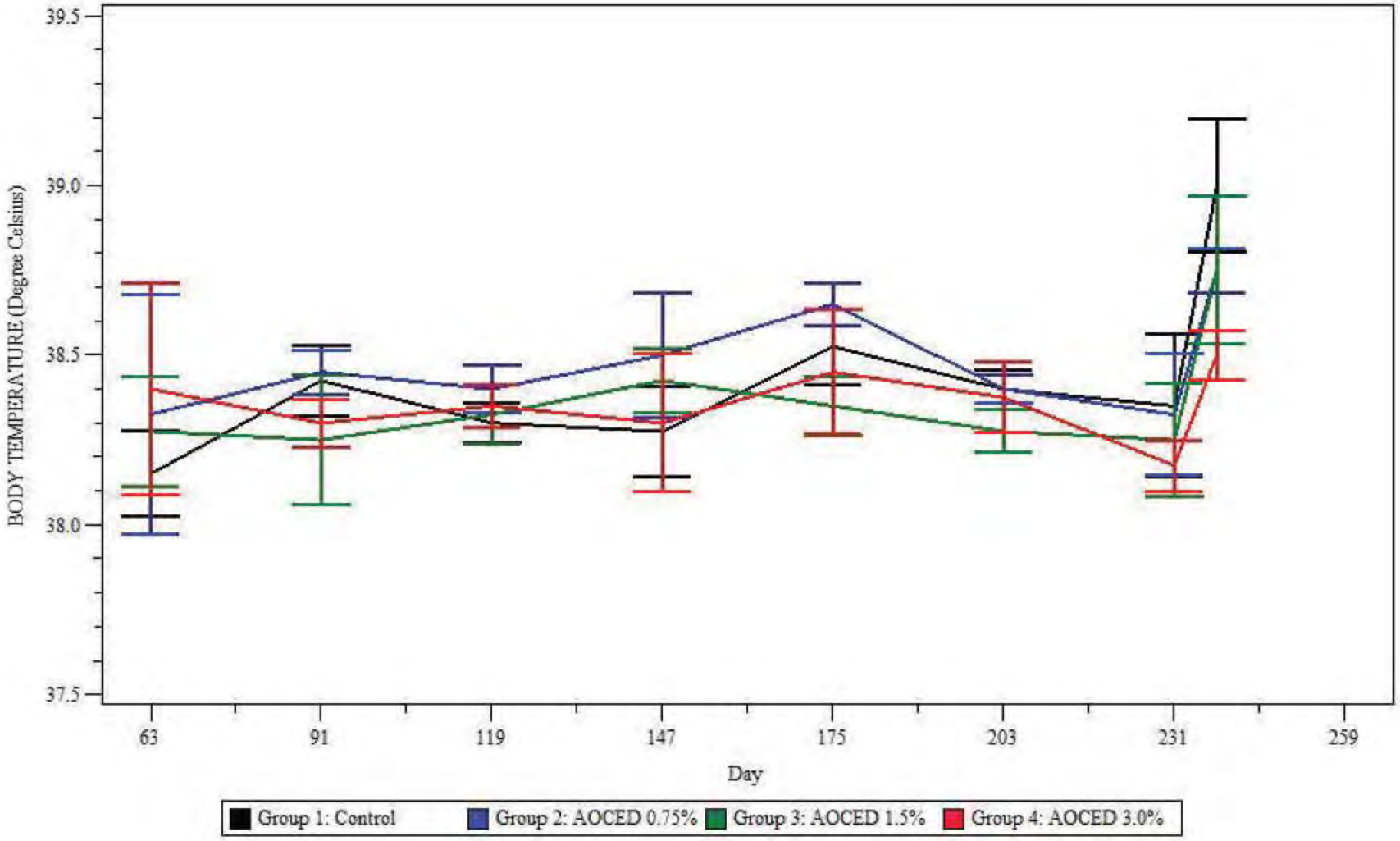
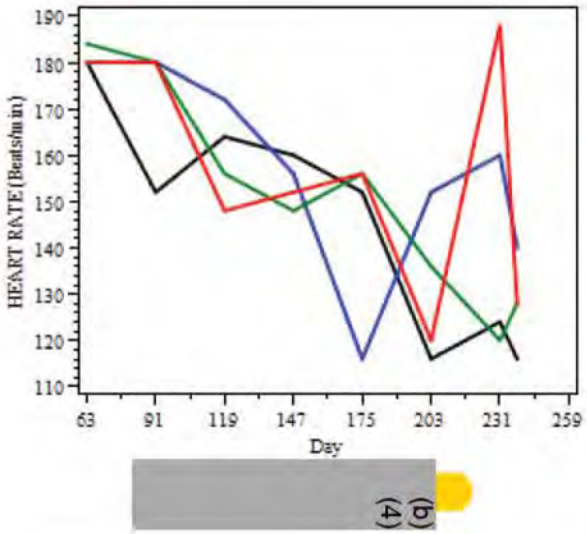
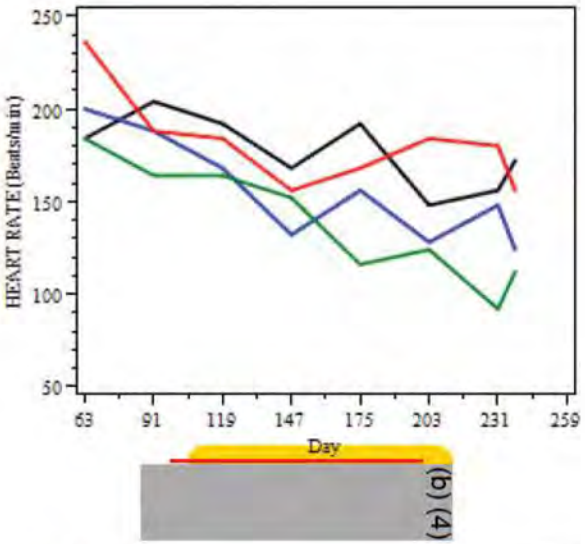
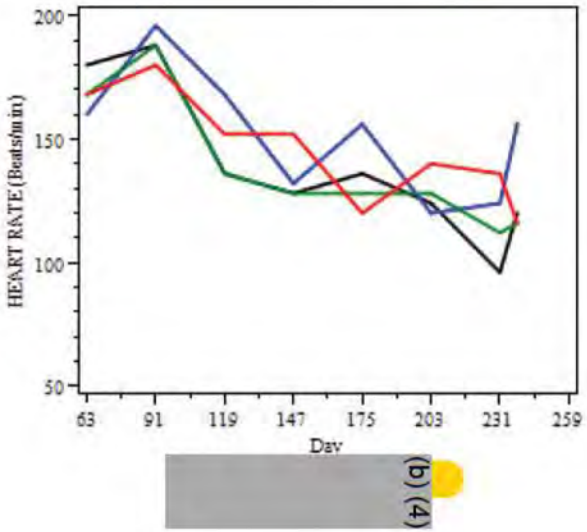


FIGURE NO. 95

GENERATION F1, POST WEANING - PUPPIES
MALES







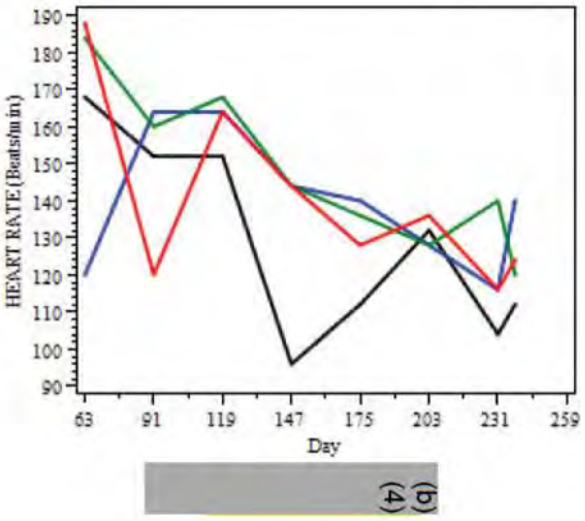
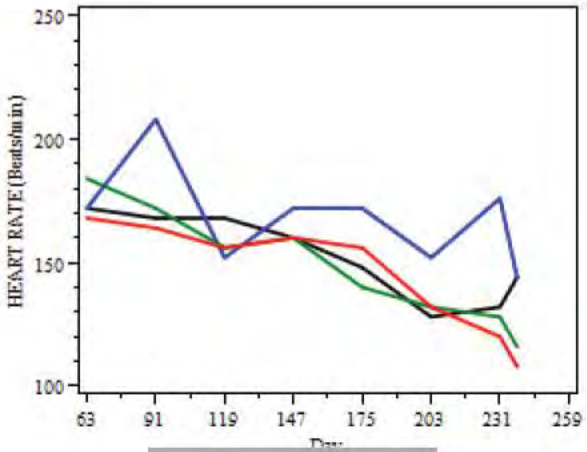
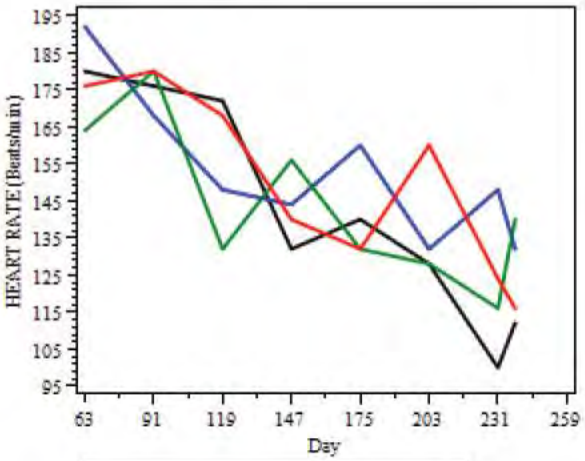


FIGURE NO. 96

[redacted]

GENERATION F1, POST WEANING - PUPPIES
FEMALES





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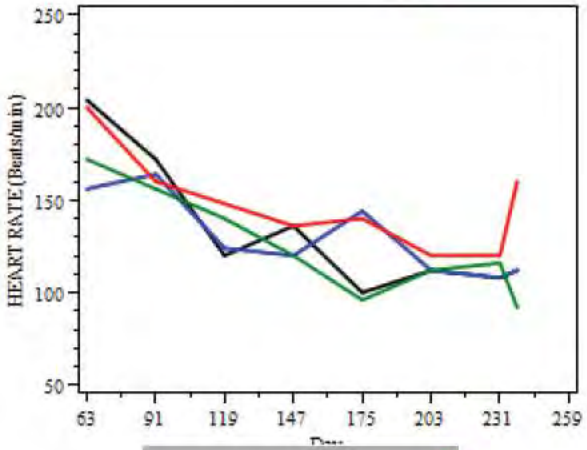

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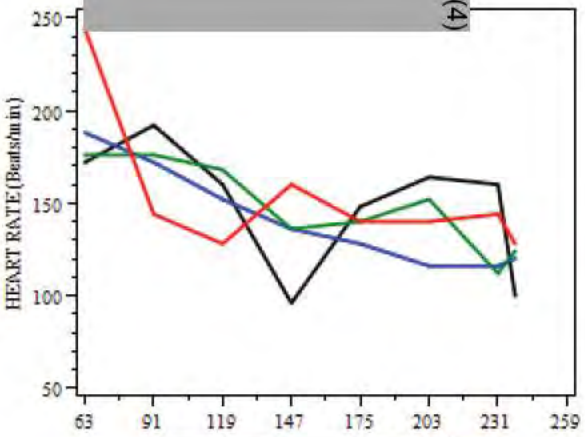


[redacted]

FIGURE NO. 97

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

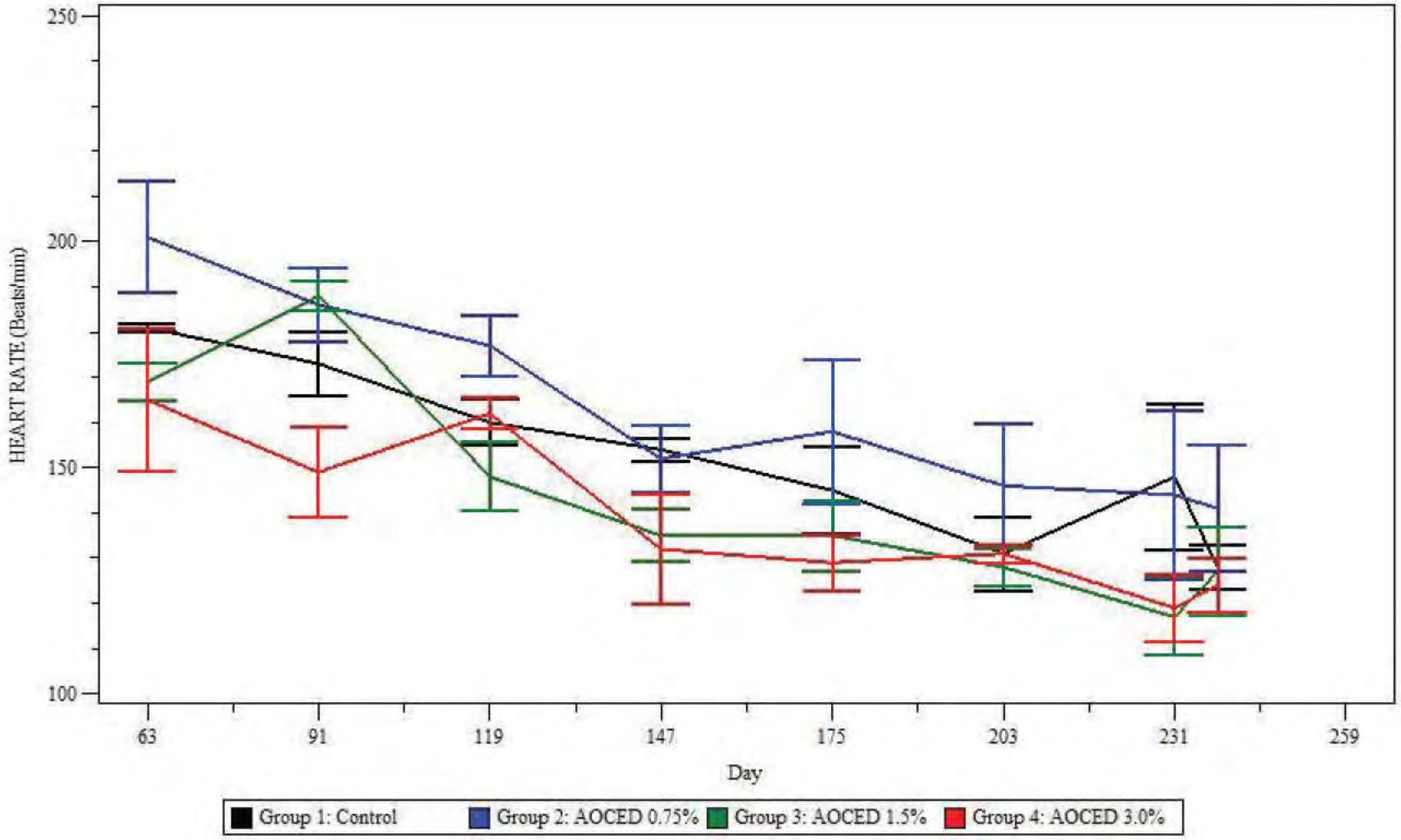


FIGURE NO. 98

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

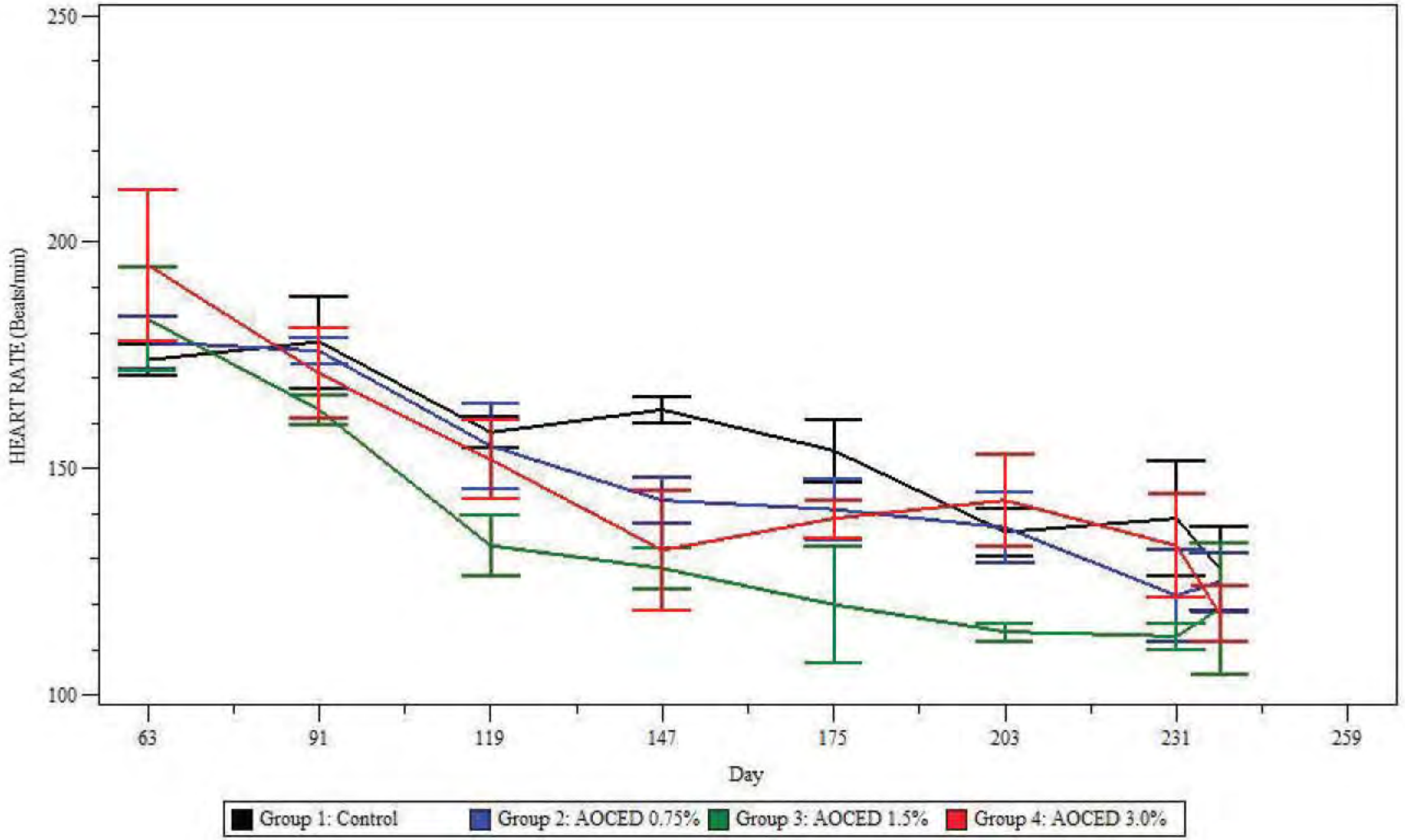
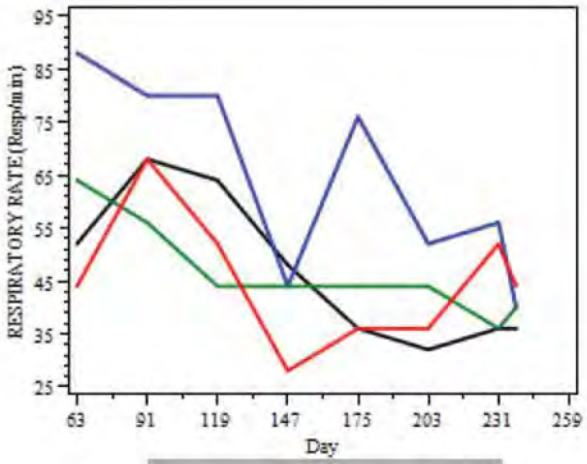


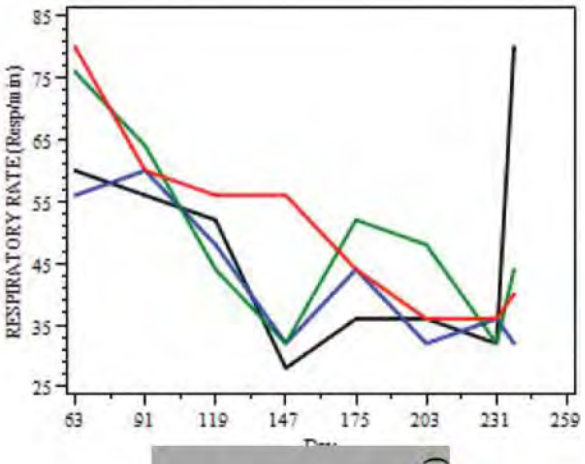
FIGURE NO. 99

(b) (4)

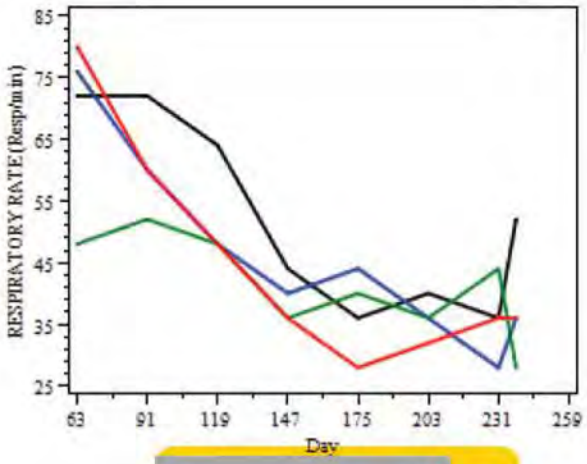
GENERATION F1, POST WEANING - PUPPIES
MALES



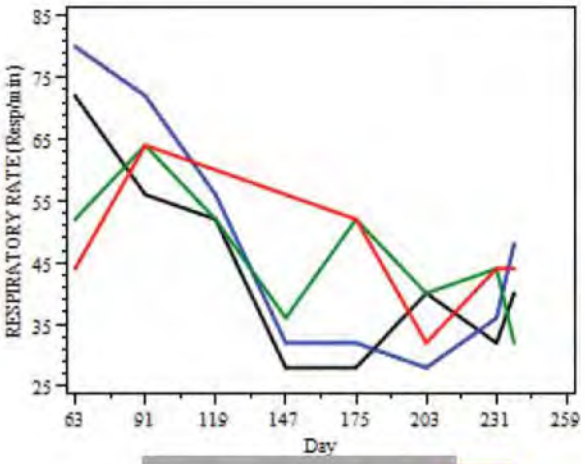
(b) (4)



(b) (4)



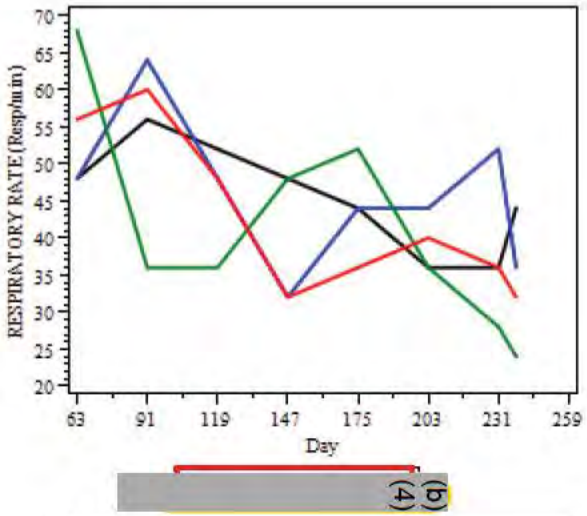
(b) (4)

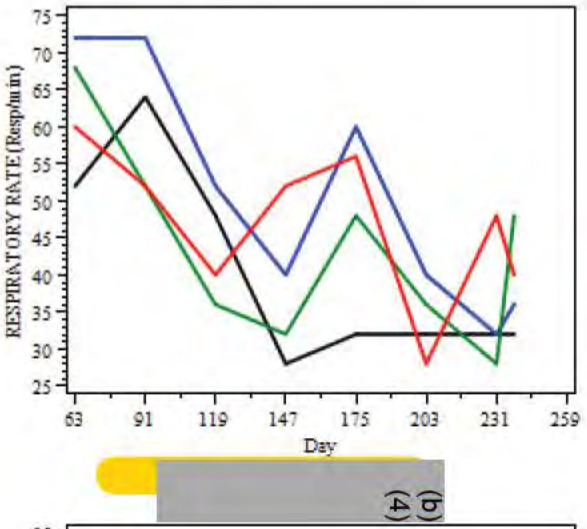


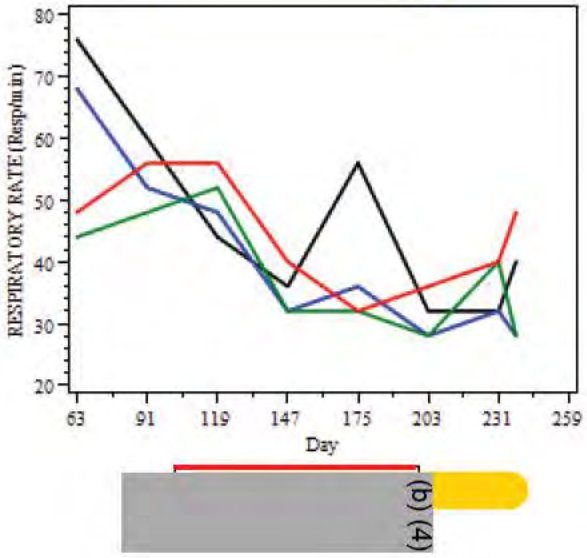
(b) (4)

FIGURE NO. 100

GENERATION F1, POST WEANING - PUPPIES
FEMALES







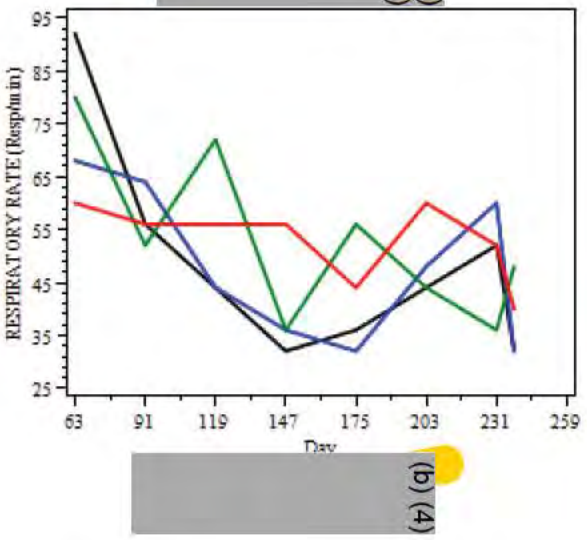


FIGURE NO. 101

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

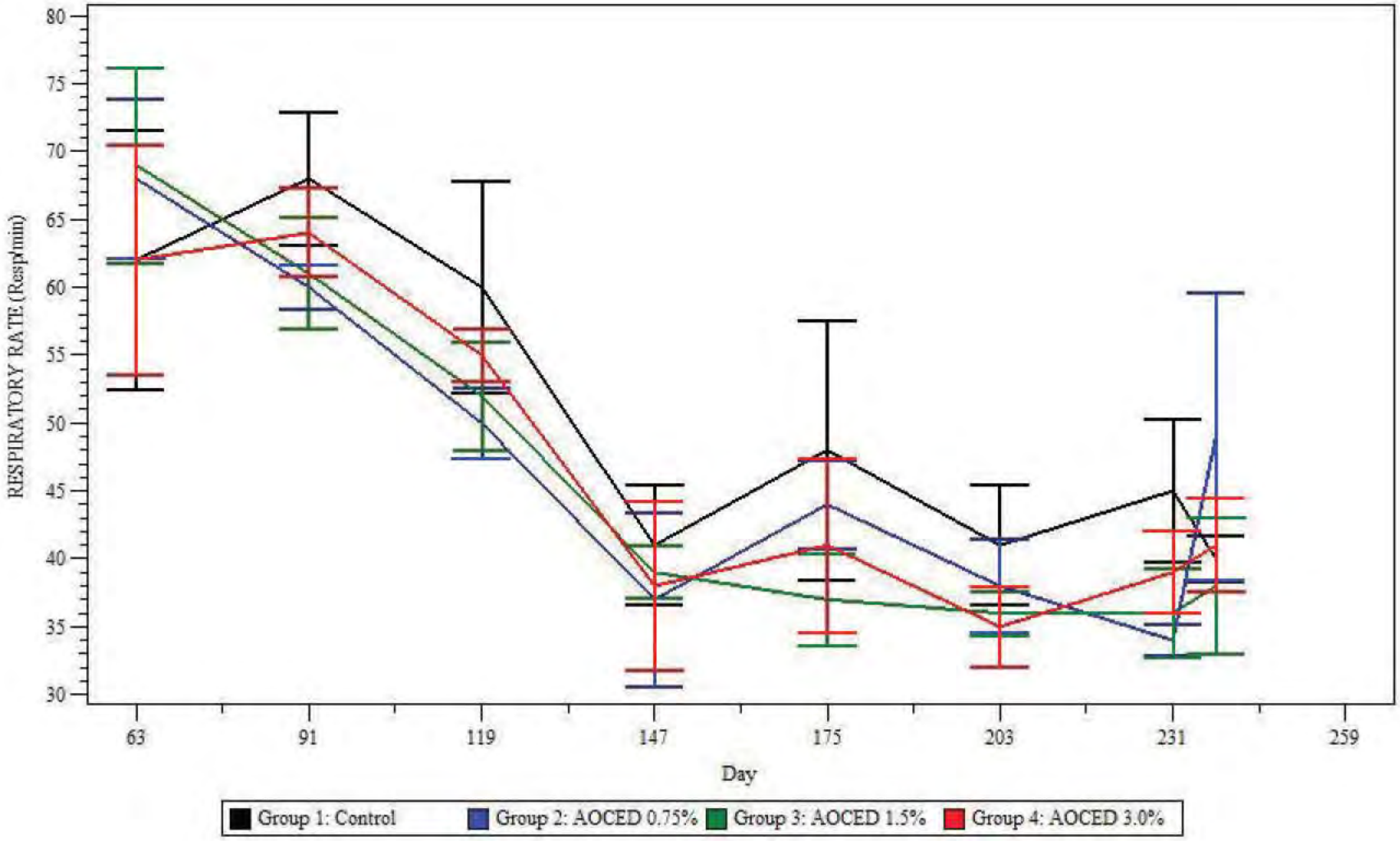


FIGURE NO. 102

(b) (4)

GENERATION F1, POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM

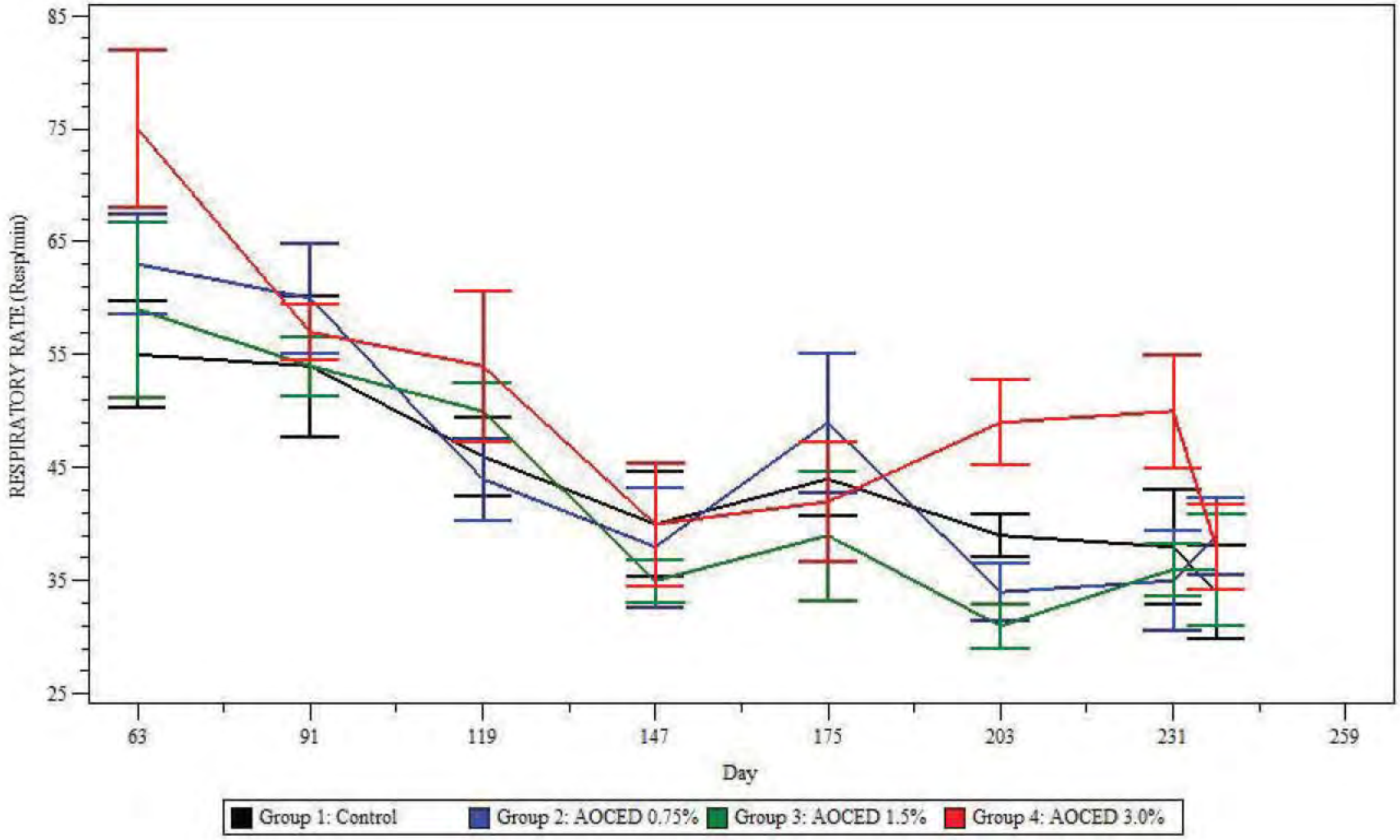
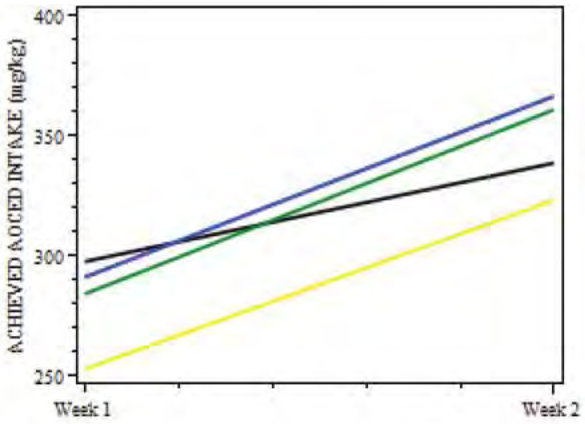


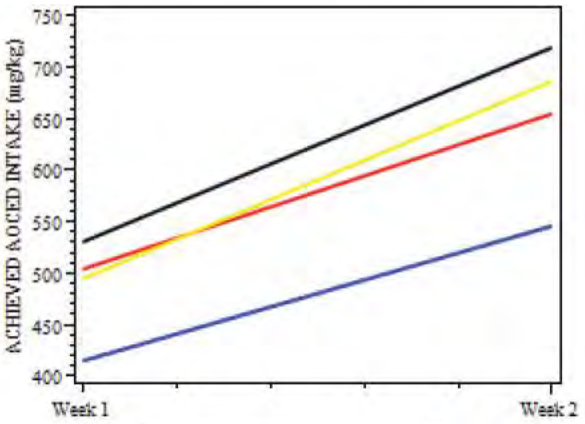
FIGURE NO. 103

(b) (4)

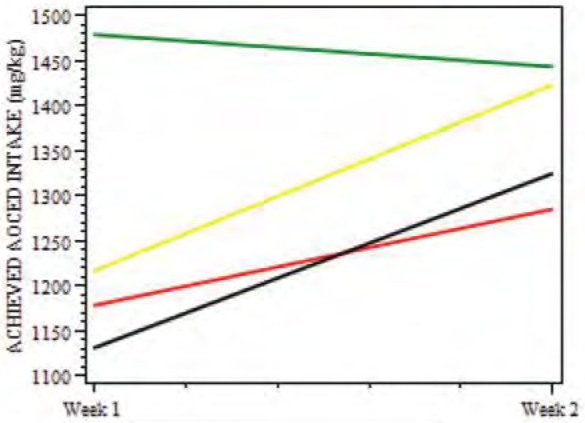
GENERATION F1, FIRST 2 WEEKS POST-WEANING - PUPPIES
CAGES (MALES AND FEMALES)



(b) (4)



(b) (4)



(b) (4)

FIGURE NO. 104

(b) (4)

GENERATION F1, FIRST 2 WEEKS POST-WEANING - PUPPIES
CAGES (MALES AND FEMALES)
Treatment Means ± SEM

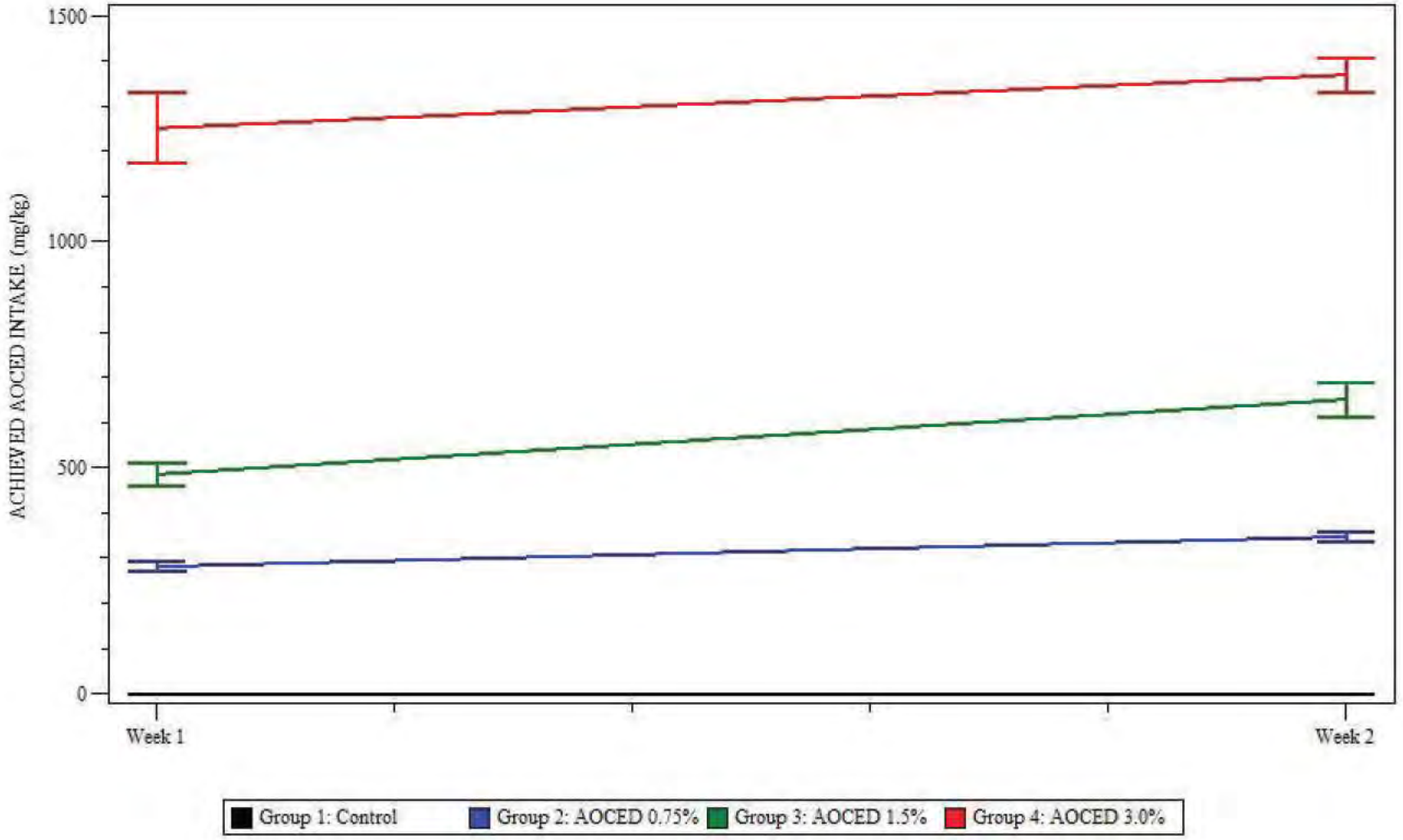
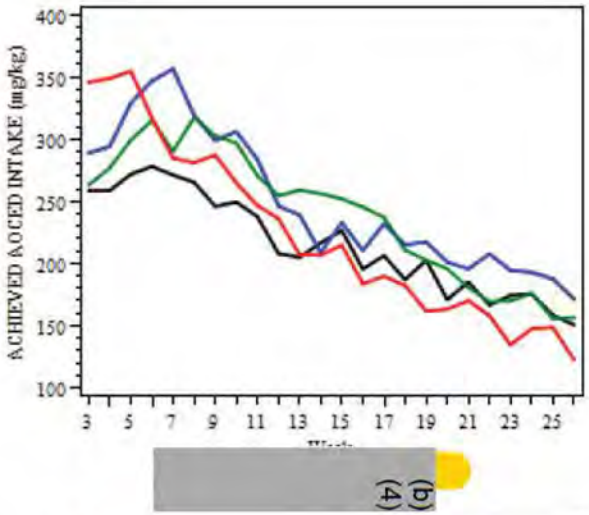


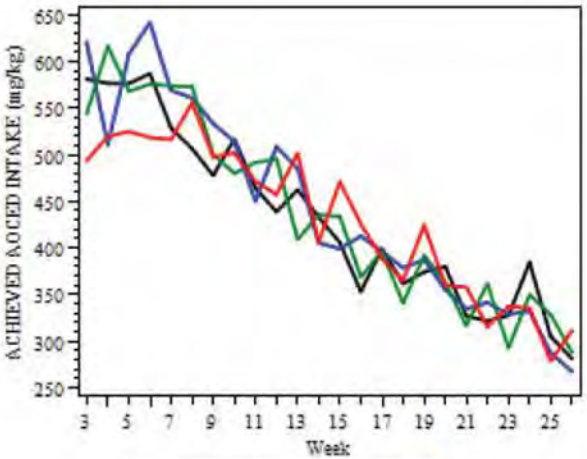
FIGURE NO. 105

(b) (4)

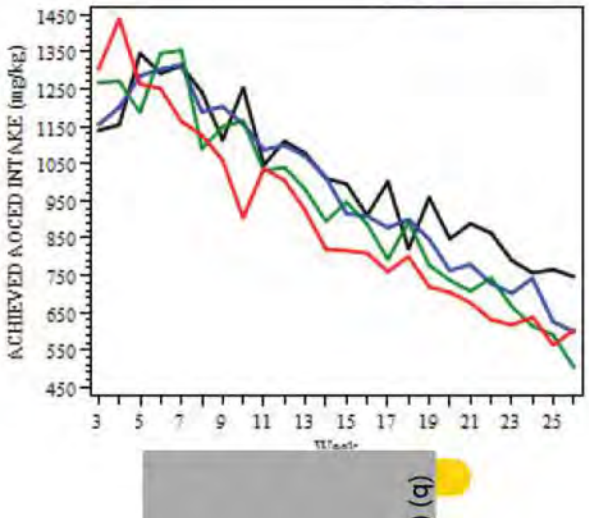
GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
MALES



(b) (4)



(b) (4)

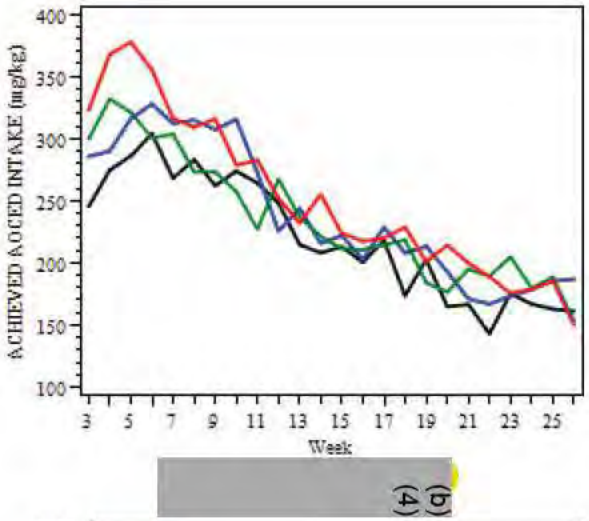


(b) (4)

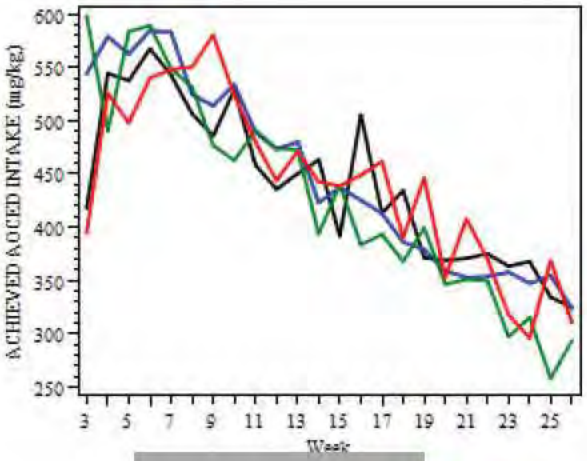
FIGURE NO. 106

GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
FEMALES

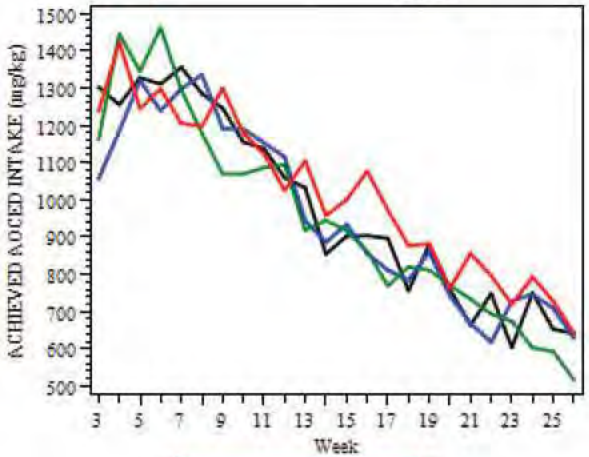
(b) (4)



(b) (4)



(b) (4)

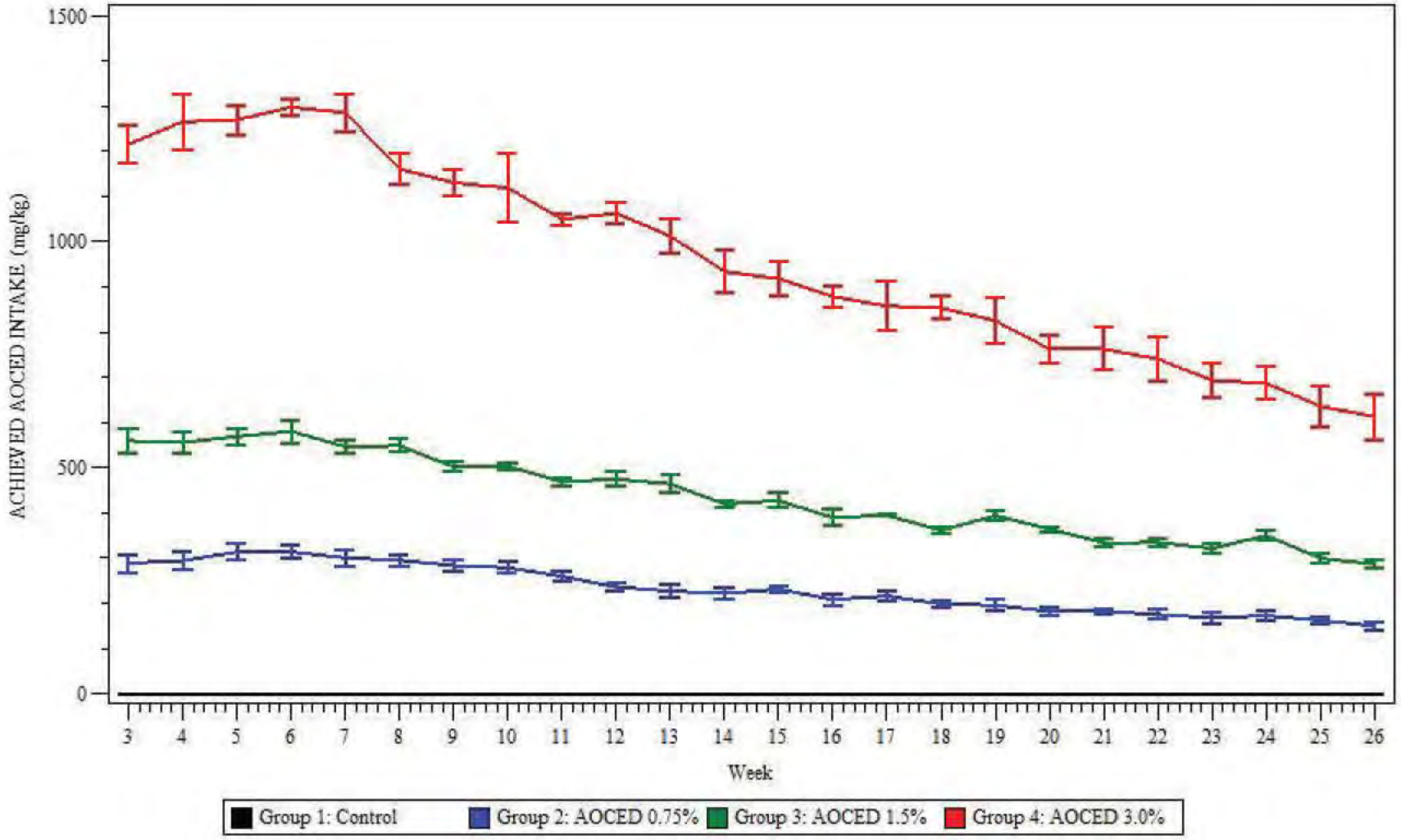


(b) (4)

FIGURE NO. 107

(b) (4)

GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
MALES
Treatment Means ± SEM

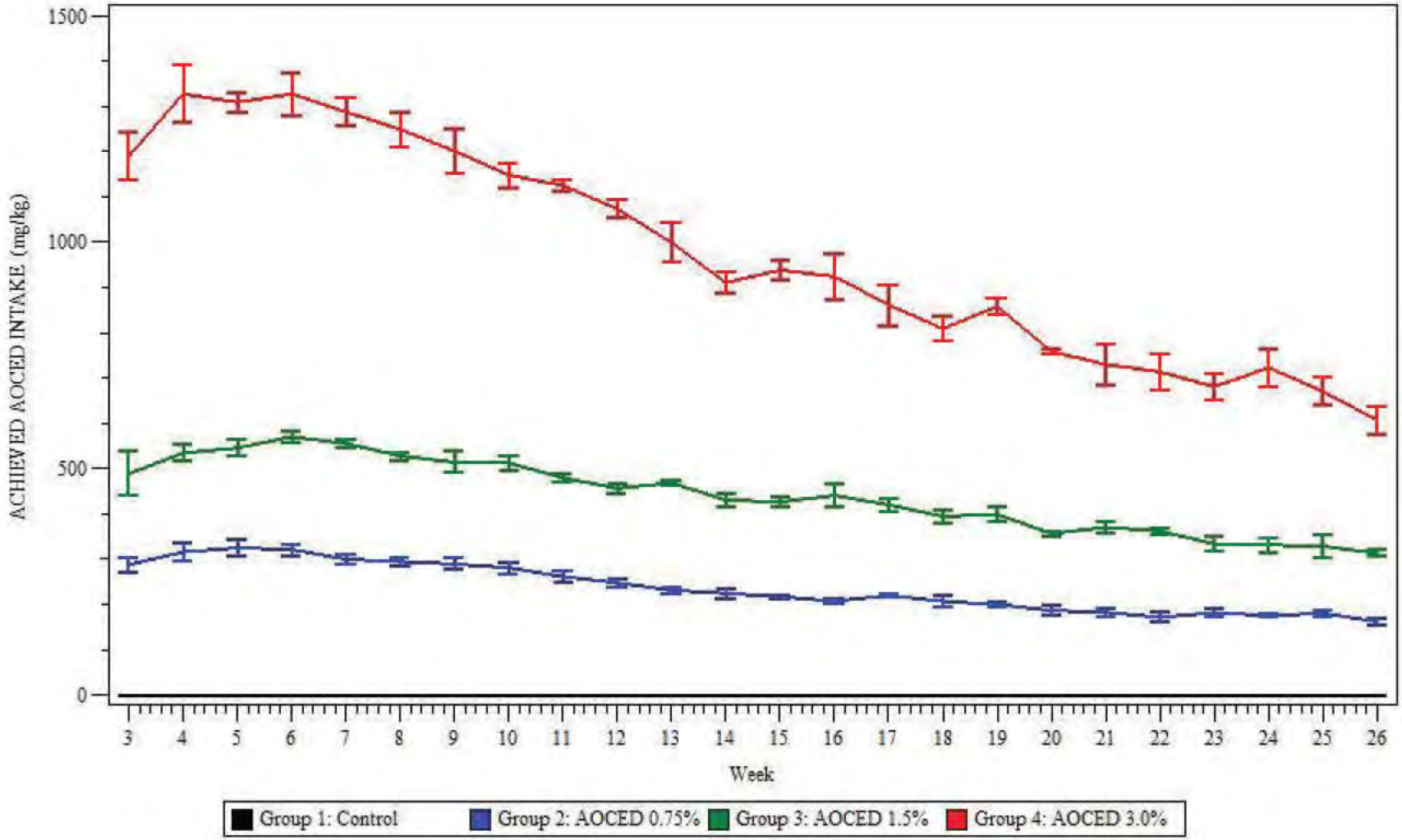


176 of 1567

FIGURE NO. 108

(b) (4)

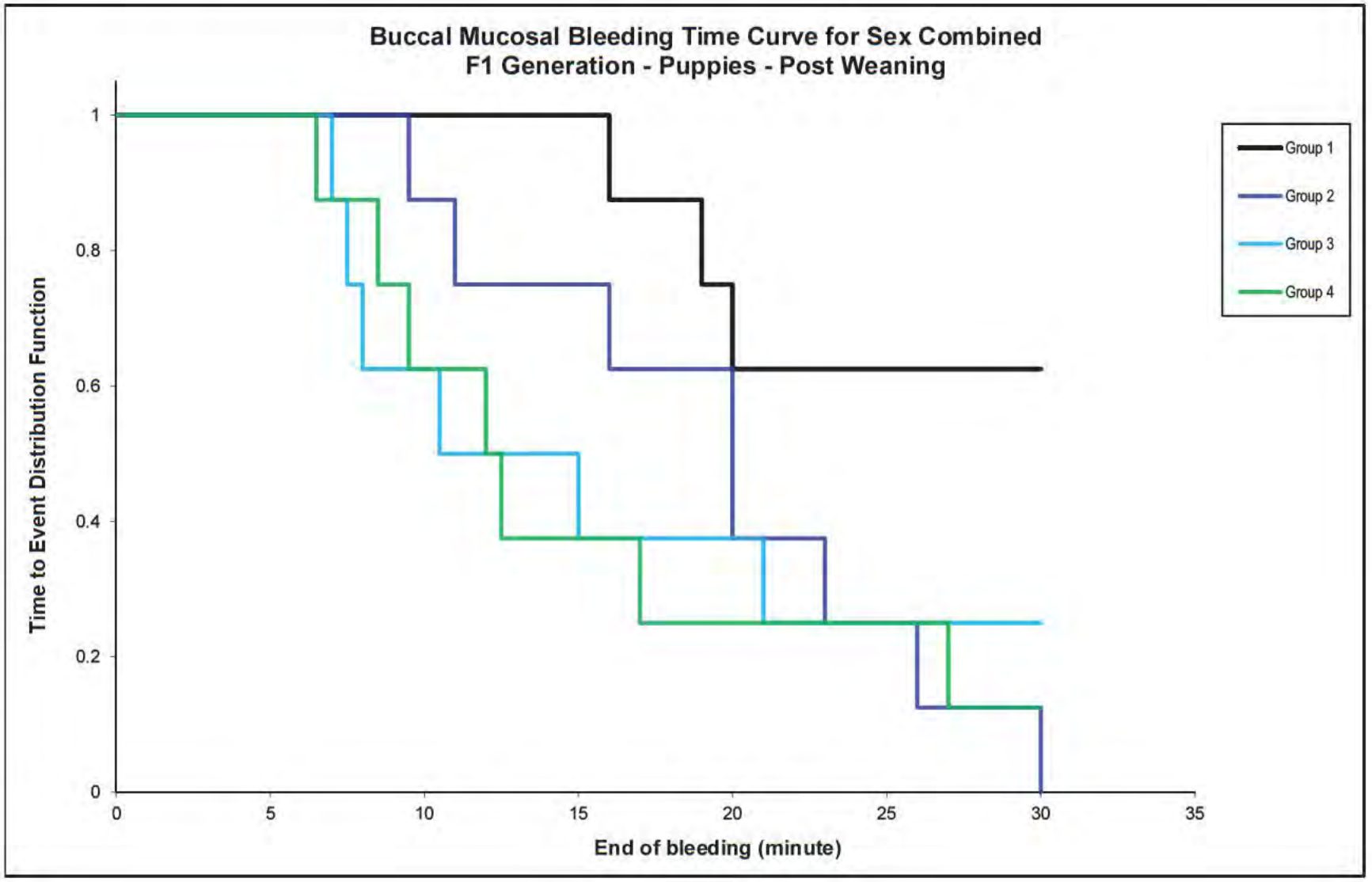
GENERATION F1, AFTER FIRST 2 WEEKS POST WEANING - PUPPIES
FEMALES
Treatment Means ± SEM



177 of 1567

FIGURE NO. 109

[redacted] (b) (4)



(b) (4)

SUMMARY TABLES
F0 GENERATION

TABLE NO. 1

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

		GROUP NO.			
CLINICAL SIGN		1 N= 5	2 N= 5	3 N= 5	4 N= 5
Lump	Number of Animal-Days	2	0	0	2
	Number of Animals	1	0	0	1
	Days from - to	-7 to 0	NA	NA	0 to 7
Circling	Number of Animal-Days	0	1	0	1
	Number of Animals	0	1	0	1
	Days from - to	NA	34 to 34	NA	54 to 54
Retching	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56
Discharge, Brown	Number of Animal-Days	0	0	1	1
	Number of Animals	0	0	1	1
	Days from - to	NA	NA	42 to 42	54 to 54
Discharge, Clear	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	42 to 42	NA	NA
Discharge, Green	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 1

(4) (b)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 5
Discharge, Red	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	54 to 54
Discharge, White	Number of Animal-Days	1	0	0	0
	Number of Animals	1	0	0	0
	Days from - to	42 to 42	NA	NA	NA
Sclera Red	Number of Animal-Days	0	1	0	1
	Number of Animals	0	1	0	1
	Days from - to	NA	50 to 50	NA	54 to 54
Fur Thin	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	42 to 42	NA
Feces Black	Number of Animal-Days	0	0	0	8
	Number of Animals	0	0	0	2
	Days from - to	NA	NA	NA	53 to 64
Feces Green	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	58 to 58
Feces Red	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	60 to 60

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 1

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 5
Feces Soft	Number of Animal-Days	5	20	7	8
	Number of Animals	3	4	3	3
	Days from - to	11 to 64	-2 to 59	10 to 53	14 to 64
Feces Loose	Number of Animal-Days	8	28	27	19
	Number of Animals	3	5	4	5
	Days from - to	13 to 70	-6 to 66	-1 to 66	4 to 66
Feces Liquid	Number of Animal-Days	12	27	25	17
	Number of Animals	4	5	3	4
	Days from - to	3 to 51	-6 to 49	-4 to 39	-4 to 58
Feces, Output	Number of Animal-Days	162	147	150	178
	Number of Animals	5	5	5	5
	Days from - to	-7 to 54	-8 to 48	-5 to 61	-7 to 64
Material Dry Black	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	53 to 53
Material Dry Green	Number of Animal-Days	0	0	0	2
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	53 to 54
Material Dry Red	Number of Animal-Days	0	0	1	1
	Number of Animals	0	0	1	1
	Days from - to	NA	NA	45 to 45	55 to 55

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 1

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 5
Material Frothy Clear	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	7 to 7
Material Frothy Yellow	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	64 to 64	NA
Material Liquid Black	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56
Material Liquid Brown	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	54 to 54
Material Liquid Clear	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56
Material Liquid Green	Number of Animal-Days	1	0	1	1
	Number of Animals	1	0	1	1
	Days from - to	64 to 64	NA	62 to 62	56 to 56
Material Liquid Red	Number of Animal-Days	0	1	0	2
	Number of Animals	0	1	0	2
	Days from - to	NA	51 to 51	NA	51 to 54

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 1

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 5
Material Liquid Yellow	Number of Animal-Days	0	2	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	51 to 53	NA	NA
Material Mucoid Brown	Number of Animal-Days	0	4	3	3
	Number of Animals	0	2	2	1
	Days from - to	NA	40 to 66	43 to 66	36 to 62
Material Mucoid Clear	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	45 to 45	NA
Material Mucoid Red	Number of Animal-Days	0	1	1	0
	Number of Animals	0	1	1	0
	Days from - to	NA	51 to 51	52 to 52	NA
Material Mucoid Yellow	Number of Animal-Days	0	1	1	0
	Number of Animals	0	1	1	0
	Days from - to	NA	51 to 51	52 to 52	NA
Activity Decreased	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 1

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 5
Broken Nail/Claw	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	7 to 7	NA
Tremors	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56
Capillary refill time	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56
Skin Lump	Number of Animal-Days	4	0	1	1
	Number of Animals	1	0	1	1
	Days from - to	-7 to 14	NA	28 to 28	-4 to -4
Skin Pallor	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	56 to 56
Swelling Soft	Number of Animal-Days	0	1	1	0
	Number of Animals	0	1	1	0
	Days from - to	NA	42 to 42	42 to 42	NA
Skin Wound with Discharge	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	41 to 41	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 1

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

		GROUP NO.			
CLINICAL SIGN		1 N= 5	2 N= 5	3 N= 5	4 N= 5
Littered	Number of Animal-Days	5	5	5	4
	Number of Animals	5	5	5	4
	Days from - to	64 to 72	60 to 69	62 to 67	60 to 67

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group.

TABLE NO. 1

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
PRE-TREATMENT AND GESTATION PERIOD – FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 5
Released	Number of Animal-Days	5	5	5	5
	Number of Animals	5	5	5	5
	Days from - to	64 to 72	60 to 69	62 to 67	60 to 67
Direct Pupillary Reflex	Number of Animal-Days	10	10	10	10
	Number of Animals	5	5	5	5
	Days from - to	35 to 42	42 to 42	42 to 42	42 to 42
Consensual Pupillary Reflex	Number of Animal-Days	10	10	10	10
	Number of Animals	5	5	5	5
	Days from - to	35 to 42	42 to 42	42 to 42	42 to 42

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group.

TABLE NO. 2

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS – LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 4
Discharge, Brown	Number of Animal-Days	2	2	6	5
	Number of Animals	2	2	3	3
	Days from - to	0 to 56	0 to 28	0 to 56	0 to 56
Discharge, Clear	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	28 to 28	NA
Discharge, Red	Number of Animal-Days	4	4	2	5
	Number of Animals	4	2	2	3
	Days from - to	0 to 56	0 to 2	5 to 28	0 to 28
Discharge, Yellow	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	0 to 0	NA	NA
Eye Conjunctiva Red	Number of Animal-Days	0	3	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	0 to 2	NA	NA
Fur Dull	Number of Animal-Days	0	4	0	3
	Number of Animals	0	2	0	1
	Days from - to	NA	0 to 2	NA	0 to 56

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 2

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS – LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 4
Fur Loss	Number of Animal-Days	0	3	0	1
	Number of Animals	0	1	0	1
	Days from - to	NA	0 to 2	NA	0 to 0
Fur Stained Brown	Number of Animal-Days	2	1	2	1
	Number of Animals	2	1	1	1
	Days from - to	0 to 0	0 to 0	0 to 2	0 to 0
Fur Stained Green	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	0 to 0	NA
Fur Stained Red	Number of Animal-Days	0	1	1	0
	Number of Animals	0	1	1	0
	Days from - to	NA	2 to 2	0 to 0	NA
Fur Thin	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	28 to 28	NA
Feces Yellow	Number of Animal-Days	1	0	0	0
	Number of Animals	1	0	0	0
	Days from - to	52 to 52	NA	NA	NA
Feces Soft	Number of Animal-Days	3	9	8	8
	Number of Animals	2	3	2	3
	Days from - to	2 to 18	2 to 39	21 to 47	1 to 39

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 2

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS – LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 4
Feces Loose	Number of Animal-Days	9	11	23	9
	Number of Animals	4	4	3	4
	Days from - to	5 to 52	2 to 44	3 to 45	1 to 35
Feces Liquid	Number of Animal-Days	0	3	0	1
	Number of Animals	0	2	0	1
	Days from - to	NA	0 to 1	NA	1 to 1
Feces, Output	Number of Animal-Days	5	3	5	5
	Number of Animals	4	3	4	3
	Days from - to	1 to 7	1 to 25	0 to 23	5 to 35
Material Dry Red	Number of Animal-Days	3	1	3	2
	Number of Animals	3	1	2	2
	Days from - to	1 to 32	1 to 1	22 to 34	2 to 4
Material Liquid Red	Number of Animal-Days	1	1	4	0
	Number of Animals	1	1	1	0
	Days from - to	24 to 24	1 to 1	7 to 18	NA
Material Mucoid Brown	Number of Animal-Days	2	0	0	0
	Number of Animals	2	0	0	0
	Days from - to	31 to 55	NA	NA	NA
Material Mucoid Red	Number of Animal-Days	0	0	1	2
	Number of Animals	0	0	1	1
	Days from - to	NA	NA	19 to 19	38 to 39

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 2

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS – LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 4
Material Mucoid Yellow	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	25 to 25	NA
Material Vomitus Brown	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	2 to 2	NA	NA
Activity Decreased	Number of Animal-Days	0	2	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	0 to 1	NA	NA
Backbone Prominent	Number of Animal-Days	0	1	1	0
	Number of Animals	0	1	1	0
	Days from - to	NA	28 to 28	12 to 12	NA
Thin	Number of Animal-Days	0	4	4	0
	Number of Animals	0	2	2	0
	Days from - to	NA	0 to 56	0 to 28	NA
Tremors	Number of Animal-Days	0	3	2	1
	Number of Animals	0	2	1	1
	Days from - to	NA	0 to 31	1 to 2	0 to 0
Warm to Touch	Number of Animal-Days	0	2	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	0 to 1	NA	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 2

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS – LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 5	2 N= 5	3 N= 5	4 N= 4
Weak	Number of Animal-Days	0	2	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	0 to 1	NA	NA
Skin, Brown	Number of Animal-Days	0	0	1	1
	Number of Animals	0	0	1	1
	Days from - to	NA	NA	56 to 56	56 to 56
Skin Dry	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	28 to 28	NA
Skin Red	Number of Animal-Days	7	7	10	4
	Number of Animals	4	3	4	3
	Days from - to	28 to 56	0 to 56	0 to 56	28 to 56
Swelling Soft	Number of Animal-Days	2	1	2	0
	Number of Animals	2	1	1	0
	Days from - to	0 to 28	0 to 0	28 to 56	NA
Skin Wound with Discharge	Number of Animal-Days	1	0	0	0
	Number of Animals	1	0	0	0
	Days from - to	28 to 28	NA	NA	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 2

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS – LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

		GROUP NO.			
CLINICAL SIGN		1 N= 5	2 N= 5	3 N= 5	4 N= 4
Teeth Broken	Number of Animal-Days	0	2	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	28 to 56	NA	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 3 (b) (4)

BODY TEMPERATURE SUMMARY – PRE-TREATMENT AND GESTATION
AXILLARY (Degree Celsius)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day -8 *	Day -7 *	Day -6 *	Day -5 *	Day -4*	Day -1 *	Day 0 *	Pre-treatment average (Days -8 to 0)
1	MEAN	38.89	38.22	39.33	--	38.22	38.33	38.31	38.42
	SD	NA	0 16	NA	--	NA	NA	0.22	0 30
	MIN	38.9	38.1	39.3	--	38.2	38.3	38.0	38.1
	MAX	38.9	38.3	39.3	--	38.2	38.3	38.5	38.9
	N	1	2	1	--	1	1	5	5
2	MEAN	39.22	38.83	--	39.00	38.28	38.56	38.49	38.58
	SD	NA	NA	--	NA	0.08	NA	0.07	0 21
	MIN	39.2	38.8	--	39.0	38.2	38.6	38.4	38.3
	MAX	39.2	38.8	--	39.0	38.3	38.6	38.6	38.8
	N	1	1	--	1	2	1	5	5
3	MEAN	--	--	--	38.44	38.67	--	38.43	38.48
	SD	--	--	--	0.38	0.47	--	0.19	0 26
	MIN	--	--	--	38.2	38.3	--	38.3	38.3
	MAX	--	--	--	38.9	39.0	--	38.8	38.9
	N	--	--	--	3	2	--	5	5
4	MEAN	--	--	38.53	38.44	38.61	--	38.37	38.39
	SD	--	--	0.27	NA	NA	--	0.47	0 35
	MIN	--	--	38.3	38.4	38.6	--	37.9	38.0
	MAX	--	--	38.7	38.4	38.6	--	39.1	38.9
	N	--	--	2	1	1	--	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)
* - No statistical comparisons were performed
NA - Not applicable

TABLE NO. 3 (b) (4)

BODY TEMPERATURE SUMMARY – PRE-TREATMENT AND GESTATION
AXILLARY/RECTAL (Degree Celsius)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
1	MEAN	38.38	38.43	38.42	38.60	38.26	37.93
	SD	0.42	0.39	0.46	0.41	0.49	0.25
	MIN	37.8	38.0	37.8	38.2	37.9	37.6
	MAX	38.8	39.0	38.9	39.1	39.1	38.2
	N	5	5	5	5	5	4
2	MEAN	38.41	38.56	38.65	38.52	38.24	38.00
	SD	0.31	0.45	0.59	0.41	0.28	0.10
	MIN	38.2	38.1	37.9	37.9	38.0	37.9
	MAX	38.9	39.3	39.4	39.0	38.6	38.1
	N	5	5	4	5	4	5
3	MEAN	38.42	38.59	38.46	38.34	38.21	37.88
	SD	0.18	0.20	0.33	0.17	0.17	0.25
	MIN	38.2	38.3	37.9	38.1	38.0	37.5
	MAX	38.7	38.9	38.7	38.6	38.4	38.1
	N	5	5	5	5	5	5
4	MEAN	38.27	38.39	38.67	38.42	38.19	37.70
	SD	0.25	0.15	0.47	0.33	0.37	0.25
	MIN	38.0	38.2	38.3	38.0	37.9	37.5
	MAX	38.6	38.6	39.4	38.9	38.6	38.1
	N	5	5	5	5	3	5

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 3 (b) (4)

BODY TEMPERATURE SUMMARY – PRE-TREATMENT AND GESTATION
RECTAL (Degree Celsius)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (7 to 42)
1	MEAN	38.34
	SD	0.33
	MIN	38.0
	MAX	38.8
	N	5
2	MEAN	38.37
	SD	0.31
	MIN	38.1
	MAX	38.8
	N	5
3	MEAN	38.32
	SD	0.13
	MIN	38.1
	MAX	38.4
	N	5
4	MEAN	38.29
	SD	0.19
	MIN	38.1
	MAX	38.6
	N	5

TABLE NO. 4 (b) (4)2

BODY TEMPERATURE SUMMARY – LACTATION PERIOD
BODY TEMPERATURE (RECTAL) (Degree Celsius)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0	Day 2 *	Day 5 *	Day 28	Day 56
1	MEAN	38.48	--	--	38.22	38.00
	SD	0.41	--	--	0.38	0.60
	MIN	37.8	--	--	37.8	37.3
	MAX	38.9	--	--	38.8	38.8
	N	5	--	--	5	5
2	MEAN	38.68	38.40	--	38.58	38.23
	SD	0.97	NA	--	0.22	0.48
	MIN	37.9	38.4	--	38.4	37.8
	MAX	40.3	38.4	--	38.9	38.9
	N	5	1	--	4	4
3	MEAN	38.16	--	38.50	38.20	38.23
	SD	0.38	--	NA	0.18	0.21
	MIN	37.5	--	38.5	38.0	38.0
	MAX	38.4	--	38.5	38.4	38.5
	N	5	--	1	4	4
4	MEAN	38.58	--	--	38.13	38.35
	SD	0.22	--	--	0.26	0.17
	MIN	38.3	--	--	37.9	38.2
	MAX	38.8	--	--	38.4	38.6
	N	4	--	--	4	4

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
*- No statistical comparisons were performed
NA: Not applicable

TABLE NO. 4 (b) (4)

BODY TEMPERATURE SUMMARY – LACTATION PERIOD
BODY TEMPERATURE (RECTAL) (Degree Celsius)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (0, 28 and 56)
1	MEAN	38.23
	SD	0.33
	MIN	37.9
	MAX	38.8
	N	5
2	MEAN	38.75
	SD	0.89
	MIN	38.1
	MAX	40.3
	N	5
3	MEAN	38.21
	SD	0.07
	MIN	38.1
	MAX	38.3
	N	5
4	MEAN	38.35
	SD	0.13
	MIN	38.2
	MAX	38.5
	N	4

TABLE NO. 5 (b) (4)

HEART RATE SUMMARY – PRE-TREATMENT AND GESTATION
HEART RATE (Beats/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day -8 *	Day -7 *	Day -6 *	Day -5 *	Day -4 *	Day -1 *	Day 0 *	Pre-treatment average (Days -8 to 0)
1	MEAN	80.0	100.0	80.0	--	120.0	110.0	96.0	97.7
	SD	NA	14.1	NA	--	NA	NA	13.4	14.5
	MIN	80	90	80	--	120	110	80	80
	MAX	80	110	80	--	120	110	110	115
	N	1	2	1	--	1	1	5	5
2	MEAN	130.0	120.0	--	100.0	95.0	100.0	102.0	103.3
	SD	NA	NA	--	NA	7.1	NA	14.8	12.0
	MIN	130	120	--	100	90	100	80	85
	MAX	130	120	--	100	100	100	120	117
	N	1	1	--	1	2	1	5	5
3	MEAN	--	--	--	106.7	105.0	--	110.0	108.0
	SD	--	--	--	15.3	7.1	--	10.0	7.6
	MIN	--	--	--	90	100	--	100	100
	MAX	--	--	--	120	110	--	120	120
	N	--	--	--	3	2	--	5	5
4	MEAN	--	100.0	95.0	140.0	110.0	--	112.0	110.0
	SD	--	NA	7.1	NA	NA	--	21.7	14.6
	MIN	--	100	90	140	110	--	100	95
	MAX	--	100	100	140	110	--	150	130
	N	--	1	2	1	1	--	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)
* - No statistical comparisons were performed
NA - Not applicable

TABLE NO. 5 (b) (4)

HEART RATE SUMMARY – PRE-TREATMENT AND GESTATION
HEART RATE (Beats/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
1	MEAN	98.0	110.0	114.0	108.0	104.8	97.0
	SD	8.4	21.2	18.2	13.0	21.6	8.9
	MIN	90	80	90	90	80	88
	MAX	110	130	130	120	130	108
	N	5	5	5	5	5	4
2	MEAN	99.2	95.2	105 2	118.0	107.5	112.0
	SD	21.1	11.2	6.7	13.0	17.1	13.3
	MIN	76	80	96	110	90	92
	MAX	130	110	110	140	130	128
	N	5	5	5	5	4	5
3	MEAN	102.0	94.0	101 2	110.0	106.0	107.2
	SD	11.0	16.7	13.3	15.8	15.2	20.9
	MIN	90	80	90	90	80	80
	MAX	120	120	120	130	120	128
	N	5	5	5	5	5	5
4	MEAN	95.6	120.0	116.0	118.0	113.3	122.4
	SD	22.1	18.7	11.4	16.4	25.2	18.7
	MIN	64	100	100	100	90	96
	MAX	120	150	130	130	140	148
	N	5	5	5	5	3	5

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 5 (b) (4)

HEART RATE SUMMARY – PRE-TREATMENT AND GESTATION
HEART RATE (Beats/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (7 to 42)
1	MEAN	105.6
	SD	10.3
	MIN	90
	MAX	119
	N	5
2	MEAN	105.8
	SD	10.5
	MIN	96
	MAX	123
	N	5
3	MEAN	103.4
	SD	12.4
	MIN	88
	MAX	120
	N	5
4	MEAN	114.0
	SD	12.8
	MIN	98
	MAX	130
	N	5

TABLE NO. 6 (b) (4)

HEART RATE SUMMARY – LACTATION PERIOD
HEART RATE (Beats/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0	Day 2 *	Day 5 *	Day 28	Day 56
1	MEAN	129.6	--	--	100.8	96.8
	SD	16.1	--	--	15.6	10.4
	MIN	112	--	--	88	84
	MAX	152	--	--	128	108
	N	5	--	--	5	5
2	MEAN	124.0	96.0	--	106.0	107.0
	SD	19.8	NA	--	7.7	15.4
	MIN	92	96	--	100	92
	MAX	140	96	--	116	128
	N	5	1	--	4	4
3	MEAN	109.6	--	136.0	99.0	85.0
	SD	33.1	--	NA	15.1	8.9
	MIN	60	--	136	84	76
	MAX	152	--	136	120	96
	N	5	--	1	4	4
4	MEAN	133.0	--	--	108.0	99.0
	SD	25.0	--	--	9.8	12.4
	MIN	108	--	--	96	88
	MAX	160	--	--	120	116
	N	4	--	--	4	4

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
*- No statistical comparisons were performed
NA: Not applicable

TABLE NO. 6 (b) (4)

HEART RATE SUMMARY – LACTATION PERIOD
HEART RATE (Beats/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (0, 28 and 56)
1	MEAN	109.1
	SD	9.8
	MIN	95
	MAX	119
	N	5
2	MEAN	116.8
	SD	14.0
	MIN	104
	MAX	140
	N	5
3	MEAN	99.5
	SD	12.9
	MIN	79
	MAX	111
	N	5
4	MEAN	113.3
	SD	7.9
	MIN	105
	MAX	124
	N	4

TABLE NO. 7 (b) (4)

RESPIRATORY RATE SUMMARY – PRE-TREATMENT AND GESTATION
RESPIRATORY RATE (Resp/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day -8 *	Day -7 *	Day -6 *	Day -5 *	Day -4 *	Day -1 *	Day 0 *	Pre-treatment average (Days -8 to 0)
1	MEAN	28.0	26.0	28.0	--	28.0	24.0	25.6	26.1
	SD	NA	2.8	NA	--	NA	NA	4.6	1.4
	MIN	28	24	28	--	28	24	20	24
	MAX	28	28	28	--	28	24	32	28
	N	1	2	1	--	1	1	5	5
2	MEAN	40.0	40.0	--	28.0	30.0	36.0	28.0	30.7
	SD	NA	NA	--	NA	2.8	NA	6.3	5.7
	MIN	40	40	--	28	28	36	20	24
	MAX	40	40	--	28	32	36	36	37
	N	1	1	--	1	2	1	5	5
3	MEAN	--	--	--	30.7	30.0	--	26.4	28.4
	SD	--	--	--	4.6	8.5	--	6.1	5.4
	MIN	--	--	--	28	24	--	20	24
	MAX	--	--	--	36	36	--	36	36
	N	--	--	--	3	2	--	5	5
4	MEAN	--	24.0	24.0	20.0	40.0	--	25.6	26.0
	SD	--	NA	0.0	NA	NA	--	4.6	5.3
	MIN	--	24	24	20	40	--	20	20
	MAX	--	24	24	20	40	--	32	34
	N	--	1	2	1	1	--	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
* - No statistical comparisons were performed
NA - Not applicable

TABLE NO. 7 (b) (4)

RESPIRATORY RATE SUMMARY – PRE-TREATMENT AND GESTATION
RESPIRATORY RATE (Resp/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
1	MEAN	24.0	25.6	22.4	25.6	27.2	22.0
	SD	4.9	4.6	3.6	4.6	5.2	2.3
	MIN	20	20	20	20	24	20
	MAX	32	32	28	32	36	24
	N	5	5	5	5	5	4
2	MEAN	24.8	28.8	28.0	24.0	30.0	24.0
	SD	4.4	7.7	7.5	4.9	5.2	2.8
	MIN	20	20	20	20	24	20
	MAX	28	40	36	32	36	28
	N	5	5	5	5	4	5
3	MEAN	28.8	25.6	27.2	26.4	29.6	27.2
	SD	8.7	8 3	5.9	6.1	8.8	5.2
	MIN	20	20	20	20	20	24
	MAX	40	40	36	36	44	36
	N	5	5	5	5	5	5
4	MEAN	23.6	28.8	28.0	26.4	34.7	27.2
	SD	5.7	6.6	7.5	8.3	22.0	3.3
	MIN	16	20	20	20	20	24
	MAX	30	36	40	40	60	32
	N	5	5	5	5	3	5

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 7 (b) (4)

RESPIRATORY RATE SUMMARY – PRE-TREATMENT AND GESTATION
RESPIRATORY RATE (Resp/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (7 to 42)
1	MEAN	24.7
	SD	2.4
	MIN	22
	MAX	28
	N	5
2	MEAN	26.6
	SD	2.8
	MIN	23
	MAX	30
	N	5
3	MEAN	27.5
	SD	6.3
	MIN	24
	MAX	39
	N	5
4	MEAN	27.7
	SD	5.5
	MIN	23
	MAX	34
	N	5

TABLE NO. 8 (b) (4)

RESPIRATORY RATE SUMMARY – LACTATION PERIOD
RESPIRATORY RATE (Resp/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0	Day 2 *	Day 5 *	Day 28	Day 56
1	MEAN	37.6	--	--	32.8	27.2
	SD	8.3	--	--	4.4	3.3
	MIN	32	--	--	28	24
	MAX	52	--	--	40	32
	N	5	--	--	5	5
2	MEAN	37.6	44.0	--	37.0	29.0
	SD	12.2	NA	--	5.0	5.0
	MIN	24	44	--	32	24
	MAX	52	44	--	44	36
	N	5	1	--	4	4
3	MEAN	32.0	--	60.0	40.0	29.0
	SD	6.3	--	NA	11.8	3.8
	MIN	24	--	60	28	24
	MAX	40	--	60	52	32
	N	5	--	1	4	4
4	MEAN	29.0	--	--	32.0	29.0
	SD	5.0	--	--	10.8	6.0
	MIN	24	--	--	24	24
	MAX	36	--	--	48	36
	N	4	--	--	4	4

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
*- No statistical comparisons were performed
NA: Not applicable

TABLE NO. 8 (b) (4)

RESPIRATORY RATE SUMMARY – LACTATION PERIOD
RESPIRATORY RATE (Resp/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (0, 28 and 56)
1	MEAN	32.5
	SD	5.1
	MIN	28
	MAX	41
	N	5
2	MEAN	36.5
	SD	8.8
	MIN	29
	MAX	48
	N	5
3	MEAN	34.4
	SD	4.0
	MIN	29
	MAX	40
	N	5
4	MEAN	30.0
	SD	4.9
	MIN	24
	MAX	36
	N	4

TABLE NO. 9 (b) (4)

BODY WEIGHT (kg) SUMMARY
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day -8 *	Day -7 *	Day -6 *	Day -5 *	Day -4 *	Day -1 *	Day 0 *	Pre-treatment average (Days -8 to 0)
1	MEAN	9.40	10.70	10.00	--	9.80	9.60	10.06	10.10
	SD	NA	1.56	NA	--	NA	NA	0.90	0 92
	MIN	9.4	9.6	10.0	--	9.8	9.6	9.4	9.5
	MAX	9.4	11.8	10.0	--	9.8	9.6	11.6	11.7
	N	1	2	1	--	1	1	5	5
2	MEAN	11.20	9.90	--	9.50	10.75	11.00	10.22	10.32
	SD	NA	NA	--	NA	0.07	NA	0.69	0.69
	MIN	11.2	9.9	--	9.5	10.7	11.0	9.3	9.4
	MAX	11.2	9.9	--	9.5	10.8	11.0	10.9	11.0
	N	1	1	--	1	2	1	5	5
3	MEAN	--	--	--	10.80	10.20	--	10.36	10.46
	SD	--	--	--	0.82	0.42	--	0.70	0.69
	MIN	--	--	--	9.9	9.9	--	9.8	9.9
	MAX	--	--	--	11.5	10.5	--	11.5	11.5
	N	--	--	--	3	2	--	5	5
4	MEAN	--	10.00	10.65	10.00	11.30	--	10.46	10.49
	SD	--	NA	1.34	NA	NA	--	0.78	0.82
	MIN	--	10.0	9.7	10.0	11.3	--	9.7	9.7
	MAX	--	10.0	11.6	10.0	11.3	--	11.4	11.5
	N	--	1	2	1	1	--	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)
* - No statistical comparisons were performed
NA - Not applicable

TABLE NO. 9 (b) (4)

BODY WEIGHT (kg) SUMMARY
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56	Day 63	Day 70 #
1	MEAN	10.18	10.40	10.30	10.00	9.74	10.30	11.34	12.00	12.65	12.00
	SD	0.72	0.72	0.71	0.66	0.55	0.93	0.91	0.94	1.05	NA
	MIN	9.6	9.8	9.6	9.3	9.0	8.7	10.0	10.6	11.6	12.0
	MAX	11.4	11.6	11.4	10.9	10.4	11.1	12.5	13.2	14.1	12.0
	N	5	5	5	5	5	5	5	5	4	1
2	MEAN	10.22	10.58	10.30	9 92	10.12	11.14	12.12	12.68	13.18	--
	SD	0.83	0.88	0.81	0.76	0.97	1.16	1.29	1.10	1.36	--
	MIN	9.3	9.4	9.2	8.8	9.0	9.8	10.7	11.2	11.6	--
	MAX	11.2	11.6	11.3	10.8	11.6	12.8	13.7	13.9	14.5	--
	N	5	5	5	5	5	5	5	5	4	--
3	MEAN	10.40	10.54	10.36	9 92	10.36	11.16	11.86	12.64	12.95	--
	SD	0.61	0.67	0.70	0.69	0.88	0.88	1.08	1.46	0.78	--
	MIN	9.8	10.0	9.5	8.9	9.2	10.2	11.0	11.5	12.4	--
	MAX	11.2	11.6	11.4	10.8	11.3	12.1	13.5	15.0	13.5	--
	N	5	5	5	5	5	5	5	5	2	--
4	MEAN	10.46	11.06	10.82	10.52	10.58	11.62	12.96	13.28	13.90	--
	SD	1.26	1.21	1.07	0 96	0.72	0.98	1.08	0.80	1.13	--
	MIN	9.0	9.8	9.6	9.5	9.7	10.1	11.5	12.4	13.1	--
	MAX	12.0	12.4	12.3	11.8	11.4	12.7	14.1	14.4	14.7	--
	N	5	5	5	5	5	5	5	5	2	--

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
#: Excluded from statistical comparison
NA - Not applicable

TABLE NO. 9 (b) (4)

BODY WEIGHT (kg) SUMMARY
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (7 to 63)
1	MEAN	10.72
	SD	0.74
	MIN	9.8
	MAX	11.8
	N	5
2	MEAN	11.12
	SD	0.89
	MIN	10.1
	MAX	12.1
	N	5
3	MEAN	10.99
	SD	0.80
	MIN	10.1
	MAX	11.9
	N	5
4	MEAN	11.52
	SD	0.87
	MIN	10.8
	MAX	12.7
	N	5

TABLE NO. 10 (b) (4)

BODY WEIGHT (kg) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56
1	MEAN	9.54	9.22	9.68	9.92	9.98	10.26	10.38	10.62	10.42
	SD	0.73	0.80	0.79	0.54	0.33	0.57	0.56	0.36	0.59
	MIN	8.8	8.3	8.6	9.3	9.5	9.4	9.7	10.1	9.8
	MAX	10.6	10.5	10.7	10.6	10.4	11.0	11.2	11.0	11.4
	N	5	5	5	5	5	5	5	5	5
2	MEAN	9.82	9.38	9.65	9.98	10.05	10.35	10.30	10.43	9.85
	SD	0.58	0.71	0.82	0.86	0.95	1.11	0.90	1.13	0.90
	MIN	9.0	8.4	8.5	8.7	8.8	8.8	9.1	8.9	8.6
	MAX	10.5	10.0	10.4	10.6	11.0	11.2	11.2	11.5	10.6
	N	5	4	4	4	4	4	4	4	4
3	MEAN	9.92	9.48	9.58	9.88	9.85	10.23	10.33	10.35	9.93
	SD	0.94	0.85	0.51	0.64	0.31	0.33	0.51	0.31	0.29
	MIN	8.6	8.4	8.9	9.0	9.6	9.9	9.7	9.9	9.7
	MAX	11.2	10.4	10.1	10.4	10.3	10.6	10.9	10.6	10.3
	N	5	4	4	4	4	4	4	4	4
4	MEAN	9.93	9.63	9.73	10.20	10.33	10.88	11.20	11.15	10.93
	SD	1.06	1.22	1.21	1.35	1.15	1.08	1.36	1.41	1.45
	MIN	8.9	8.6	8.8	9.2	9.4	9.9	10.2	10.0	9.7
	MAX	11.4	11.4	11.5	12.2	12.0	12.3	13.2	13.2	13.0
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 10 (b) (4)

BODY WEIGHT (kg) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (0 to 56)
1	MEAN	10.00
	SD	0.56
	MIN	9.3
	MAX	10.8
	N	5
2	MEAN	10.01
	SD	0.75
	MIN	8.8
	MAX	10.6
	N	5
3	MEAN	10.17
	SD	0.69
	MIN	9.3
	MAX	11.2
	N	5
4	MEAN	10.44
	SD	1.24
	MIN	9.4
	MAX	12.2
	N	4

TABLE NO. 11 (b) (4)

BODY WEIGHT CHANGE (kg) SUMMARY
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day -8 to -1 *	Day -7 to 0 *	Day -6 to 0 *	Day -5 to 0 *	Day -4 to 0 *	Day -1 to 0 *	Day 0 to 7	Day 7 to 14
1	MEAN	0.20	-0.05	0.10	--	-0.30	-0.20	0.12	0.22
	SD	NA	0.21	NA	--	NA	NA	0.22	0.08
	MIN	0.2	-0.2	0.1	--	-0.3	-0.2	-0.2	0.1
	MAX	0.2	0.1	0.1	--	-0.3	-0.2	0.4	0.3
	N	1	2	1	--	1	1	5	5
2	MEAN	-0.20	-0.20	--	-0.20	-0.15	-0.10	0.00	0.36
	SD	NA	NA	--	NA	0.07	NA	0.21	0.18
	MIN	-0.2	-0.2	--	-0.2	-0.2	-0.1	-0.3	0.1
	MAX	-0.2	-0.2	--	-0.2	-0.1	-0.1	0.3	0.6
	N	1	1	--	1	2	1	5	5
3	MEAN	--	--	--	-0.20	-0.20	--	0.04	0.14
	SD	--	--	--	0.26	0.14	--	0.30	0.25
	MIN	--	--	--	-0.5	-0.3	--	-0.3	-0.1
	MAX	--	--	--	0.0	-0.1	--	0.4	0.4
	N	--	--	--	3	2	--	5	5
4	MEAN	--	-0.10	-0.10	0.10	-0.10	--	0.00	0.60
	SD	--	NA	0.14	NA	NA	--	0.51	0.20
	MIN	--	-0.1	-0.2	0.1	-0.1	--	-0.7	0.4
	MAX	--	-0.1	0.0	0.1	-0.1	--	0.6	0.8
	N	--	1	2	1	1	--	5	5

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
* - No statistical comparisons were performed
NA - Not applicable

TABLE NO. 11 (b) (4)

BODY WEIGHT CHANGE (kg) SUMMARY
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56	Day 56 to 63	Day 63 to 70 #
1	MEAN	-0.10	-0.30	-0.26	0.56	1.04	0.66	0.65	0.40
	SD	0.14	0.23	0.23	0.52	0.32	0.17	0.37	NA
	MIN	-0.3	-0.5	-0.5	-0.3	0.6	0.4	0 2	0.4
	MAX	0.0	0.1	0.1	1.1	1.4	0.8	1.0	0.4
	N	5	5	5	5	5	5	4	1
2	MEAN	-0.28	-0.38	0.20	1.02	0.98	0.56	0.80	--
	SD	0.15	0.13	0.35	0.48	0.43	0.43	0.39	--
	MIN	-0.5	-0.5	0.0	0.2	0.4	0.2	0.4	--
	MAX	-0.1	-0.2	0.8	1.4	1.6	1.2	1 3	--
	N	5	5	5	5	5	5	4	--
3	MEAN	-0.18	-0.44	0.44	0.80	0.70	0.78	0.65	--
	SD	0.22	0.17	0.47	0.54	0.45	0.41	0.35	--
	MIN	-0.5	-0.6	-0.1	0.1	0.3	0.5	0.4	--
	MAX	0.1	-0.2	1.1	1.5	1.4	1.5	0 9	--
	N	5	5	5	5	5	5	2	--
4	MEAN	-0.24	-0.30	0.06	1.04	1.34	0.32	0.50	--
	SD	0.44	0.16	0.68	0.44	0.47	0.86	0.28	--
	MIN	-1.0	-0.5	-0.6	0.4	0.9	-1.2	0 3	--
	MAX	0.1	-0.1	1.0	1.5	2.1	0.9	0.7	--
	N	5	5	5	5	5	5	2	--

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
#: Excluded from statistical comparison
NA - Not applicable

TABLE NO. 11 (b) (4)

BODY WEIGHT CHANGE (kg) SUMMARY
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (0 to 63)
1	MEAN	0.28
	SD	0.04
	MIN	0.2
	MAX	0.3
	N	5
2	MEAN	0.35
	SD	0.09
	MIN	0.2
	MAX	0.4
	N	5
3	MEAN	0.31
	SD	0.14
	MIN	0.2
	MAX	0.6
	N	5
4	MEAN	0.36
	SD	0.11
	MIN	0.2
	MAX	0.5
	N	5

TABLE NO. 12 (b) (4)

BODY WEIGHT CHANGE (kg) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0 to 7	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	-0.32	0.46	0.24	0.06	0.28	0.12	0.24	-0.20
	SD	0.32	0.36	0.40	0.30	0.25	0.19	0.27	0.38
	MIN	-0.7	0.2	-0.2	-0.2	-0.1	-0.2	-0.2	-0.6
	MAX	0.1	1.1	0.7	0.5	0.6	0.3	0.5	0.4
	N	5	5	5	5	5	5	5	5
2	MEAN	-0.35	0.28	0.33	0.08	0.30	-0.05	0.13	-0.58
	SD	0.37	0.35	0.19	0.34	0.32	0.29	0.24	0.25
	MIN	-0.6	-0.1	0.2	-0.4	0.0	-0.4	-0.2	-0.9
	MAX	0.2	0.7	0.6	0.4	0.7	0.3	0.3	-0.3
	N	4	4	4	4	4	4	4	4
3	MEAN	-0.13	0.10	0.30	-0.03	0.38	0.10	0.03	-0.43
	SD	0.43	0.34	0.16	0.46	0.30	0.36	0.24	0.33
	MIN	-0.7	-0.3	0.1	-0.5	0.1	-0.2	-0.3	-0.8
	MAX	0.2	0.5	0.5	0.6	0.8	0.5	0.2	-0.1
	N	4	4	4	4	4	4	4	4
4	MEAN	-0.30	0.10	0.48	0.13	0.55	0.33	-0.05	-0.23
	SD	0.22	0.14	0.17	0.25	0.31	0.45	0.19	0.25
	MIN	-0.5	-0.1	0.3	-0.2	0.3	-0.2	-0.2	-0.5
	MAX	0.0	0.2	0.7	0.4	1.0	0.9	0.2	0.1
	N	4	4	4	4	4	4	4	4

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 12 (b) (4)

BODY WEIGHT CHANGE (kg) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED DAYS (0 to 56)
1	MEAN	0.11
	SD	0.03
	MIN	0.1
	MAX	0.2
	N	5
2	MEAN	0.02
	SD	0.06
	MIN	-0.1
	MAX	0.1
	N	4
3	MEAN	0.04
	SD	0.07
	MIN	0.0
	MAX	0.1
	N	4
4	MEAN	0.13
	SD	0.06
	MIN	0.1
	MAX	0.2
	N	4

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day -8 to -7	Day -7 to -6	Day -6 to -5	Day -5 to -4	Day -4 to -3	Day -3 to -2	Day -2 to -1	Day -1 to 0	Pre-treatment Average (Days -8 to 0)
1	MEAN	156.0	206.0	148.5	177.3	159.6	163.2	150.4	165.5	158.7
	SD	NA	51.0	83.8	98.2	68.9	74.3	73.0	68.3	51.0
	MIN	156	148	86	110	92	76	90	100	104
	MAX	156	244	272	290	264	272	260	248	220
	N	1	3	4	3	5	5	5	4	5
2	MEAN	108.0	150.0	169.0	131.3	207.0	175.2	167.2	166.4	174.8
	SD	NA	138.6	91.9	59.0	58.9	65.1	55.3	62.5	53.8
	MIN	108	52	104	86	126	128	106	106	128
	MAX	108	248	234	198	266	286	242	270	266
	N	1	2	2	3	4	5	5	5	5
3	MEAN	--	--	--	126.7	197.3	190.8	161.6	106.5	156.9
	SD	--	--	--	3.1	126.3	56.9	39.3	39.4	18.8
	MIN	--	--	--	124	66	104	96	56	130
	MAX	--	--	--	130	318	250	198	150	177
	N	--	--	--	3	3	5	5	4	5
4	MEAN	--	166.0	138.7	201.5	147.5	153.2	137.2	146.8	153.7
	SD	--	NA	95.9	39.5	62.2	73.4	30.0	40.0	20.3
	MIN	--	166	28	150	92	88	90	94	118
	MAX	--	166	196	238	224	278	172	188	168
	N	--	1	3	4	4	5	5	5	5

NA - Not applicable

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0 to 1	Day 1 to 2	Day 2 to 3	Day 3 to 4	Day 4 to 5	Day 5 to 6	Day 6 to 7	Day 7 to 8
1	MEAN	150.5	147.2	124.8	166.8	178.0	177.6	215.6	140.4
	SD	90.6	51.9	49.2	49.8	58.2	56.4	47.2	84.7
	MIN	62	84	72	94	78	124	146	0
	MAX	260	224	196	222	230	262	278	222
	N	4	5	5	5	5	5	5	5
2	MEAN	184.4	178.4	219.6	250.8	249.6	201.6	210.4	221.2
	SD	73.4	61.1	25.3	54.6	38.6	68.0	42.6	54.3
	MIN	128	76	202	170	186	102	162	156
	MAX	292	234	262	302	284	264	274	296
	N	5	5	5	5	5	5	5	5
3	MEAN	133.2	124.5	168.4	174.0	177.6	178.0	142.8	159.2
	SD	36.7	30.7	80.3	42.6	53.1	52.4	80.4	110.7
	MIN	92	106	70	118	104	96	12	0
	MAX	182	170	278	228	232	230	220	310
	N	5	4	5	5	5	5	5	5
4	MEAN	168.0	120.0	186.4	197.2	143.2	132.0	206.0	281.2
	SD	45.4	103.3	99.4	115.4	19.8	52.4	140.4	97.6
	MIN	98	14	116	74	118	64	46	166
	MAX	222	248	360	374	172	180	392	424
	N	5	5	5	5	5	5	5	5

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 8 to 9	Day 9 to 10	Day 10 to 11	Day 11 to 12	Day 12 to 13	Day 13 to 14	Day 14 to 15	Day 15 to 16
1	MEAN	229.6	237.6	206.0	224.0	208.4	236.4	214.4	211.6
	SD	44.9	55.0	55.6	51.0	14.7	54.2	81.6	46.4
	MIN	154	168	132	174	190	176	152	144
	MAX	274	306	272	296	230	294	352	272
	N	5	5	5	5	5	5	5	5
2	MEAN	251.2	269.6	272.4	284.8	259.6	263.2	219.6	250.8
	SD	47.0	45.2	21.8	69.4	55.4	29.9	49.6	49.1
	MIN	206	226	244	166	206	218	156	198
	MAX	324	340	296	332	348	298	292	302
	N	5	5	5	5	5	5	5	5
3	MEAN	186.4	222.0	278.8	214.4	249.6	260.8	151.6	150.4
	SD	70.8	107.5	99.1	104.8	66.3	129.9	113.3	71.2
	MIN	82	90	194	62	162	158	0	48
	MAX	256	344	420	322	348	482	258	240
	N	5	5	5	5	5	5	5	5
4	MEAN	239.6	276.8	244.4	315.2	238.0	234.0	218.4	220.0
	SD	75.1	94.2	61.5	70.5	89.0	54.5	115.3	86.0
	MIN	166	152	146	216	96	180	136	116
	MAX	362	386	310	384	340	302	418	346
	N	5	5	5	5	5	5	5	5

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 16 to 17	Day 17 to 18	Day 18 to 19	Day 19 to 20	Day 20 to 21	Day 21 to 22	Day 22 to 23	Day 23 to 24
1	MEAN	223.6	157.2	195.2	216.8	170.8	130.0	150.4	140.4
	SD	84.6	64.4	25.3	76.6	46.1	60.0	38.8	48.7
	MIN	116	90	168	132	110	52	110	72
	MAX	338	230	222	314	216	212	208	196
	N	5	5	5	5	5	5	5	5
2	MEAN	206.8	199.6	179.6	123.6	182.8	117.2	143.6	142.0
	SD	34.3	39.6	81.1	44.4	50.4	35.2	42.4	56.5
	MIN	166	146	72	72	98	60	74	68
	MAX	248	242	274	172	222	146	180	206
	N	5	5	5	5	5	5	5	5
3	MEAN	204.8	162.8	179.2	149.0	151.2	156.8	121.6	124.0
	SD	92.9	68.0	50.2	32.7	23.3	55.7	51.8	24.1
	MIN	98	60	120	120	120	98	64	102
	MAX	354	242	242	188	182	240	164	158
	N	5	5	5	4	5	5	5	4
4	MEAN	180.0	158.4	205.6	139.2	146.8	118.0	137.6	136.8
	SD	76.0	118.9	51.8	59.6	85.2	51.9	35.1	55.1
	MIN	84	2	132	64	2	58	112	78
	MAX	280	266	266	220	210	184	194	196
	N	5	5	5	5	5	5	5	5

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 24 to 25	Day 25 to 26	Day 26 to 27	Day 27 to 28	Day 28 to 29	Day 29 to 30	Day 30 to 31	Day 31 to 32
1	MEAN	111.6	137.6	127.2	101.6	85.2	75.2	68.8	85.6
	SD	42.9	59.5	48.9	79.8	47.0	47.8	44.3	25.7
	MIN	48	86	58	2	30	24	34	56
	MAX	164	214	192	220	154	130	142	122
	N	5	5	5	5	5	5	5	5
2	MEAN	182.0	93.6	77.6	86.0	91.6	66.4	93.2	108.8
	SD	96.7	52.7	31.0	43.3	75.4	27.7	40.5	33.2
	MIN	86	16	24	28	4	34	46	76
	MAX	344	158	98	136	194	100	126	154
	N	5	5	5	5	5	5	5	5
3	MEAN	98.0	113.6	77.6	129.0	96.8	114.8	109.2	106.4
	SD	55.5	27.8	59.2	55.3	42.2	91.9	50.1	67.5
	MIN	6	88	0	66	50	0	48	42
	MAX	156	158	152	192	138	222	172	220
	N	5	5	5	4	5	5	5	5
4	MEAN	87.2	116.5	103.6	87.2	47.6	108.0	69.2	107.2
	SD	26.6	26.3	24.4	37.3	31.0	85.0	47.6	78.4
	MIN	56	88	68	64	2	20	12	30
	MAX	116	146	128	152	82	222	130	232
	N	5	4	5	5	5	4	5	5

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 32 to 33	Day 33 to 34	Day 34 to 35	Day 35 to 36	Day 36 to 37	Day 37 to 38	Day 38 to 39	Day 39 to 40
1	MEAN	84.6	121.8	77.8	101.5	120.0	132.0	111.6	180.6
	SD	35.9	58.8	48.8	75.9	82.9	93.5	73.6	108.7
	MIN	42	64	14	16	26	28	26	50
	MAX	120	190	150	181	234	244	198	314
	N	5	5	5	4	5	5	5	5
2	MEAN	143.2	113.2	161.6	171.6	199.2	242.0	225.4	199.4
	SD	51.0	43.7	36.1	107.2	34.2	67.1	61.6	35.1
	MIN	90	56	104	66	146	140	129	145
	MAX	198	168	190	284	228	312	290	231
	N	5	5	5	5	5	5	5	5
3	MEAN	135.2	195.6	191.8	162.8	161.4	233.6	228.8	209.6
	SD	75.4	56.9	119.7	43.2	91.1	96.7	109.3	63.9
	MIN	68	144	86	126	54	114	115	114
	MAX	254	280	356	232	260	358	374	278
	N	5	5	4	5	5	5	5	5
4	MEAN	124.4	129.4	112.0	141.8	163.4	251.0	185.6	196.0
	SD	96.7	120.2	96.4	90.6	96.1	172.6	83.8	136.2
	MIN	38	32	16	20	32	30	53	1
	MAX	278	312	232	270	291	454	255	334
	N	5	5	5	5	5	5	5	5

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 40 to 41	Day 41 to 42	Day 42 to 43	Day 43 to 44	Day 44 to 45	Day 45 to 46	Day 46 to 47	Day 47 to 48
1	MEAN	210.4	200.8	243.2	270.0	270.0	256.0	223.4	220.6
	SD	102.8	64.4	95.9	76.6	86.1	18.9	94.4	64.4
	MIN	37	99	114	137	147	242	103	126
	MAX	288	267	379	331	349	288	344	296
	N	5	5	5	5	5	5	5	5
2	MEAN	192.0	263.2	233.8	234.8	171.2	233.4	220.2	282.0
	SD	94.5	42.1	46.9	56.7	79.4	82.5	73.5	57.5
	MIN	70	214	166	159	59	136	141	199
	MAX	308	330	277	312	265	340	306	332
	N	5	5	5	5	5	5	5	5
3	MEAN	274.8	186.4	219.0	191.4	281.4	211.4	193.8	193.0
	SD	133.7	72.0	94.7	62.6	93.1	50.4	45.0	70.4
	MIN	117	90	118	107	184	153	130	71
	MAX	427	259	350	266	387	278	239	242
	N	5	5	5	5	5	5	5	5
4	MEAN	247.8	210.4	287.8	231.2	282.2	235.4	240.6	270.6
	SD	119.0	54.0	70.7	100.2	110.0	86.7	81.7	113.1
	MIN	90	126	224	167	118	152	147	185
	MAX	422	248	367	409	417	362	331	428
	N	5	5	5	5	5	5	5	5

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 48 to 49	Day 49 to 50	Day 50 to 51	Day 51 to 52	Day 52 to 53	Day 53 to 54	Day 54 to 55	Day 55 to 56
1	MEAN	264.0	200.0	216.6	233.6	206.8	205.2	246.4	189.0
	SD	40.2	60.3	47.2	53.4	75.5	47.7	63.1	97.9
	MIN	204	138	180	170	86	163	144	74
	MAX	308	278	299	291	289	284	301	313
	N	5	5	5	5	5	5	5	5
2	MEAN	233.4	180.0	216.6	222.0	222.8	259.6	215.6	222.0
	SD	131.6	39.9	88.3	62.3	84.8	50.8	61.6	30.8
	MIN	105	130	96	140	120	195	125	185
	MAX	412	241	312	283	306	312	288	254
	N	5	5	5	5	5	5	5	5
3	MEAN	191.8	222.8	260.6	189.6	211.8	177 2	188.6	216.0
	SD	49.2	46.2	23.6	84.3	83.6	86.8	31.3	90.2
	MIN	135	163	236	74	92	96	156	140
	MAX	260	280	295	273	317	312	224	369
	N	5	5	5	5	5	5	5	5
4	MEAN	237.8	291.4	102.4	212.8	169.4	216.8	132.6	173.6
	SD	58.8	95.4	89.4	124.8	96.0	145.2	89.5	87.3
	MIN	189	178	2	66	3	3	2	41
	MAX	337	406	231	405	241	384	237	285
	N	5	5	5	5	5	5	5	5

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 56 to 57	Day 57 to 58	Day 58 to 59	Day 59 to 60	Day 60 to 61	Day 61 to 62	Day 62 to 63	Day 63 to 64	Post treatment Average (Days 0 to 63)
1	MEAN	219.0	268.6	209.0	198.6	162.6	196.3	175.0	161.7	179.1
	SD	79.1	73.4	69.6	85.7	73.9	48.2	56.0	90.7	79.9
	MIN	133	167	128	113	95	137	131	95	0
	MAX	316	347	304	303	276	237	238	265	379
	N	5	5	5	5	5	4	3	3	310
2	MEAN	203.2	232.4	245.5	215.3	203.0	232.8	258.5	138.0	198.4
	SD	21.2	82.2	72.1	24.9	41.6	57.7	116.2	36.4	77.2
	MIN	179	158	166	180	161	171	122	99	4
	MAX	227	352	341	236	252	301	361	171	412
	N	5	5	4	4	4	4	4	3	310
3	MEAN	206.2	263.6	159.4	185.4	149.0	164.4	184.5	154.0	180.0
	SD	29.7	136.4	50.0	62.3	66.1	118.5	218.5	56.6	83.7
	MIN	161	140	107	110	61	0	30	114	0
	MAX	240	481	229	250	204	288	339	194	482
	N	5	5	5	5	5	5	2	2	307
4	MEAN	114.2	161.0	148.8	166.5	181.5	65.3	60.7	--	178.0
	SD	110.7	68.4	31.2	20.7	104.9	57.6	53.7	--	101.5
	MIN	0	88	115	148	102	2	18	--	0
	MAX	224	257	187	195	326	133	121	--	454
	N	5	5	4	4	4	4	3	--	307

TABLE NO. 13 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 64 to 65	Day 65 to 66	Day 66 to 67	Day 67 to 68	Day 68 to 69	Day 69 to 70
1	MEAN	183.0	98.0	2.0	294.0	115.0	195.0
	SD	NA	NA	NA	NA	NA	NA
	MIN	183	98	2	294	115	195
	MAX	183	98	2	294	115	195
	N	1	1	1	1	1	1
2	MEAN	192.5	--	--	99.0	54.0	--
	SD	16.3	--	--	NA	NA	--
	MIN	181	--	--	99	54	--
	MAX	204	--	--	99	54	--
	N	2	--	--	1	1	--
3	MEAN	144.0	--	100.0	--	--	--
	SD	NA	--	NA	--	--	--
	MIN	144	--	100	--	--	--
	MAX	144	--	100	--	--	--
	N	1	--	1	--	--	--

NA - Not applicable

TABLE NO. 13 (b) (4)

FOOD CONSUMPTION (g) SUMMARY
F0 GENERATION
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		PRETREATMENT AVERAGE (WEEK)
1	MEAN	160.1
	SD	50.5
	MIN	104
	MAX	220
	N	5
2	MEAN	171.2
	SD	56.4
	MIN	128
	MAX	266
	N	5
3	MEAN	156.9
	SD	18.8
	MIN	130
	MAX	177
	N	5
4	MEAN	153.7
	SD	20.3
	MIN	118
	MAX	168
	N	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

TABLE NO. 13 (b) (4)

FOOD CONSUMPTION (g)
F0 GENERATION – GESTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 1	Week 2	Week 3	Week 4	Week 5
1	MEAN	166.0	211.8	198.5	128.4	85.6
	SD	42.9	39.4	49.2	48.5	24.1
	MIN	103	167	139	81	55
	MAX	216	264	259	197	114
	N	5	5	5	5	5
2	MEAN	213.5	260 3	194.7	120.3	111.1
	SD	25.0	21.2	32.7	33.1	28.4
	MIN	183	230	162	72	88
	MAX	243	277	238	155	144
	N	5	5	5	5	5
3	MEAN	157.2	224 5	164.0	115.1	133.5
	SD	30.1	36.3	32.2	27.5	58.1
	MIN	122	168	124	88	78
	MAX	197	261	208	153	199
	N	5	5	5	5	5
4	MEAN	164.7	261 3	181.2	111.7	97.8
	SD	71.5	48.7	64.3	15.2	58.1
	MIN	95	198	100	91	39
	MAX	265	311	256	129	173
	N	5	5	5	5	5

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 13 (b) (4)

FOOD CONSUMPTION (g)
F0 GENERATION – GESTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 6	Week 7	Week 8	Week 9	Week 10
1	MEAN	153.5	249.6	213.9	206.6	154.1
	SD	72.9	36.3	39.2	32.4	90.3
	MIN	40	199	183	151	50
	MAX	217	289	263	228	265
	N	5	5	5	5	4
2	MEAN	213.3	229.8	219.8	219.9	140.4
	SD	27.3	49.2	31.5	23.8	43.3
	MIN	173	178	175	180	77
	MAX	248	294	261	238	171
	N	5	5	5	5	4
3	MEAN	208.2	211.7	209.5	186.9	138.0
	SD	42.2	33.9	25.7	59.4	12.7
	MIN	148	164	174	107	129
	MAX	266	244	234	256	147
	N	5	5	5	5	2
4	MEAN	199.4	255 1	185.6	138.0	--
	SD	89.6	65.7	74.2	28.1	--
	MIN	68	186	61	98	--
	MAX	293	352	249	176	--
	N	5	5	5	5	--

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 13 (b) (4)

FOOD CONSUMPTION (g)
F0 GENERATION – GESTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED (WEEKS 1 to 9)	COMBINED (WEEKS 1 to 10)
1	MEAN	179.3	177.7
	SD	31.8	34.2
	MIN	140	144
	MAX	221	226
	N	5	5
2	MEAN	198.1	193 3
	SD	16.8	12.2
	MIN	180	179
	MAX	218	208
	N	5	5
3	MEAN	178.9	177 9
	SD	21.6	22.4
	MIN	158	157
	MAX	203	203
	N	5	5
4	MEAN	177.2	177 2
	SD	24.5	24.5
	MIN	136	136
	MAX	196	196
	N	5	5

TABLE NO. 14 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0 to 1	Day 1 to 2	Day 2 to 3	Day 3 to 4	Day 4 to 5	Day 5 to 6	Day 6 to 7	Day 7 to 8
1	MEAN	135.8	171.5	261.8	268.8	206.4	256.8	286.4	315.2
	SD	114.9	114.2	37.5	75.9	85.7	72.3	58.0	80.2
	MIN	1	85	217	147	60	158	220	209
	MAX	261	334	298	351	280	336	377	429
	N	4	4	5	5	5	5	5	5
2	MEAN	184.3	222.8	279.5	434.5	388.8	334.3	374.0	393.0
	SD	158.4	212.0	101.6	23.4	113.7	139.4	41.5	64.3
	MIN	1	0	128	411	298	213	327	343
	MAX	324	473	339	467	555	494	418	486
	N	4	5	4	4	4	4	4	4
3	MEAN	104.8	136.5	265.8	281.8	298.3	371.7	403.0	368.5
	SD	110.3	100.7	165.0	192.5	212.0	145.6	198.1	69.1
	MIN	1	61	104	21	60	274	273	265
	MAX	285	284	496	485	505	539	631	409
	N	5	4	4	4	4	3	3	4
4	MEAN	222.7	144.7	344.0	269.3	277.5	291.0	321.0	304.7
	SD	292.5	94.6	152.3	23.6	159.1	200.8	79.0	143.2
	MIN	20	57	174	247	165	149	243	219
	MAX	558	245	468	294	390	433	401	470
	N	3	3	3	3	2	2	3	3

TABLE NO. 14 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 8 to 9	Day 9 to 10	Day 10 to 11	Day 11 to 12	Day 12 to 13	Day 13 to 14	Day 14 to 15	Day 15 to 16
1	MEAN	411.6	335.0	372.8	387.2	356.6	497.4	334.6	413.0
	SD	74.1	61.3	138.7	99.2	138.3	180.2	114.6	63.6
	MIN	330	272	154	302	186	305	149	344
	MAX	481	420	502	529	538	686	444	514
	N	5	5	5	5	5	5	5	5
2	MEAN	478.0	423.0	348.0	465.0	447.3	509.3	421.0	418.3
	SD	93.6	130.0	32.6	32.1	69.6	54.6	132.0	113.1
	MIN	388	288	312	420	379	451	267	268
	MAX	568	567	379	495	529	582	532	524
	N	4	4	4	4	4	4	4	4
3	MEAN	332.5	341.8	387.0	451.0	385.0	509.0	570.8	406.8
	SD	112.8	147.6	119.7	115.0	130.9	87.2	90.0	203.4
	MIN	199	212	280	349	199	428	436	249
	MAX	450	547	547	612	487	624	624	702
	N	4	4	4	4	4	4	4	4
4	MEAN	321.0	352.3	421.8	378.3	397.0	451.5	494.0	345.0
	SD	141.9	165.9	101.7	82.1	121.6	197.2	77.5	188.9
	MIN	165	178	291	260	244	286	389	151
	MAX	463	556	532	450	530	718	567	574
	N	4	4	4	4	4	4	4	4

TABLE NO. 14 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 16 to 17	Day 17 to 18	Day 18 to 19	Day 19 to 20	Day 20 to 21	Day 21 to 22	Day 22 to 23	Day 23 to 24
1	MEAN	485.2	418.0	536.8	477.0	515.6	395.8	491.0	556.6
	SD	121.1	156.2	128.1	125.7	55.9	90.7	85.5	52.9
	MIN	365	174	413	329	439	299	401	474
	MAX	624	591	754	601	578	506	610	611
	N	5	5	5	5	5	5	5	5
2	MEAN	526.5	499.0	446.5	498.5	521.3	553.5	613.3	518.0
	SD	74.7	114.1	94.7	97.5	116.1	160.3	64.9	181.8
	MIN	449	341	380	369	359	363	537	294
	MAX	591	610	586	602	618	755	677	721
	N	4	4	4	4	4	4	4	4
3	MEAN	525.5	586.0	496.8	517.5	490.8	506.8	565.3	621.0
	SD	172.2	130.0	154.5	130.6	184.6	63.5	169.7	118.0
	MIN	382	430	279	392	258	417	400	497
	MAX	766	747	627	641	709	565	786	776
	N	4	4	4	4	4	4	4	4
4	MEAN	471.3	505.3	465.3	464.0	479.0	526.3	509.8	528.0
	SD	128.1	159.5	44.9	99.2	15.3	73.9	98.4	110.2
	MIN	301	330	421	356	464	419	402	420
	MAX	592	716	527	582	500	578	640	659
	N	4	4	4	4	4	4	4	4

TABLE NO. 14 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 24 to 25	Day 25 to 26	Day 26 to 27	Day 27 to 28	Day 28 to 29	Day 29 to 30	Day 30 to 31	Day 31 to 32
1	MEAN	494.4	557.2	434.8	536.4	575.0	433.4	544.2	543.8
	SD	82.8	117.1	121.4	82.8	104.8	117.7	132.1	81.6
	MIN	386	465	303	420	443	269	338	431
	MAX	571	725	592	623	723	564	664	639
	N	5	5	5	5	5	5	5	5
2	MEAN	574.0	461.0	621.8	511.3	528.8	550.5	504.0	559.0
	SD	91.3	115.8	98.5	137.5	139.6	90.7	85.5	72.0
	MIN	455	374	499	353	397	427	394	494
	MAX	674	625	718	656	662	645	597	646
	N	4	4	4	4	4	4	4	4
3	MEAN	456.3	601.8	559.0	551.0	641.8	518.5	687.3	446.3
	SD	98.3	75.3	158.0	62.6	146.4	131.9	75.9	132.8
	MIN	389	515	476	465	436	356	580	278
	MAX	602	694	796	615	767	679	758	578
	N	4	4	4	4	4	4	4	4
4	MEAN	551.0	593.3	600.5	500.8	591.5	589.0	555.3	556.8
	SD	26.5	121.1	105.8	165.9	177.4	31.1	42.9	119.4
	MIN	516	473	471	311	452	553	511	383
	MAX	574	700	711	685	844	628	614	652
	N	4	4	4	4	4	4	4	4

TABLE NO. 14 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 32 to 33	Day 33 to 34	Day 34 to 35	Day 35 to 36	Day 36 to 37	Day 37 to 38	Day 38 to 39	Day 39 to 40
1	MEAN	504.0	618.6	514.4	557.0	631.2	584.2	675.8	620.2
	SD	93.9	98.6	109.0	127.2	66.8	112.7	89.5	158.9
	MIN	393	482	400	360	535	425	567	341
	MAX	589	753	643	710	696	707	761	727
	N	5	5	5	5	5	5	5	5
2	MEAN	626.8	536.0	604.3	525.5	595.8	611.3	695.0	689.3
	SD	145.3	69.4	92.0	119.3	83.2	150.8	194.9	91.7
	MIN	431	466	509	356	513	465	521	622
	MAX	776	615	716	631	709	778	877	821
	N	4	4	4	4	4	4	4	4
3	MEAN	673.0	678.3	566.5	543.3	603.5	672.8	594.3	636.3
	SD	120.3	202.6	148.5	100.4	156.3	128.3	153.9	141.4
	MIN	499	380	396	465	407	486	410	462
	MAX	755	806	746	680	786	766	772	767
	N	4	4	4	4	4	4	4	4
4	MEAN	546.5	616.5	565.0	653.0	665.3	571.8	663.5	680.0
	SD	69.8	118.4	52.0	66.7	184.7	69.6	130.0	103.8
	MIN	472	512	510	580	449	492	551	568
	MAX	631	723	634	741	900	652	848	798
	N	4	4	4	4	4	4	4	4

TABLE NO. 14 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 40 to 41	Day 41 to 42	Day 42 to 43	Day 43 to 44	Day 44 to 45	Day 45 to 46	Day 46 to 47	Day 47 to 48
1	MEAN	557.6	728.0	631.0	694.4	593.0	733.2	794.6	642.2
	SD	113.6	136.6	127.5	95.4	118.2	144.4	120.1	181.3
	MIN	390	541	494	592	449	590	585	324
	MAX	676	891	810	837	769	900	893	768
	N	5	5	5	5	5	5	5	5
2	MEAN	562.5	628.0	679.5	625.3	629.8	706.0	775.8	576.5
	SD	91.6	127.1	68.4	132.5	101.9	111.9	148.6	257.6
	MIN	451	511	606	431	553	585	604	274
	MAX	665	770	770	728	780	856	900	846
	N	4	4	4	4	4	4	4	4
3	MEAN	699.5	721.3	609.3	712.0	657.8	690.5	716.0	704.5
	SD	55.7	94.3	151.2	35.9	91.4	187.8	224.7	173.2
	MIN	638	612	480	662	534	525	407	539
	MAX	773	841	812	741	734	900	900	858
	N	4	4	4	4	4	4	4	4
4	MEAN	739.0	721.0	644.8	683.5	670.3	844.3	720.8	777.3
	SD	107.2	10.9	71.9	121.2	118.1	65.1	131.3	125.0
	MIN	639	712	553	540	514	752	565	601
	MAX	891	736	702	833	780	900	885	890
	N	4	4	4	4	4	4	4	4

TABLE NO. 14 (b) (4)

DAILY FOOD CONSUMPTION (g) SUMMARY
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 48 to 49	Day 49 to 50	Day 50 to 51	Day 51 to 52	Day 52 to 53	Day 53 to 54	Day 54 to 55	Post treatment average (Days 0 to 55)
1	MEAN	690.8	622.2	749.2	629.6	783.0	706.6	739.6	511.8
	SD	147.7	132.1	139.5	120.9	127.3	159.6	153.6	188.6
	MIN	526	448	591	450	607	487	490	1
	MAX	818	757	900	751	900	893	900	900
	N	5	5	5	5	5	5	5	273
2	MEAN	752.0	628.8	750.3	797.8	726.3	696.8	651.3	538.2
	SD	156.3	52.5	85.2	53.3	112.0	63.7	157.8	169.6
	MIN	527	560	654	734	617	621	495	0
	MAX	873	688	858	847	879	768	845	900
	N	4	4	4	4	4	4	4	221
3	MEAN	750.0	653.8	727.5	726.8	755.0	626.8	633.8	540.1
	SD	119.0	168.6	109.9	163.0	157.7	54.1	37.4	197.0
	MIN	623	517	568	512	545	573	607	1
	MAX	900	897	816	900	887	700	689	900
	N	4	4	4	4	4	4	4	219
4	MEAN	680.5	762.0	662.3	698.0	747.8	638.3	722.3	548.8
	SD	111.4	107.7	190.1	64.7	115.5	61.2	104.5	183.5
	MIN	555	613	422	644	609	582	618	20
	MAX	823	850	846	790	886	713	853	900
	N	4	4	4	4	4	4	4	210

TABLE NO. 14 (b) (4)

FOOD CONSUMPTION (g)
F0 GENERATION – LACTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
1	MEAN	233.3	382.3	454.3	495.2	533.3	622.0	682.7	705.0
	SD	60.5	56.3	79.5	64.3	39.8	71.9	93.8	114.0
	MIN	154	340	349	412	498	499	553	556
	MAX	284	446	554	575	600	688	785	833
	N	5	5	5	5	5	5	5	5
2	MEAN	269.8	437.6	475.9	550.4	558.5	615.3	677.8	708.5
	SD	158.6	31.6	65.3	58.6	58.1	57.4	53.4	34.9
	MIN	1	401	411	503	494	559	645	665
	MAX	388	470	553	631	632	694	758	748
	N	5	4	4	4	4	4	4	4
3	MEAN	247.4	396.4	513.4	551.6	601.6	638.7	691.4	687.3
	SD	146.6	78.4	113.4	73.1	69.0	50.0	55.5	36.5
	MIN	85	349	454	509	514	589	643	648
	MAX	477	513	683	661	657	687	771	727
	N	5	4	4	4	4	4	4	4
4	MEAN	269.2	376.5	460.5	544.2	574.4	670.5	717.3	705.1
	SD	127.3	100.8	73.3	46.0	22.2	25.3	52.4	69.5
	MIN	155	297	404	507	547	638	653	645
	MAX	397	524	568	606	597	697	772	783
	N	4	4	4	4	4	4	4	4

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 14 (b) (4)

FOOD CONSUMPTION (g)
F0 GENERATION – LACTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		COMBINED WEEKS (1 to 8)
1	MEAN	513.5
	SD	64.1
	MIN	423
	MAX	582
	N	5
2	MEAN	436.2
	SD	245.8
	MIN	1
	MAX	579
	N	5
3	MEAN	453.8
	SD	213.6
	MIN	85
	MAX	635
	N	5
4	MEAN	539.7
	SD	46.7
	MIN	506
	MAX	609
	N	4

TABLE NO. 15 (b) (4)

HEMATOLOGY SUMMARY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	7.132	169.6	0.542	75.94	23.78	313.6	12.40	252.6
	SD	0.310	9.7	0.033	2.34	0.67	12.9	0.55	21.7
	MIN	6.72	158	0.51	72.8	23.0	302	11.9	227
	MAX	7.54	181	0.59	78.6	24.8	330	13.3	284
	N	5	5	5	5	5	5	5	5
2	MEAN	7.128	164.4	0.542	76.06	23.08	303.6	12.86	251.4
	SD	0.426	9.0	0.040	1.84	0.23	9 3	0.54	38.2
	MIN	6.68	155	0.49	72.8	22.8	298	12.4	206
	MAX	7.83	179	0.60	77.2	23.3	320	13.5	287
	N	5	5	5	5	5	5	5	5
3	MEAN	7.562	171.8	0.552	73.12	22.74	311.6	13.06	232.2
	SD	0.485	10.1	0.038	4.76	1.11	11.9	1.02	18.7
	MIN	7.01	164	0.51	65.0	21.1	300	12.2	215
	MAX	8.27	186	0.61	77.4	24.0	325	14.6	258
	N	5	5	5	5	5	5	5	5
4	MEAN	6.990	161.6	0.513	73.50	23.14	315.0	12.66	301.0 **B**
	SD	0.348	8.2	0.023	2.58	0.46	11.7	0.75	45.7
	MIN	6.65	153	0.48	71.4	22.6	300	11.8	256
	MAX	7.37	173	0.53	77.7	23.6	326	13.6	370
	N	5	5	5	5	5	5	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

TABLE NO. 15 (b) (4)

HEMATOLOGY SUMMARY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	9.144	5.968	2.412	0.458	0.246	0.032	0.026
	SD	1.744	1.506	0.339	0.036	0.092	0.013	0.018
	MIN	7.63	4.22	2.04	0.42	0.16	0.02	0.01
	MAX	11.87	8.16	2.75	0 50	0.40	0.05	0.05
	N	5	5	5	5	5	5	5
2	MEAN	8.916	6.202	2.024 **A**	0.392	0.260	0.024	0.018
	SD	0.343	0.297	0.370	0.084	0.119	0.011	0.004
	MIN	8.52	5.92	1.68	0 34	0.13	0.01	0.01
	MAX	9.28	6.68	2.50	0 54	0.44	0.04	0.02
	N	5	5	5	5	5	5	5
3	MEAN	11.218	8.132	2.246	0.522	0.252	0.040	0.026
	SD	2.181	1.676	0.284	0.180	0.156	0.012	0.013
	MIN	9.08	6.34	1.92	0 25	0.09	0.02	0.01
	MAX	13.82	10.29	2.64	0.72	0.43	0.05	0.04
	N	5	5	5	5	5	5	5
4	MEAN	10.366	6.946	2.726	0.450	0.188	0.030	0.026
	SD	2.206	2.120	0.293	0.070	0.076	0.012	0.009
	MIN	6.65	3.60	2.44	0 33	0.09	0.01	0.02
	MAX	12.32	8.93	3.21	0 50	0.27	0.04	0.04
	N	5	5	5	5	5	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

TABLE NO. 15 (b) (4)

HEMATOLOGY SUMMARY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	64.70	26.84	5.12	2.66	0.38	0.32	NA	NA
	SD	5.54	4.95	0.67	0.56	0.20	0.22	NA	NA
	MIN	55.3	22.6	4.2	2.1	0.2	0 1	NA	NA
	MAX	68.8	35.0	5.9	3.4	0.7	0.6	NA	NA
	N	5	5	5	5	5	5	0	0
2	MEAN	69.58	22.64	4.40	2.96	0.28	0.18	NA	NA
	SD	2.36	3.48	1.09	1.43	0.13	0.04	NA	NA
	MIN	67.0	19.5	3.6	1.4	0.1	0 1	NA	NA
	MAX	72.8	27.0	6.3	5.1	0.4	0 2	NA	NA
	N	5	5	5	5	5	5	0	0
3	MEAN	72.40	20.24 B	4.62	2.14	0.36	0.24	NA	NA
	SD	2.55	1.75	1.32	1.02	0.11	0.11	NA	NA
	MIN	69.8	17.5	2.4	1.0	0.2	0 1	NA	NA
	MAX	75.7	22.2	5.8	3.2	0.5	0.4	NA	NA
	N	5	5	5	5	5	5	0	0
4	MEAN	65.74	27.48	4.42	1.80	0.34	0.26	NA	NA
	SD	8.06	7.50	0.55	0.63	0.15	0.09	NA	NA
	MIN	54.1	21.5	3.8	1.1	0.1	0 2	NA	NA
	MAX	72.5	38.8	5.0	2.7	0.5	0.4	NA	NA
	N	5	5	5	5	5	5	0	0

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)
NA - Not applicable

TABLE NO. 16 (b) (4)

HEMATOLOGY - LACTATION PERIOD SUMMARY
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	7.200	171.2	0.506	70.36	23.82	338.4	12.36	324.0
	SD	0.610	11.4	0.040	1.27	0.53	2.6	0.95	60.2
	MIN	6.62	158	0.46	68.8	23.0	334	11.4	223
	MAX	8.23	189	0.57	72.1	24.4	341	13.7	376
	N	5	5	5	5	5	5	5	5
2	MEAN	7.503	174.0	0.525	69.65	23.20	333.5	12.38	302.0
	SD	0.856	20.2	0.064	0.64	0.36	3.7	0.51	74.3
	MIN	6.77	156	0.47	69.0	22.9	329	11.8	214
	MAX	8.43	193	0.59	70.5	23.7	337	13.0	393
	N	4	4	4	4	4	4	4	4
3	MEAN	7.013	158.5	0.473	67.65	22.63	334.3	13.20	305.5
	SD	0.498	12.1	0.039	2.45	0.91	2 2	1.36	36.7
	MIN	6.40	148	0.44	65.0	21.7	332	12.0	276
	MAX	7.48	173	0.52	70.2	23.5	337	14.7	356
	N	4	4	4	4	4	4	4	4
4	MEAN	7.093	162.8	0.483	68.40	22.95	335.8	13.18	332.0
	SD	0.304	12.6	0.034	3.81	1.39	2.4	1.61	56.4
	MIN	6.78	152	0.45	62.9	21.0	334	11.8	267
	MAX	7.45	181	0.53	71.7	24.3	339	15.5	384
	N	4	4	4	4	4	4	4	4

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

TABLE NO. 16 (b) (4)

HEMATOLOGY - LACTATION PERIOD SUMMARY
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	7.518	4.014	2.294	0.402	0.746	0.034	0.032
	SD	1.718	0.934	0.682	0.082	0.523	0.011	0.015
	MIN	5.08	3.09	1.24	0 27	0.34	0.02	0.01
	MAX	9.46	5.16	2.97	0.48	1.56	0.05	0.05
	N	5	5	5	5	5	5	5
2	MEAN	7.698	5.000 **B**	1.868	0.308	0.463	0.038	0.020
	SD	0.393	0.337	0.632	0.045	0.254	0.013	0.000
	MIN	7.22	4.58	1.25	0 25	0.29	0.02	0.02
	MAX	8.03	5.37	2.73	0 36	0.84	0.05	0.02
	N	4	4	4	4	4	4	4
3	MEAN	9.925	6.425 **C**	2.063	0.528	0.835	0.035	0.035
	SD	1.336	0.676	0.464	0.135	0.588	0.006	0.006
	MIN	8.62	5.51	1.60	0 34	0.27	0.03	0.03
	MAX	11.79	7.13	2.60	0.63	1.65	0.04	0.04
	N	4	4	4	4	4	4	4
4	MEAN	8.085	4.998 **A**	2.228	0.440	0.378	0.025	0.020
	SD	1.435	1.272	0.452	0.133	0.105	0.006	0.008
	MIN	6.23	3.12	1.74	0 32	0.30	0.02	0.01
	MAX	9.53	5.82	2.78	0.63	0.53	0.03	0.03
	N	4	4	4	4	4	4	4

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

TABLE NO. 16 (b) (4)

HEMATOLOGY - LACTATION PERIOD SUMMARY
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	53.78	30.10	5.48	9.74	0.42	0.44	29.40	0.42
	SD	6.53	3.79	1.45	6.49	0.16	0.22	5.91	0.11
	MIN	43.0	24.5	3.9	5.3	0.3	0 3	20.8	0.3
	MAX	60.8	33.9	7.5	20.8	0.7	0.8	33.8	0.5
	N	5	5	5	5	5	5	5	5
2	MEAN	65.28	24.03	3.98	5.93	0.48	0.28	30.35	0.38
	SD	7.67	7.08	0.51	3.08	0.13	0.05	18.50	0.21
	MIN	57.1	17.3	3.5	4.0	0.3	0 2	14.0	0.2
	MAX	74.5	33.9	4.7	10.5	0.6	0 3	50.8	0.6
	N	4	4	4	4	4	4	4	4
3	MEAN	64.98	20.78	5.38	8.18	0.35	0.35	32.20	0.48
	SD	3.69	3.97	1.51	4.77	0.06	0.06	3.72	0.05
	MIN	60.5	18.4	3.5	2.8	0.3	0 3	28.6	0.4
	MAX	69.2	26.7	7.2	14.0	0.4	0.4	36.6	0.5
	N	4	4	4	4	4	4	4	4
4	MEAN	61.15	28.18	5.40	4.73	0.33	0.28	26.48	0.38
	SD	8.13	7.36	1.19	1.06	0.10	0.05	18.25	0.22
	MIN	50.1	22.5	4.1	3.4	0.2	0 2	14.8	0.2
	MAX	68.4	38.2	6.6	6.0	0.4	0 3	53.7	0.7
	N	4	4	4	4	4	4	4	4

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.02$, C - $p \leq 0.002$ (Dunnett)
D - $p \leq 0.1$, E - $p \leq 0.02$, F - $p \leq 0.002$ (Dunn)
Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

TABLE NO. 17

(b) (4)

CLINICAL CHEMISTRY SUMMARY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	26.6	32.6	50.6	5.81	4.714	0.479	4.14	3 57	44.2
	SD	5.9	7.9	23.7	0.94	0.478	0.068	0.31	0.44	6.3
	MIN	21	23	32	5.1	4.17	0.41	3.7	3 2	35
	MAX	35	44	83	6.8	5.26	0.58	4.4	4 3	53
	N	5	5	5	5	5	5	5	5	5
2	MEAN	27.0	28.8	38.4	4.79	5.714 **A**	0.475	3.56	3.71	47.7
	SD	3.4	3.1	6.8	0.76	0.164	0.083	0.47	0 54	7.9
	MIN	23	25	29	3.4	5.49	0.41	2.9	3 2	35
	MAX	31	32	46	5.1	5.91	0.61	4.3	4 3	53
	N	5	5	5	5	5	5	5	5	5
3	MEAN	23.8	28.2	42.8	5.47	6 123 **B**	0.538	3.62	3.43	51.5
	SD	2.5	7.1	7.3	0.76	1.296	0.114	0.27	0 96	7.1
	MIN	20	21	34	5.1	4.71	0.40	3.4	2 5	44
	MAX	26	37	53	6.8	8.00	0.66	3.9	5.0	62
	N	5	5	5	5	5	5	5	5	5
4	MEAN	27.6	33.0	40.8	5.81	5.475	0.509	4.10	3.79	44.2
	SD	3.3	4.2	7.4	0.94	0.843	0.092	0.67	1 17	0.0
	MIN	23	27	31	5.1	4.01	0.37	3.2	1.8	44
	MAX	32	38	48	6.8	6.09	0.60	4.9	4.6	44
	N	5	5	5	5	5	5	5	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

TABLE NO. 17 (b) (4)

CLINICAL CHEMISTRY SUMMARY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	61.60	32.60	29.00	1.140	2.640	1.247	146.2	4.360	112.4
	SD	5.50	2.07	4.30	0.152	0.095	0.106	0.4	0.241	1.1
	MIN	54.0	29.0	25.0	0.90	2.50	1.13	146	4 10	111
	MAX	69.0	34.0	36.0	1.30	2.75	1.36	147	4.70	114
	N	5	5	5	5	5	5	5	5	5
2	MEAN	59.80	33.20	26.60	1.260 A	2.685	1.214	145.8	4.520	113.0
	SD	1.10	1.10	1.82	0.114	0.052	0.109	1.3	0.148	1.2
	MIN	58.0	32.0	25.0	1.10	2.60	1.10	144	4 30	112
	MAX	61.0	35.0	29.0	1.40	2.73	1.39	147	4.70	115
	N	5	5	5	5	5	5	5	5	5
3	MEAN	62.80	34.80 B	28.00	1.260 A	2.700	1.266	147.0	4.240	112.6
	SD	3.11	1.48	1.87	0.055	0.047	0.090	1.6	0.182	0.9
	MIN	60.0	33.0	26.0	1.20	2.63	1.16	145	4.00	112
	MAX	68.0	37.0	31.0	1.30	2.75	1.36	149	4 50	114
	N	5	5	5	5	5	5	5	5	5
4	MEAN	61.60	32.60	29.20	1.120	2.650	1.298	146.4	4.520	113.6
	SD	1.34	0.89	1.10	0.084	0.047	0.126	0.5	0.377	2.3
	MIN	60.0	32.0	28.0	1.00	2.60	1.16	146	4 10	111
	MAX	63.0	34.0	31.0	1.20	2.73	1.49	147	5 10	117
	N	5	5	5	5	5	5	5	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

TABLE NO. 17 (b) (4)

CLINICAL CHEMISTRY SUMMARY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		LDHI2 (U/L)	CK (U/L)	GGT (U/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	92.6	138 2	7.2	517.2	0.855
	SD	48.8	57.3	1.6	65.0	0.034
	MIN	46	69	5	454	0.82
	MAX	165	216	9	614	0.90
	N	5	5	5	5	5
2	MEAN	105.2	171.0	6.2	580.2	0.871
	SD	19.5	36.3	1.1	49.6	0.034
	MIN	83	123	5	505	0.82
	MAX	127	211	7	642	0.90
	N	5	5	5	5	5
3	MEAN	92.0	120 2	6.6	610.6	0.855
	SD	32.3	52.1	0.9	129.1	0.018
	MIN	66	68	6	467	0.82
	MAX	147	185	8	803	0.86
	N	5	5	5	5	5
4	MEAN	111.0	165.0	6.8	665.2	0.847
	SD	36.7	63.8	1.5	228.8	0.037
	MIN	52	89	5	400	0.82
	MAX	142	257	9	1010	0.90
	N	5	5	5	5	5

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

TABLE NO. 18 (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD SUMMARY
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	26.6	32.4	97.6	NA	6.940	0.512	5.44	5 54	46.0
	SD	3.2	10.6	53.4	NA	0.845	0.064	0.18	0 92	4.2
	MIN	23	26	49	NA	5.67	0.42	5.2	4 3	42
	MAX	31	51	187	NA	7.65	0.59	5.6	6.7	53
	N	5	5	5	0	5	5	5	5	5
2	MEAN	27.3	42.8	99.3	NA	6.823 **A**	0.405	4.73 **A**	5.45	47.8
	SD	4.6	22.9	22.9	NA	0.644	0.068	0.15	1 39	10.6
	MIN	22	30	77	NA	6.24	0.35	4.6	3 9	34
	MAX	32	77	120	NA	7.74	0.49	4.9	6.9	57
	N	4	4	4	0	4	4	4	4	4
3	MEAN	24.3	31.0	91.5	NA	6 995 **B**	0.385	5.75 **B**	6 25	48.8
	SD	1.7	5.5	30.6	NA	2.190	0.039	0.40	2.01	16.1
	MIN	22	27	60	NA	5.03	0.33	5.2	4 5	36
	MAX	26	39	131	NA	10.08	0.42	6.1	8 9	71
	N	4	4	4	0	4	4	4	4	4
4	MEAN	32.3	35.8	80.8	NA	5.670 **C**	0.433	5.43	5.68	39.3
	SD	6.1	3.3	9.9	NA	0.866	0.111	0.61	1 13	3.1
	MIN	26	32	68	NA	4.91	0.29	4.9	4.0	35
	MAX	38	40	92	NA	6.91	0.56	6.3	6.4	42
	N	4	4	4	0	4	4	4	4	4

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
NA - Not applicable

TABLE NO. 18 (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD SUMMARY
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	61.30	34.36	26.94	1.278	2.548	1.102	146.2	4.602	106.6
	SD	2.94	1.77	1.64	0.075	0.041	0.141	1.1	0.176	2.0
	MIN	56.3	31.5	24.8	1.17	2.50	0.90	145	4 34	104
	MAX	63.8	35.9	28.9	1.38	2.61	1.23	148	4.81	109
	N	5	5	5	5	5	5	5	5	5
2	MEAN	60.03	35.55	24.48	1.458	2.550	1.240	147.3	4.713	108 1
	SD	1.54	1.30	1.60	0.128	0.170	0.324	1.5	0.473	0.8
	MIN	58.1	34.1	22.9	1.30	2.43	0.94	146	4 30	107
	MAX	61.5	36.7	26.7	1.60	2.80	1.69	149	5 36	109
	N	4	4	4	4	4	4	4	4	4
3	MEAN	61.58	35.60	25.98	1.370	2.538	1.103	147.5	4.640	107 1
	SD	1.58	1.70	0.46	0.076	0.084	0.112	1.9	0.428	2.6
	MIN	60.0	33.8	25.5	1.29	2.46	0.97	146	4 23	104
	MAX	63.6	37.9	26.5	1.47	2.62	1.23	150	5 24	110
	N	4	4	4	4	4	4	4	4	4
4	MEAN	61.00	34.58	26.43	1.310	2.505	1.093	146.3	4.700	107.0
	SD	2.63	1.56	1.64	0.086	0.013	0.125	0.5	0.115	1.1
	MIN	58.7	32.4	24.4	1.23	2.49	0.91	146	4.63	106
	MAX	64.5	36.1	28.4	1.43	2.52	1.19	147	4.87	108
	N	4	4	4	4	4	4	4	4	4

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

TABLE NO. 18 (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD SUMMARY
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		LDHI2 (U/L)	CK (U/L)	GGT (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	98.4	153.8	NA	1.70	391.8	0.846
	SD	38.7	32.6	NA	0.28	27.5	0.050
	MIN	55	102	NA	1.5	352	0.80
	MAX	161	185	NA	1.9	418	0.92
	N	5	5	0	2	5	5
2	MEAN	94.5	155.8	NA	1.15	389 5	0.860
	SD	52.4	51.4	NA	0.21	43.8	0.042
	MIN	42	115	NA	1.0	330	0.81
	MAX	152	231	NA	1.3	435	0.90
	N	4	4	0	2	4	4
3	MEAN	59.0	112 3	NA	4.00	475 3	0.830
	SD	21.1	15.8	NA	4.24	97.7	0.022
	MIN	37	93	NA	1.0	380	0.81
	MAX	79	131	NA	7.0	585	0.86
	N	4	4	0	2	4	4
4	MEAN	112.0	170 3	NA	1.80	780.8	0.835
	SD	58.0	42.9	NA	NA	426.7	0.029
	MIN	31	113	NA	1.8	430	0.81
	MAX	164	216	NA	1.8	1389	0.86
	N	4	4	0	1	4	4

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)
NA - Not applicable

TABLE NO. 19 (b) (4)

MATERNAL SUMMARY
PERCENTAGE LIVE PUPS
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0
1	MEAN	89.286
	SD	14.725
	MIN	71.43
	MAX	100.00
	N	5
2	MEAN	96.111
	SD	5.415
	MIN	88.89
	MAX	100.00
	N	5
3	MEAN	96.364
	SD	8.131
	MIN	81.82
	MAX	100.00
	N	5
4	MEAN	100.000
	SD	0.000
	MIN	100.00
	MAX	100.00
	N	4

Significant difference when compared to group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

SUMMARY TABLES
F1 PUPPIES PRE-WEANING

TABLE NO. 20

(b) (4)

SUMMARY OF CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST PARTUM

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN	GROUP 1 LITTER/		GROUP 2 LITTER/		GROUP 3 LITTER/		GROUP 4 LITTER/	
	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
Activity Decreased	1/2	0/0	0/0	0/0	2/2	0/0	0/0	0/0
Backbone Prominent	0/0	0/0	0/0	0/0	0/0	0/0	1/1	1/1
Cold To Touch	2/4	1/1	1/3	1/3	2/3	1/2	1/1	0/0
Discharge Red	0/0	0/0	1/1	1/1	0/0	0/0	1/1	0/0
Fur Dull	1/3	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Fur Stained Brown	0/0	0/0	0/0	0/0	0/0	1/2	0/0	0/0
Fur Stained Red	0/0	0/0	0/0	1/1	0/0	0/0	0/0	0/0
Fur Stained Yellow	0/0	0/0	0/0	0/0	0/0	2/2	0/0	0/0
Fur Wet	0/0	0/0	0/0	0/0	0/0	1/1	0/0	0/0
Lying on Cage Floor	1/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Material Vomitus Beige	0/0	1/1	0/0	0/0	0/0	0/0	0/0	0/0
Respiration Labored	0/0	0/0	0/0	0/0	0/0	1/1	1/1	0/0
Respiratory Rate	1/2	0/0	0/0	0/0	0/0	0/0	1/1	0/0
Retching	0/0	0/0	0/0	0/0	0/0	0/0	1/1	0/0
Skin Blue	0/0	0/0	0/0	0/0	1/1	0/0	1/1	0/0
Skin Dry	1/2	1/2	1/1	1/3	0/0	0/0	0/0	0/0
Skin Lump	0/0	0/0	1/1	1/2	0/0	0/0	1/1	1/2
Skin Red	3/4	3/3	3/5	2/3	2/4	3/4	2/3	2/3
Skin Scab	4/6	1/1	2/2	3/4	1/3	2/2	4/6	2/2
Skin Turgor Slow	3/6	2/5	0/0	3/3	2/5	3/3	3/4	2/5
Skin Wound	1/1	0/0	0/0	2/2	2/2	1/1	0/0	0/0
Skin Wound with Discharge	1/1	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Swelling Firm	5/11	4/7	4/5	4/8	2/5	3/3	3/5	2/4

TABLE NO. 20

(b) (4)

SUMMARY OF CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST PARTUM

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN	GROUP 1 LITTER/		GROUP 2 LITTER/		GROUP 3 LITTER/		GROUP 4 LITTER/	
	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
Swelling Soft	3/6	3/5	3/4	2/4	2/4	3/3	4/8	4/7
Tail Kinked	0/0	0/0	0/0	0/0	0/0	0/0	1/1	0/0
Thin	2/6	3/3	0/0	3/4	3/5	3/3	2/2	2/2
Tremors	0/0	0/0	0/0	0/0	0/0	0/0	1/1	0/0
Weak	1/1	0/0	1/3	1/3	0/0	0/0	0/0	0/0

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0 $	Day 0	Day 4 $	Day 4	Day 7	Day 10	Day 14	Day 17
1	MEAN	227.30	228.97	328.97	320.00	443.40	587.60	784.27	925.93
	SD	35.21	31.47	60.56	62.18	90.32	113.14	134.46	157.94
	MIN	177.3	187.5	251.0	251.0	347.0	460.0	650.3	746.7
	MAX	263.5	263.5	386.5	386 5	563.0	734.0	961.5	1132.5
	N	5	5	5	5	5	5	5	5
2	MEAN	247 10 **E**	258.88	410.25	406 38	598.00	766.75	963.25 **A**[3]	1109.00 **A**[3]
	SD	36.40	19.33	47.51	51.59	80.92	69.43	62.31	76.23
	MIN	192.5	237.0	380.0	362 5	534.5	716.0	905.5	1035.5
	MAX	284.0	284.0	481.0	481.0	714.0	865.0	1028.0	1196.0
	N	5	5	4	4	4	4	4	4
3	MEAN	270.30 **F**	284.58	405.65	415.63	580.33	735.88	944.75 **B**[3]	1105.33 **B**[3]
	SD	20.43	17.69	63.79	51.94	81.84	78.64	101.37	128.06
	MIN	253.8	263.3	322.3	352.0	508.3	654.0	857.0	999.3
	MAX	303.0	303.0	477.0	477.0	688.5	839.0	1091.0	1291.5
	N	5	4	4	4	4	4	4	4
4	MEAN	235.27	230.45	337.67	322.71	450.38	590.92	790.54	938.54
	SD	15.29	17.03	32.14	18.79	59.22	72.30	103.92	143.02
	MIN	222.6	216.5	313.3	305 5	397.5	533.5	696.0	809.0
	MAX	256.0	253.3	384.0	343.0	532.0	696.5	922.0	1112.5
	N	4	4	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
$: Not considered in the repeated measures analysis, based on litter means calculated on all puppies.

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 21	Day 24	Day 27	Day 30	Day 33	Day 37
1	MEAN	1127.90	1260.60	1368.20	1487.77	1605.17	1756.73
	SD	164.88	152.67	156.36	139.16	121.63	113.59
	MIN	951.0	1088.0	1167.0	1312.3	1444.3	1588.7
	MAX	1354.5	1468.5	1562.5	1675.5	1760.0	1895.0
	N	5	5	5	5	5	5
2	MEAN	1318.13 A^3	1452.63 A^3	1582.75 B^3	1702.63 B^3	1833.50 B^3	1988.75 B^3
	SD	91.07	67.95	81.31	88.48	103.53	88.66
	MIN	1226.5	1397.0	1487.5	1598.0	1701.5	1860.5
	MAX	1443.0	1546.0	1682.0	1809.0	1951.0	2064.5
	N	4	4	4	4	4	4
3	MEAN	1337.25 B^3	1465.58 B^3	1604.13 C^3	1738.58 C^3	1886.13 C^3	2071.17 C^3
	SD	111.86	159.97	148.28	161.05	137.39	143.66
	MIN	1273.0	1331.3	1496.0	1611.3	1786.5	1949.5
	MAX	1504.5	1697.5	1821.0	1969.5	2088.0	2266.0
	N	4	4	4	4	4	4
4	MEAN	1124.33	1249.42	1382.50	1505.17	1623.71	1786.29
	SD	139.65	157.40	180.36	188.54	179.54	195.20
	MIN	967.5	1059.5	1168.5	1277.5	1394.5	1532.0
	MAX	1253.0	1398.5	1553.5	1694.0	1783.5	1956.0
	N	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 40	Day 43	Day 47	Day 50	Day 53	Day 56
1	MEAN	1894.73	2046.97	2273.20	2481.90	2673.53	2747.53
	SD	126.49	135.26	171.19	195.16	226.47	255.04
	MIN	1699.7	1825.3	1998.0	2160.0	2333.7	2411.7
	MAX	2014.0	2179.0	2429.0	2666.5	2849.5	3042.0
	N	5	5	5	5	5	5
2	MEAN	2151.75 B^3	2307.00 B^3	2525.38 A^3	2712.50 A^3	2908.13 A^3	2964.63
	SD	87.51	126.69	162.79	117.87	139.70	167.67
	MIN	2058.0	2188.5	2393.5	2602.0	2814.0	2854.5
	MAX	2257.0	2482.0	2739.5	2869.5	3114.5	3214.5
	N	4	4	4	4	4	4
3	MEAN	2216.50 C^3	2374.21 C^3	2553.04 C^3	2733.33 B^3	2862.71 A^3	2945.29
	SD	134.36	131.63	85.26	37.18	91.20	28.94
	MIN	2064.0	2221.5	2442.0	2688.5	2741.5	2918.0
	MAX	2379.5	2522.0	2630.5	2773.0	2962.5	2972.5
	N	4	4	4	4	4	4
4	MEAN	1952.17	2103.75	2347.46	2511.88	2695.83	2728.33
	SD	151.19	150.71	137.83	159.88	144.42	134.13
	MIN	1783.0	1914.5	2203.0	2379.0	2556.0	2612.0
	MAX	2111.0	2278.5	2528.0	2741.5	2845.5	2907.5
	N	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0 [$]	Day 0	Day 4 [$]	Day 4	Day 7	Day 10	Day 14	Day 17
1	MEAN	208.43	219.25	312.98	311.75	431.00	568.38	748.50	884.50
	SD	34.83	30.55	42.03	40.10	53.62	66.11	115.39	139.64
	MIN	166.0	178.5	260.5	260 5	380.0	499.5	630.0	722.0
	MAX	241.3	251.0	355.7	347 5	484.5	640.5	880.5	1033.0
	N	5	4	4	4	4	4	4	4
2	MEAN	225.45 **E**	235.46	369.58	370.71	528.63	682.67	874.17 **A**[3]	1002.63 **A**[3]
	SD	42.94	21.17	18.71	17.51	19.35	34.19	41.73	52.49
	MIN	158.3	211.5	351.0	351.0	511.0	649.5	830.5	935.5
	MAX	259.3	259.3	393.3	393 3	551.0	730.5	931.0	1060.0
	N	5	4	4	4	4	4	4	4
3	MEAN	250.08 **F**	264.13	329.75	360 50	519.25	680.38	904.25 **B**[3]	1035.50 **B**[3]
	SD	34.83	48.02	104.22	116.01	167.27	187.46	236.14	290.17
	MIN	222.7	225.0	216.0	288.0	394.0	522.0	684.0	799.0
	MAX	307.0	328.5	500.3	533.0	764.5	952.0	1239.0	1458.5
	N	5	4	5	4	4	4	4	4
4	MEAN	213.85	227.75	275.29	308 13	419.00	543.75	700.38	854.25
	SD	10.82	19.87	36.15	21.24	49.28	64.01	65.49	75.39
	MIN	204.7	210.5	236.5	279 5	373.5	491.0	657.5	776.0
	MAX	225.7	256.0	312.3	325.0	486.0	627.0	798.0	953.0
	N	4	4	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
[$]: Not considered in the repeated measures analysis, based on litter means calculated on all puppies.

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 21	Day 24	Day 27	Day 30	Day 33	Day 37
1	MEAN	1099.63	1227.00	1329.63	1433.13	1519.00	1671.50
	SD	184.40	212.90	204.60	197.12	163.57	153.32
	MIN	870.5	971.0	1072.0	1195.5	1304.0	1462.5
	MAX	1303.5	1481.5	1563.5	1674.5	1688.5	1823.5
	N	4	4	4	4	4	4
2	MEAN	1181.21 A^3	1325.08 A^3	1450.13 B^3	1554.25 B^3	1659.21 B^3	1802.79 B^3
	SD	51.62	69.57	108.56	103.29	120.08	134.33
	MIN	1104.0	1226.0	1294.0	1400.0	1481.5	1606.0
	MAX	1212.3	1388.3	1541.0	1619.0	1745.0	1907.0
	N	4	4	4	4	4	4
3	MEAN	1230.88 B^3	1386.13 B^3	1506.63 C^3	1651.13 C^3	1764.13 C^3	1897.63 C^3
	SD	325.68	373.50	365.28	407.71	410.20	426.77
	MIN	935.5	1061.0	1203.0	1315.5	1447.0	1632.5
	MAX	1695.0	1924.0	2036.5	2242.0	2365.0	2531.5
	N	4	4	4	4	4	4
4	MEAN	1028.13	1154.00	1283.50	1402.63	1478.50	1627.75
	SD	79.70	103.87	131.55	145.20	128.57	139.36
	MIN	926.5	1043.5	1109.5	1190.0	1302.0	1449.0
	MAX	1118.5	1277.0	1391.0	1496.5	1597.5	1789.5
	N	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 40	Day 43	Day 47	Day 50	Day 53	Day 56
1	MEAN	1801.38	1969.88	2192.13	2360.75	2538.25	2679.00
	SD	143.13	138.01	176.68	170.01	230.14	131.30
	MIN	1600.0	1764.0	1930.0	2111.0	2207.0	2510.0
	MAX	1928.0	2052.0	2313.0	2490.5	2723.5	2830.5
	N	4	4	4	4	4	4
2	MEAN	1930.13 B^3	2046.71 B^3	2215.58 A^3	2371.25 A^3	2553.38 A^3	2549.92
	SD	138.19	147.16	166.02	163.46	154.80	149.20
	MIN	1754.5	1853.5	2035.0	2201.0	2396.5	2365.0
	MAX	2085.0	2203.5	2400.5	2586.5	2761.0	2721.0
	N	4	4	4	4	4	4
3	MEAN	2025.00 C^3	2163.00 C^3	2329.13 C^3	2457.25 B^3	2582.63 A^3	2639.13
	SD	443.88	470.01	474.65	504.15	519.76	555.94
	MIN	1730.5	1855.5	1980.0	2115.5	2265.0	2283.0
	MAX	2684.0	2862.0	3030.5	3206.5	3359.5	3468.5
	N	4	4	4	4	4	4
4	MEAN	1773.00	1896.63	2105.50	2240.13	2395.38	2432.38
	SD	123.41	162.51	231.90	268.22	312.31	292.02
	MIN	1625.5	1730.5	1913.0	1978.0	2107.5	2188.5
	MAX	1925.0	2089.0	2389.0	2567.5	2780.0	2806.5
	N	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0 [$]	Day 0	Day 4	Day 7	Day 10	Day 14	Day 17
1	MEAN	219.28	223.42	309.80	428.80	567.15	756.57	891.43
	SD	28.28	27.29	52.65	73.48	91.13	117.09	140.46
	MIN	177.6	183.0	251.0	347.0	460.0	650.3	746.7
	MAX	245.0	253.8	363.0	523.8	687.3	921.0	1082.8
	N	5	5	5	5	5	5	5
2	MEAN	234.39 **E**	245.63	383.06	553.13	713.00	908.63 **A**[3]	1044.94 **A**[3]
	SD	37.66	17.53	24.24	31.27	29.14	42.71	51.42
	MIN	175.4	224.3	356.8	524.3	684.5	868.0	985.5
	MAX	265.5	265.5	415.3	591.8	748.5	968.0	1104.5
	N	5	4	4	4	4	4	4
3	MEAN	261.38 **F**	276.44	391.50	554.19	710.56	925.69 **B**[3]	1074.81 **B**[3]
	SD	22.80	22.93	77.41	119.39	127.33	163.12	203.17
	MIN	243.4	255.0	338.3	460.3	612.5	801.5	928.8
	MAX	297.2	303.0	505.0	726.5	895.5	1165.0	1375.0
	N	5	4	4	4	4	4	4
4	MEAN	224.77	228.94	316.00	436.56	567.31	748.38	897.19
	SD	9.65	17.96	20.01	53.97	65.76	80.04	107.80
	MIN	212.8	214.5	292.5	395.0	514.8	676.8	792.5
	MAX	236.2	254.0	333.3	509.0	661.8	860.0	1032.8
	N	4	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)
3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
[$]: Not considered in the repeated measures analysis, based on litter means calculated on all puppies.

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 21	Day 24	Day 27	Day 30	Day 33	Day 37
1	MEAN	1098.90	1229.90	1332.65	1448.37	1554.62	1705.83
	SD	158.98	163.14	164.65	150.27	124.78	114.97
	MIN	951.0	1088.0	1167.0	1312.3	1436.3	1588.7
	MAX	1329.0	1475.0	1563.0	1675.0	1724.3	1859.3
	N	5	5	5	5	5	5
2	MEAN	1235.25 A^3	1379.00 A^3	1507.63 B^3	1615.13 B^3	1730.56 B^3	1884.88 B^3
	SD	47.60	49.37	80.71	77.77	93.36	108.10
	MIN	1165.3	1311.5	1390.8	1499.0	1591.5	1733.3
	MAX	1270.0	1427.8	1576.3	1664.3	1786.5	1962.5
	N	4	4	4	4	4	4
3	MEAN	1290.40 B^3	1430.38 B^3	1563.63 C^3	1703.25 C^3	1839.63 C^3	2004.44 C^3
	SD	212.52	257.62	246.29	270.85	261.78	263.45
	MIN	1114.8	1243.8	1389.3	1520.3	1650.5	1859.5
	MAX	1599.8	1810.8	1928.8	2105.8	2226.5	2398.8
	N	4	4	4	4	4	4
4	MEAN	1078.00	1207.00	1335.88	1453.88	1557.19	1713.13
	SD	106.64	126.86	154.10	163.10	151.16	162.54
	MIN	947.0	1051.5	1139.0	1233.8	1348.3	1490.5
	MAX	1185.8	1337.8	1472.3	1594.5	1673.0	1872.8
	N	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 21 (b) (4)

BODY WEIGHTS SUMMARY
LITTER MEAN BODY WEIGHTS - PUPPIES (g)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 40	Day 43	Day 47	Day 50	Day 53	Day 56
1	MEAN	1837.88	1993.97	2213.25	2401 25	2585.43	2686 53
	SD	120.02	125.82	164.32	173.73	213.70	198.48
	MIN	1699.7	1825.3	1998.0	2160.0	2333.7	2411.7
	MAX	1971.0	2115.5	2352.5	2578.5	2783.5	2936.3
	N	5	5	5	5	5	5
2	MEAN	2028.44 B^3	2163.25 B^3	2353.00 A^3	2520.56 A^3	2709.38 A^3	2733 50
	SD	113.97	130.83	172.67	144.52	124.90	147.39
	MIN	1906 3	2021.0	2194.3	2390.3	2575.5	2609.8
	MAX	2135.0	2290.8	2521.0	2659.5	2840.3	2905.8
	N	4	4	4	4	4	4
3	MEAN	2143.56 C^3	2292.94 C^3	2464.94 C^3	2626.00 B^3	2755.88 A^3	2825.75
	SD	262.32	269.84	252.46	244.34	253.59	272.69
	MIN	1974.8	2113.5	2294.0	2444.3	2555.8	2600.5
	MAX	2531.8	2692.0	2830.5	2979.5	3119.5	3218.3
	N	4	4	4	4	4	4
4	MEAN	1867.63	2007.31	2236.88	2385 19	2562.88	2594.81
	SD	129.63	151.49	188.27	214.29	240.60	219.90
	MIN	1704 3	1822.5	2058.0	2178.5	2331.8	2400.3
	MAX	2018.0	2183.8	2458.5	2654.5	2812.8	2857.0
	N	4	4	4	4	4	4

2-way ANOVA on PPD0:
Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (t-test)

3-way nested repeated measures ANOVA:
Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0 to 4 [$]	Day 0 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21
1	MEAN	96.90	91.03	123.40	144.20	196.67	141.67	201.97
	SD	45.76	42.39	31.67	23.51	24.77	28.84	12.02
	MIN	38.7	38.7	96.0	113.0	165.0	96.3	193.5
	MAX	154.7	139.0	176.5	171.0	227.5	171.0	222.0
	N	5	5	5	5	5	5	5
2	MEAN	150.17	147.50 C^3	191.63 C^3	168.75 B^3	196.50	145.75	209.13
	SD	35.11	37.68	33.51	14.61	31.29	16.01	37.58
	MIN	114.7	107.0	158.0	151.0	163.0	130.0	165.5
	MAX	197.0	197.0	233.0	185.0	238.5	168.0	247.0
	N	4	4	4	4	4	4	4
3	MEAN	122.63	131.04	164.71 C^3	155 54 A^3	208.88 B^3	160.58	216.50
	SD	61.54	49.44	37.19	14.13	36.12	28.11	13.10
	MIN	53.0	88.7	121.5	145.7	164.5	139.5	205.5
	MAX	199.5	199.5	211.5	176.5	252.0	200.5	235.5
	N	4	4	4	4	4	4	4
4	MEAN	102.67	92.25	127.67	140.54	199.63	148.00	185.79
	SD	33.98	23.40	42.87	25.50	46.15	39.88	43.39
	MIN	81.0	74.5	89.5	106.7	159.0	113.0	140.5
	MAX	152.7	126.5	189.0	164.5	251.5	190.5	232.5
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
[$]: Not considered in the repeated measures analysis, based on litter means calculated on all puppies.

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33	Day 33 to 37	Day 37 to 40
1	MEAN	132.70	107.60	119.57	117.40	151.57	138.00
	SD	14.55	27.38	21.97	22.39	20.31	29.57
	MIN	114.0	79.0	87.5	84.5	132.0	111.0
	MAX	154.0	141.0	145.3	143.0	173 5	180.5
	N	5	5	5	5	5	5
2	MEAN	134.50	130.13	119.88	130.88	155.25	163.00
	SD	29.57	27.17	7.43	18.67	65.85	47.26
	MIN	103.0	90.5	110.5	103.5	61.0	95.0
	MAX	170.5	151 5	127.0	143.5	203 5	197.5
	N	4	4	4	4	4	4
3	MEAN	144.75	138.54	134.46 B^3	147.54 B^3	185.04	145.33
	SD	32.36	22.23	17.21	38.91	35.75	37.22
	MIN	124.0	117.0	115.3	118.5	161.7	113.5
	MAX	193.0	164.7	149.5	204.7	237 5	187.3
	N	4	4	4	4	4	4
4	MEAN	125.08	133.08	122.67	118.54	162.58	165.88
	SD	23.38	23.31	14.65	21.46	33.03	58.38
	MIN	92.0	109.0	109.0	89.5	137 5	121.5
	MAX	145.5	155.0	140.5	139.7	207 5	251.0
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A1 - $p \leq 0.1$, B1 - $p \leq 0.05$, C1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A2 - $p \leq 0.1$, B2 - $p \leq 0.05$, C2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A3 - $p \leq 0.1$, B3 - $p \leq 0.05$, C3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A4 - $p \leq 0.1$, B4 - $p \leq 0.05$, C4 - $p \leq 0.01$ (t-test)

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
1	MEAN	152.23	226.23	208.70	191.63	74.00
	SD	30.46	57.33	64.44	67.01	76.33
	MIN	116.5	172.7	128.0	95.0	-11 5
	MAX	190.0	314.0	292.0	271.0	192.5
	N	5	5	5	5	5
2	MEAN	155.25	218.38	187.13	195.63	56.50
	SD	47.00	48.10	48.64	83.84	51.40
	MIN	124.5	156.0	130.0	81.5	-17 5
	MAX	225.0	257 5	242.0	270.0	100.0
	N	4	4	4	4	4
3	MEAN	157.71	178.83 B^3	180.29	129.38	82.58
	SD	14.63	51.34	51.86	57.16	113.95
	MIN	142.5	108 5	122.0	53.0	-44 5
	MAX	177.5	220 5	246.5	189.5	231.0
	N	4	4	4	4	4
4	MEAN	151.58	243.71	164.42	183.96	32.50
	SD	48.61	63.97	38.99	90.56	54.12
	MIN	97.0	151 5	124.7	104.0	-39.0
	MAX	210.3	288 5	213.5	300.3	84.5
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 0 to 4 [$]	Day 0 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21
1	MEAN	94.27	92.50	119.25	137.38	180.13	136.00	215.13
	SD	19.09	16.60	22.34	20.14	49.50	29.73	50.73
	MIN	82.0	82.0	90.5	109.5	130.5	92.0	148.5
	MAX	122.3	117.0	145.0	156.0	240.0	155.5	270.5
	N	4	4	4	4	4	4	4
2	MEAN	127.60	135.25 **C[3]**	157.92 **C[3]**	154.04 **B[3]**	191.50	128.46	178.58
	SD	15.68	13.70	13.93	29.42	25.82	20.72	29.76
	MIN	112.8	125.5	139.0	126.7	157.5	105.0	143.0
	MAX	146.7	155.0	172.0	192.0	219.0	155.3	212.5
	N	4	4	4	4	4	4	4
3	MEAN	63.25	96.38	158.75 **C[3]**	161.13 **A[3]**	223.88 **B[3]**	131.25	195.38
	SD	98.10	79.96	52.90	26.63	51.04	59.67	43.26
	MIN	-76.0	15.0	106.0	128.0	162.0	91.0	136.5
	MAX	193.3	204.5	231.5	187.5	287.0	219.5	236.5
	N	5	4	4	4	4	4	4
4	MEAN	61.42	80.38	110.88	124.75	156.63	153.88	173.88
	SD	41.46	17.02	34.71	17.50	30.91	30.59	19.99
	MIN	8.0	69.0	88.0	103.5	112.0	118.5	150.5
	MAX	107.7	105.0	162.5	141.0	182.0	193.0	196.0
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
[$]: Not considered in the repeated measures analysis, based on litter means calculated on all puppies.

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33	Day 33 to 37	Day 37 to 40
1	MEAN	127.38	102.63	103.50	85.88	152.50	129.88
	SD	35.17	16.13	21.06	49.67	16.19	16.93
	MIN	100.5	82.0	74.0	14.0	135.0	104.5
	MAX	178.0	121.0	123.5	126.5	172.0	139.0
	N	4	4	4	4	4	4
2	MEAN	143.88	125.04	104.13	104.96	143.58	127.33
	SD	23.09	39.69	35.05	18.49	15.76	46.80
	MIN	122.0	68.0	55.0	81.5	124 5	69.3
	MAX	176.0	152.7	136.5	126.0	162.0	178.0
	N	4	4	4	4	4	4
3	MEAN	155.25	120.50	144.50 B^3	113.00 B^3	133.50	127.38
	SD	49.45	16.03	43.75	18.12	51.81	24.95
	MIN	125.5	105.0	112.5	90.5	73.0	98.0
	MAX	229.0	142.0	205.5	131.5	185 5	152.5
	N	4	4	4	4	4	4
4	MEAN	125.88	129.50	119.13	75.88	149.25	145.25
	SD	35.29	50.76	40.20	35.75	42.98	25.74
	MIN	80.0	66.0	80.5	42.0	91.0	116.0
	MAX	158.5	182.0	175.0	112.0	192.0	176.5
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
1	MEAN	168.50	222.25	168.63	177.50	140.75
	SD	49.47	45.55	24.21	81.55	245.61
	MIN	124.0	166.0	132.5	96.0	-55 5
	MAX	238.5	261.0	183.5	290.5	475.5
	N	4	4	4	4	4
2	MEAN	116.58	168.88	155.67	182.13	-3.46
	SD	12.08	50.73	44.59	10.32	37.49
	MIN	99.0	94.0	90.0	173.5	-40.0
	MAX	125.5	203.0	186.0	195.5	31.0
	N	4	4	4	4	4
3	MEAN	138.00	166.13 B^3	128.13	125.38	56.50
	SD	26.92	40.80	40.35	30.71	38.02
	MIN	120.0	124 5	78.0	91.0	18.0
	MAX	178.0	221.0	176.0	153.0	109.0
	N	4	4	4	4	4
4	MEAN	123.63	208.88	134.63	155.25	37.00
	SD	59.08	76.33	48.75	80.40	46.18
	MIN	48.5	120.0	65.0	37.5	6.0
	MAX	177.0	300.0	178.5	212.5	105.0
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21
1	MEAN	86.38	119.00	138.35	189.42	134.87	207.47
	SD	34.21	25.27	19.51	32.78	28.75	26.71
	MIN	38.7	96.0	113.0	157.5	96.3	171.3
	MAX	128.0	160.8	163.5	233.8	161.8	246.3
	N	5	5	5	5	5	5
2	MEAN	137.44 C^3	170.06 C^3	159.88 B^3	195.63	136.31	190.31
	SD	17.20	16.59	20.85	21.30	16.92	29.81
	MIN	116.3	148.5	132.8	173.5	117.5	154.3
	MAX	153.0	187.8	183.5	219.5	158.5	222.8
	N	4	4	4	4	4	4
3	MEAN	115.06	162.69 C^3	156 38 A^3	215.13 B^3	149.13	206.77
	SD	62.64	44.56	8.49	37.13	40.60	16.07
	MIN	58.5	113.8	150.8	189.0	127.3	186.0
	MAX	202.0	221.5	169.0	269.5	210.0	224.8
	N	4	4	4	4	4	4
4	MEAN	87.06	120.56	130.75	181.06	148.81	180.81
	SD	19.14	38.27	17.39	32.02	34.12	31.26
	MIN	76.5	88.8	114.3	147.3	115.8	153.0
	MAX	115.8	175.8	152.8	216.8	183.3	208.0
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 22 (b) (4)2

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33	Day 33 to 37	Day 37 to 40
1	MEAN	131.00	102.75	115.72	106.25	151.22	132.05
	SD	13.68	21.81	23.22	32.88	16.98	21.61
	MIN	115.3	79.0	80.8	49.3	135.0	111.0
	MAX	146.0	131.0	145.3	132.0	172.8	159.5
	N	5	5	5	5	5	5
2	MEAN	143.75	128.63	107.50	115.44	154.31	143.56
	SD	11.17	33.67	24.73	17.85	28.69	46.16
	MIN	131.3	79.3	73.0	92.5	119.8	75.8
	MAX	157.8	151.5	130.5	134.8	179.8	173.0
	N	4	4	4	4	4	4
3	MEAN	149.42	133.25	139.63 B^3	136.38 B^3	164.81	139.13
	SD	41.06	16.70	26.49	29.98	35.15	26.05
	MIN	128.7	118.0	114.8	114 3	136.0	115.3
	MAX	211.0	149.8	177.0	180 3	211.5	176.3
	N	4	4	4	4	4	4
4	MEAN	129.00	128.88	118.00	103.31	155.94	154.50
	SD	20.35	32.47	18.83	22.88	36.29	41.14
	MIN	104.5	87.5	94.8	69.0	114.5	118.8
	MAX	152.0	166.5	140.3	115 3	199.8	213.8
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 22 (b) (4)

BODY WEIGHT CHANGES SUMMARY
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
1	MEAN	156.08	219.28	188.00	184.18	101.10
	SD	35.66	45.35	41.49	66.21	116.43
	MIN	125.7	172.7	130 3	95.5	-33 5
	MAX	214.3	285.8	234.8	280.8	253.0
	N	5	5	5	5	5
2	MEAN	134.81	189.75	167.56	188.81	24.13
	SD	27.48	56.00	39.15	44.94	37.63
	MIN	114.8	109.5	110.0	128.0	-24 5
	MAX	175.3	230.3	196.0	232.8	65.5
	N	4	4	4	4	4
3	MEAN	149 38	172.00 B^3	161.06	129.88	69.88
	SD	8.93	35.19	16.57	41.18	65.61
	MIN	138.8	138.5	149.0	72.0	-13 3
	MAX	160.3	215.3	184.8	169.5	140.0
	N	4	4	4	4	4
4	MEAN	139.69	229.56	148.31	177.69	31.94
	SD	56.28	65.06	33.68	79.55	51.31
	MIN	72.8	135.8	120 5	79.3	-27.8
	MAX	202.0	274.8	196.0	268.0	94.8
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 23

(b) (4)

BODY WEIGHTS - PUPPIES (g) SUMMARY

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
1	MEAN	211.5	323.6	434.6	576.0	772 1	909.6	1111.8	1244.9	1349.9	1471.8
	SD	41.7	75.5	105.5	139.3	159.0	187 1	203.2	201.2	206.2	192.2
	MIN	148	170	241	315	471	537	683	805	865	1040
	MAX	265	423	569	743	979	1180	1393	1494	1590	1707
	N	19	13	11	11	11	11	11	11	11	11
2	MEAN	239.5	396.3	581.4	752.7	954.0	1096.6	1300.3	1439.3	1568.6	1687.4
	SD	35.0	38.0	65.4	61.1	70.1	87.1	101.8	92.3	109.9	109.7
	MIN	178	345	517	684	863	971	1175	1283	1420	1544
	MAX	294	481	714	865	1044	1196	1443	1546	1699	1810
	N	17	9	7	7	7	7	7	7	7	7
3	MEAN	264.3	391.6	572.3	726.8	935.0	1093.6	1337.3	1450.7	1592.1	1724.4
	SD	39.5	79.2	95.7	96.0	127 9	143 2	135.4	185.5	195.1	197.5
	MIN	183	233	416	569	698	876	1170	1200	1352	1472
	MAX	317	508	737	880	1139	1332	1547	1781	1977	2071
	N	17	11	9	9	9	9	8	9	9	9
4	MEAN	233.7	337.7	450.8	587.6	782.7	927.0	1115.7	1242.0	1373.3	1496.7
	SD	26.6	69.2	91.1	117.6	146 1	162 5	170.7	179.4	206.5	210.0
	MIN	175	216	308	380	500	647	821	941	1032	1158
	MAX	272	466	586	772	994	1161	1309	1429	1587	1704
	N	21	12	9	9	9	9	9	9	9	9

TABLE NO. 23

BODY WEIGHTS - PUPPIES (g) SUMMARY

MALES

(b) (4)

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
1	MEAN	1590.5	1741.5	1877.0	2026.8	2248.2	2452.6	2642.6	2717.0
	SD	180.8	193.3	198.8	230.6	263 2	308.7	345.3	363.7
	MIN	1177	1309	1435	1514	1677	1804	1922	2014
	MAX	1789	1979	2128	2344	2626	2909	3227	3308
	N	11	11	11	11	11	11	11	11
2	MEAN	1816.7	1985.4	2158.1	2315.4	2542.7	2722.0	2919.0	2974.3
	SD	123.4	131.0	141.0	173.5	202.7	195.6	208.8	252.7
	MIN	1679	1847	2002	2127	2319	2493	2630	2638
	MAX	1962	2174	2368	2593	2839	2979	3245	3359
	N	7	7	7	7	7	7	7	7
3	MEAN	1878.3	2060.8	2210.8	2368.0	2550.7	2731.8	2863.2	2942.8
	SD	187.6	204.1	216.7	228.0	226 9	244.3	262.7	287.2
	MIN	1669	1794	1924	2053	2253	2393	2543	2471
	MAX	2210	2360	2492	2659	2894	3093	3326	3365
	N	9	9	9	9	9	9	9	9
4	MEAN	1617.6	1780.7	1943.2	2101.3	2349.7	2509.7	2706.6	2731.1
	SD	213.6	231.7	229.2	231.9	238 9	250.9	280.8	257.6
	MIN	1264	1402	1499	1700	1959	2067	2265	2283
	MAX	1810	2025	2198	2366	2676	2889	3078	3080
	N	9	9	9	9	9	9	9	9

TABLE NO. 23

(b) (4)

BODY WEIGHTS - PUPPIES (g) SUMMARY

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
1	MEAN	222.5	321.1	431.0	568.4	748 5	884 5	1099.6	1227.0	1329.6	1433 1
	SD	32.8	41.8	58.4	69.0	113 3	137 5	178.2	207.1	198.5	194.2
	MIN	166	258	375	485	601	679	800	891	987	1098
	MAX	265	391	520	661	901	1053	1333	1520	1611	1730
	N	15	11	8	8	8	8	8	8	8	8
2	MEAN	228.4	368.8	531.1	682.1	873 3	1004.8	1184.7	1332.1	1460.2	1558 9
	SD	45.3	49.7	54.3	74.8	80.2	82.2	98.6	118.9	141.2	148.8
	MIN	135	300	434	569	734	844	1004	1140	1191	1280
	MAX	323	444	609	790	978	1120	1298	1459	1615	1718
	N	23	13	9	9	9	9	9	9	9	9
3	MEAN	255.9	367.3	530.9	689.7	913.7	1050.7	1246.6	1404.3	1527.0	1676.0
	SD	46.2	113.0	171.8	195.8	247.8	297.7	333.9	379.2	372.4	411.3
	MIN	178	216	320	434	574	675	832	946	1083	1215
	MAX	335	543	770	961	1250	1484	1706	1931	2049	2250
	N	17	12	7	7	7	7	7	7	7	7
4	MEAN	213.0	278.8	418.3	541.3	704 3	858 9	1029.6	1162.0	1287.7	1398 9
	SD	24.6	64.8	81.5	90.4	103 5	124.7	117.3	130.4	155.9	161.7
	MIN	169	148	332	445	580	681	852	970	1033	1123
	MAX	256	385	580	726	912	1098	1244	1397	1514	1600
	N	17	11	7	7	7	7	7	7	7	7

TABLE NO. 23

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g) SUMMARY

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
1	MEAN	1519.0	1671.5	1801.4	1969.9	2192.1	2360.8	2538.3	2679.0
	SD	172.1	176.9	166.4	168.5	214.0	218.8	271.6	275.3
	MIN	1199	1317	1479	1640	1786	1950	2073	2294
	MAX	1767	1927	2028	2170	2464	2680	2844	3069
	N	8	8	8	8	8	8	8	8
2	MEAN	1663.6	1806.7	1927.6	2044.9	2205.4	2363.9	2546.3	2546.2
	SD	160.5	179.6	181.4	201.2	236.8	258.7	248.8	263.8
	MIN	1352	1501	1618	1753	1813	1959	2154	2172
	MAX	1834	2009	2168	2310	2520	2740	2859	2884
	N	9	9	9	9	9	9	9	9
3	MEAN	1789.9	1932.0	2057.1	2196.4	2354.7	2490.0	2617.9	2675.3
	SD	414.6	428.7	452.5	482.0	496 2	529.8	545.6	581.9
	MIN	1320	1478	1551	1672	1795	1890	2054	2036
	MAX	2395	2558	2743	2981	3189	3383	3565	3676
	N	7	7	7	7	7	7	7	7
4	MEAN	1479.6	1626.3	1770.4	1886.4	2091.9	2225.1	2378.1	2419.6
	SD	146.4	177.6	177.9	214.8	273 5	313.0	361.3	334.2
	MIN	1236	1283	1417	1485	1652	1688	1853	1901
	MAX	1640	1847	1940	2111	2401	2568	2803	2833
	N	7	7	7	7	7	7	7	7

TABLE NO. 24

(b) (4)

BODY WEIGHT CHANGES SUMMARY - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 17 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
1	MEAN	95.8	120.9	141.4	196.1	137 5	202.2	133.1	--	105.0	121.9	118.7
	SD	52.0	33.4	37.7	31.8	40.4	28.9	18.8	--	37.5	40.3	23.1
	MIN	2	71	74	139	66	146	101	--	39	75	82
	MAX	186	179	186	236	201	252	169	--	158	186	150
	N	13	11	11	11	11	11	11	--	11	11	11
2	MEAN	141.4	185.7	171.3	201.3	142.6	203.7	139.0	--	129.3	118.9	129.3
	SD	29.3	28.6	22.2	34.0	23.0	37.7	29.2	--	41.2	18.2	22.4
	MIN	95	154	141	163	108	164	103	--	39	82	82
	MAX	197	233	203	268	174	262	189	--	166	139	152
	N	9	7	7	7	7	7	7	--	7	7	7
3	MEAN	111.2	163.8	154.4	208.2	158.6	304.9	52.2	324.0	141.4	132.3	153.9
	SD	70.1	38.3	17.9	49.0	39.8	266.7	280.5	NA	48.1	32.4	41.1
	MIN	-54	117	125	129	96	161	-688	324	51	94	98
	MAX	210	229	191	259	208	1012	234	324	210	203	212
	N	11	9	9	9	9	9	9	1	9	9	9
4	MEAN	102.7	126.8	136.8	195.1	144 3	188.7	126.3	--	131.3	123.3	120.9
	SD	63.4	40.9	36.0	45.9	41.4	44.9	41.1	--	34.6	21.8	38.6
	MIN	-47	66	72	120	84	131	70	--	70	95	73
	MAX	205	190	186	252	214	248	183	--	165	164	211
	N	12	9	9	9	9	9	9	--	9	9	9

TABLE NO. 24

(b) (4)

BODY WEIGHT CHANGES SUMMARY - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
1	MEAN	150.9	135.5	149.8	221.4	204.5	190.0	74.4
	SD	37.5	33.1	49.9	61.1	80.2	69.0	72.8
	MIN	101	93	79	153	109	81	-55
	MAX	218	195	230	334	388	318	224
	N	11	11	11	11	11	11	11
2	MEAN	168.7	172.7	157 3	227.3	179.3	197.0	55.3
	SD	77.4	45.5	61.3	43.2	51.5	92.5	66.0
	MIN	61	95	109	156	120	38	-19
	MAX	299	232	291	279	243	318	149
	N	7	7	7	7	7	7	7
3	MEAN	182.4	150.0	157 2	182.7	181.1	131.4	79.6
	SD	46.3	47.9	26.7	60.5	55.3	110.6	141.4
	MIN	125	95	119	64	98	-138	-128
	MAX	286	229	200	235	269	244	397
	N	9	9	9	9	9	9	9
4	MEAN	163.1	162.6	158 1	248.3	160.0	196.9	24.6
	SD	38.3	67.4	47.2	67.0	40.3	99.7	59.5
	MIN	135	97	88	147	108	93	-84
	MAX	223	302	221	323	214	372	99
	N	9	9	9	9	9	9	9

TABLE NO. 24

[redacted] (b) (4)

BODY WEIGHT CHANGES SUMMARY - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
1	MEAN	96.1	119.3	137.4	180.1	136.0	215 1	127.4	102.6	103.5	85.9
	SD	19.0	23.6	19.6	49.2	33.9	50.5	50.4	21.1	27.7	58.0
	MIN	74	81	109	116	78	121	87	73	51	-9
	MAX	133	161	158	240	179	280	246	132	136	178
	N	11	8	8	8	8	8	8	8	8	8
2	MEAN	126.5	157.9	151.0	191.2	131.4	179 9	147.4	128.1	98.7	104.7
	SD	29.4	15.1	34.3	27.7	27.7	42.2	40.4	38.3	43.2	24.2
	MIN	74	134	102	150	99	108	82	51	5	72
	MAX	186	174	208	229	176	239	204	163	138	137
	N	13	9	9	9	9	9	9	9	9	9
3	MEAN	91.2	161.3	158.9	224.0	137.0	195 9	157.7	122.7	149.0	113.9
	SD	94.0	53.8	28.9	53.9	59.8	53.8	50.3	21.5	43.8	28.1
	MIN	-76	97	114	140	76	116	112	93	93	76
	MAX	221	247	202	289	234	266	233	147	210	158
	N	12	7	7	7	7	7	7	7	7	7
4	MEAN	66.3	112.6	123.0	163.0	154.6	170.7	132.4	125.7	111.1	80.7
	SD	51.2	40.9	18.6	32.6	37.5	26.2	29.5	49.5	35.1	39.0
	MIN	-53	70	94	112	101	130	80	63	71	36
	MAX	143	195	146	205	206	202	164	184	175	136
	N	11	7	7	7	7	7	7	7	7	7

TABLE NO. 24

(b) (4)

BODY WEIGHT CHANGES SUMMARY - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
1	MEAN	152.5	129.9	168 5	222.3	168.6	177.5	140.8
	SD	29.7	28.8	47.7	51.3	32.7	87.4	332.9
	MIN	110	101	106	146	121	69	-74
	MAX	199	172	255	294	216	328	927
	N	8	8	8	8	8	8	8
2	MEAN	143.1	120.9	117 3	160.6	158.4	182.4	-0.1
	SD	31.7	54.0	39.3	62.4	50.4	31.4	56.1
	MIN	95	12	63	17	54	119	-105
	MAX	182	186	180	210	220	230	81
	N	9	9	9	9	9	9	9
3	MEAN	142.1	125.1	139 3	158.3	135.3	127.9	57.4
	SD	47.4	34.5	43.9	40.9	43.9	35.5	46.6
	MIN	73	73	115	123	78	82	-18
	MAX	213	185	238	221	194	182	111
	N	7	7	7	7	7	7	7
4	MEAN	146.7	144.1	116.0	205.4	133.3	153.0	41.4
	SD	72.8	43.1	62.8	80.1	52.1	84.3	49.7
	MIN	47	93	9	78	36	19	-27
	MAX	247	219	177	310	190	235	117
	N	7	7	7	7	7	7	7

TABLE NO. 25 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS SUMMARY
GROUP LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS- PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35
1	MEAN	15.700	18.617	21.100	21.767	23.267
	SD	1.022	0.600	0.945	0.824	1.006
	MIN	14.00	17.83	19.50	20.83	22.00
	MAX	16.75	19.50	21.75	23.00	24.33
	N	5	5	5	5	5
2	MEAN	17.625 C^3	20.250 C^3	21.563	23.438	25.063 C^3
	SD	0.250	0 354	0.427	1.612	1.231
	MIN	17.50	19.75	21.00	21.50	23.25
	MAX	18.00	20.50	22.00	25.00	26.00
	N	4	4	4	4	4
3	MEAN	17.167 C^3	20.354 C^3	21.833 A^3	22.361	23.979 A^3
	SD	0.850	1.621	1.296	1.248	0.267
	MIN	16.00	19.17	20.33	21.33	23.75
	MAX	18.00	22.75	23.50	23.75	24.25
	N	4	4	4	3	4
4	MEAN	15.604	17.938	20.896	22.375	23.229
	SD	0.657	0.427	0.515	1.797	1.420
	MIN	15.00	17.50	20.25	21.00	21.75
	MAX	16.50	18.50	21.50	25.00	25.17
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 25 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 42	Day 49	Day 56
1	MEAN	24.583	25.417	26.150
	SD	0.328	0.493	0.576
	MIN	24.25	24.83	25.50
	MAX	25.00	26.00	27.00
	N	5	5	5
2	MEAN	25.750 C^3	25.938 B^3	27.188 C^3
	SD	1.258	0 921	0.944
	MIN	24.00	24.75	26.50
	MAX	27.00	27.00	28.50
	N	4	4	4
3	MEAN	25.021	25.583	26.583
	SD	0.172	0.612	0.289
	MIN	24.83	25.25	26.33
	MAX	25.25	26.50	27.00
	N	4	4	4
4	MEAN	23.896	25.313	25.917
	SD	1.487	0.826	0.553
	MIN	22.50	24.75	25.50
	MAX	25.83	26.50	26.67
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 25 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35
1	MEAN	15.688	18.188	20.583	21.625	22.500
	SD	1.028	1.048	0.804	1.601	1.837
	MIN	14.50	16.75	20.00	20.50	21.50
	MAX	17.00	19.25	21.50	24.00	25.25
	N	4	4	3	4	4
2	MEAN	17.083 C^3	19.250 C^3	20.583	22.333	24.750 C^3
	SD	0.204	0.456	1.041	1.568	1.208
	MIN	16.83	18.75	19.50	20.75	23.00
	MAX	17.25	19.75	21.83	24.33	25.75
	N	4	4	4	4	4
3	MEAN	16.875 C^3	20.063 C^3	21.313 A^3	21.167	23.375 A^3
	SD	1.436	2.401	1.599	0.764	0.777
	MIN	15.00	18.00	20.00	20.50	22.25
	MAX	18.50	23.50	23.50	22.00	24.00
	N	4	4	4	3	4
4	MEAN	15.250	17.625	20.188	22.188	22.688
	SD	0.842	0.777	0.688	1.919	1.546
	MIN	14.25	16.75	19.50	20.75	21.75
	MAX	16.25	18.50	21.00	25.00	25.00
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 25 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 42	Day 49	Day 56
1	MEAN	23.438	24.625	25.500
	SD	1.477	0.750	0.913
	MIN	22.00	24.00	24.50
	MAX	25.50	25.50	26.50
	N	4	4	4
2	MEAN	25.229 **C**[3]	25.417 **B**[3]	25.917 **C**[3]
	SD	0.826	0.612	0.842
	MIN	24.00	24.50	24.75
	MAX	25.75	25.75	26.75
	N	4	4	4
3	MEAN	24.188	24.938	25.438
	SD	0.851	1 281	1.087
	MIN	23.00	23.75	24.50
	MAX	25.00	26.75	27.00
	N	4	4	4
4	MEAN	23.875	24.500	25.125
	SD	1.548	1.061	0.629
	MIN	22.50	23.75	24.50
	MAX	26.00	26.00	26.00
	N	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 25 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE - PUPPIES (cm)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7	Day 14	Day 21	Day 28	Day 35
1	MEAN	15.525	18.367	20.808	21.617	23.067
	SD	1.040	0.595	0.919	1.079	1.373
	MIN	14.00	17.63	19.50	20.83	21.75
	MAX	16.88	18.88	21.75	23.50	24.75
	N	5	5	5	5	5
2	MEAN	17.313 C^3	19.656 C^3	21.063	22.844	24.875 C^3
	SD	0.260	0.400	0.633	1.508	1.190
	MIN	17.00	19.25	20.50	21.13	23.13
	MAX	17.63	20.00	21.88	24.50	25.63
	N	4	4	4	4	4
3	MEAN	17.031 C^3	20.219 C^3	21.594 A^3	21.889	23.719 A^3
	SD	1.082	1.972	1.390	0.896	0.483
	MIN	15.50	18.88	20.25	21.13	23.00
	MAX	18.00	23.13	23.50	22.88	24.00
	N	4	4	4	3	4
4	MEAN	15.438	17.719	20.563	22.281	22.969
	SD	0.747	0.413	0.582	1.824	1.463
	MIN	14.63	17.25	19.88	21.13	21.88
	MAX	16.38	18.25	21.25	25.00	25.13
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 25 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE - PUPPIES (cm)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 42	Day 49	Day 56
1	MEAN	24.133	25.042	25.825
	SD	0.792	0.320	0.401
	MIN	23.38	24.75	25.38
	MAX	25.25	25.50	26.38
	N	5	5	5
2	MEAN	25.469 **C**[3]	25.656 **B**[3]	26.531 **C**[3]
	SD	1.002	0.739	0.739
	MIN	24.00	24.63	25.63
	MAX	26.25	26.38	27.25
	N	4	4	4
3	MEAN	24.625	25.313	26.094
	SD	0.433	0.916	0.514
	MIN	24.00	24.50	25.50
	MAX	25.00	26.63	26.75
	N	4	4	4
4	MEAN	23.875	24.938	25.583
	SD	1.497	0.971	0.612
	MIN	22.50	24.25	25.25
	MAX	25.88	26.38	26.50
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 14 to 28 #	Day 21 to 28
1	MEAN	2 917	2.633	1.500	0.717
	SD	0.825	0.747	NA	0.591
	MIN	1.75	1.67	1.50	0.00
	MAX	3.83	3.50	1.50	1.33
	N	5	5	1	5
2	MEAN	2.625	1.313 C^3	--	1.875 B^3
	SD	0 595	0.625	--	1.199
	MIN	1.75	0.50	--	0.50
	MAX	3.00	2.00	--	3.00
	N	4	4	--	4
3	MEAN	3 188	1.479 C^3	--	1.083
	SD	1.638	0.625	--	0.878
	MIN	1.75	0.75	--	0.25
	MAX	5.25	2.00	--	2.00
	N	4	4	--	3
4	MEAN	2 333	2.958	--	1.479 A^3
	SD	0.882	0.344	--	1.796
	MIN	1.50	2.50	--	0.50
	MAX	3.50	3.33	--	4.17
	N	4	4	--	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
#- Excluded from statistical comparison
NA - Not applicable

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 21 to 35 #	Day 28 to 35	Day 35 to 42	Day 42 to 49
1	MEAN	--	1.500	1.317	0.833
	SD	--	1.146	0.771	0.738
	MIN	--	0.75	0.33	0.00
	MAX	--	3.50	2.25	1.75
	N	--	5	5	5
2	MEAN	--	1.625 **B**[3]	0.688	0.188 **C**[3]
	SD	--	0.924	0.239	0.375
	MIN	--	0.50	0.50	0.00
	MAX	--	2.75	1.00	0.75
	N	--	4	4	4
3	MEAN	0 250	1.694	1.042	0.563
	SD	NA	1.496	0.276	0.657
	MIN	0.25	0.00	0.67	0.00
	MAX	0.25	2.83	1.25	1.50
	N	1	3	4	4
4	MEAN	--	0.854 **A**[3]	0.667	1.417
	SD	--	0.554	0.514	0.965
	MIN	--	0.17	0.00	0.50
	MAX	--	1.50	1.25	2.25
	N	--	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \le 0.1$, B^1 - $p \le 0.05$, C^1 - $p \le 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \le 0.1$, B^2 - $p \le 0.05$, C^2 - $p \le 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \le 0.1$, B^3 - $p \le 0.05$, C^3 - $p \le 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \le 0.1$, B^4 - $p \le 0.05$, C^4 - $p \le 0.01$ (*t*-test)
#- Excluded from statistical comparison
NA - Not applicable

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 49 to 56
1	MEAN	0.733
	SD	0.356
	MIN	0.25
	MAX	1.25
	N	5
2	MEAN	1.250
	SD	0.540
	MIN	0.50
	MAX	1.75
	N	4
3	MEAN	1.000
	SD	0.736
	MIN	0.00
	MAX	1.75
	N	4
4	MEAN	0.604
	SD	0.292
	MIN	0.17
	MAX	0.75
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 14 to 28 #	Day 21 to 28
1	MEAN	2 500	2.750	1.750	1.250
	SD	0 289	0.866	NA	1.090
	MIN	2.25	1.75	1.75	0.50
	MAX	2.75	3.25	1.75	2.50
	N	4	3	1	3
2	MEAN	2 167	1.333 C^3	--	1.750 B^3
	SD	0.471	1.047	--	1.339
	MIN	1.50	0.50	--	0.50
	MAX	2.50	2.83	--	3.25
	N	4	4	--	4
3	MEAN	3 188	1.250 C^3	--	0.750
	SD	1 281	0.979	--	0.901
	MIN	2.00	0.00	--	0.00
	MAX	5.00	2.25	--	1.75
	N	4	4	--	3
4	MEAN	2 375	2.563	--	2.000 A^3
	SD	1 233	0.427	--	1.860
	MIN	1.00	2.00	--	0.25
	MAX	3.75	3.00	--	4.50
	N	4	4	--	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
#- Excluded from statistical comparison
NA - Not applicable

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 21 to 35 #	Day 28 to 35	Day 35 to 42	Day 42 to 49
1	MEAN	--	0.875	0.938	1.188
	SD	--	0.433	0.800	0.987
	MIN	--	0.50	0.25	0.00
	MAX	--	1.25	1.75	2.00
	N	--	4	4	4
2	MEAN	--	2.417 B^3	0.479	0.188 C^3
	SD	--	1.467	0.443	0.239
	MIN	--	0.67	0.00	0.00
	MAX	--	4.25	1.00	0.50
	N	--	4	4	4
3	MEAN	1.250	1.917	0.813	0.750
	SD	1.061	1.465	0.239	0.736
	MIN	0.50	0.25	0.50	0.00
	MAX	2.00	3.00	1.00	1.75
	N	2	3	4	4
4	MEAN	--	0.500 A^3	1.188	0.625
	SD	--	0.456	0.625	0.520
	MIN	--	0.00	0.50	0.00
	MAX	--	1.00	2.00	1.25
	N	--	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)
#- Excluded from statistical comparison

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 49 to 56
1	MEAN	0.875
	SD	0.479
	MIN	0.50
	MAX	1.50
	N	4
2	MEAN	0.500
	SD	0.354
	MIN	0.25
	MAX	1.00
	N	4
3	MEAN	0.500
	SD	0.204
	MIN	0.25
	MAX	0.75
	N	4
4	MEAN	0.938
	SD	1.087
	MIN	0.00
	MAX	2.50
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35
1	MEAN	2.842	2.575	0.917	1.450
	SD	0.706	0.604	0.670	1.188
	MIN	2.00	1.67	0 25	0.63
	MAX	3.83	3.25	1.88	3.50
	N	5	5	5	5
2	MEAN	2.344	1.406 C^3	1.781 B^3	2.031 B^3
	SD	0.504	0.825	1.205	1.174
	MIN	1.63	0.50	0.63	0.63
	MAX	2.75	2.50	3.00	3.50
	N	4	4	4	4
3	MEAN	3.188	1.375 C^3	0.972	1.778
	SD	1.423	0.791	0.858	1.457
	MIN	2.00	0.38	0 17	0.13
	MAX	5.13	2.13	1.88	2.88
	N	4	4	3	3
4	MEAN	2.281	2.844	1.719 A^3	0.688 A^3
	SD	0.986	0.188	1.751	0.484
	MIN	1.25	2.63	0 38	0.13
	MAX	3.63	3.00	4 25	1.25
	N	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 26 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)
PUPS SEX: COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	1.067	0.908	0.783
	SD	0.693	0.817	0.217
	MIN	0.33	0.00	0.63
	MAX	2.00	1.88	1.13
	N	5	5	5
2	MEAN	0.594	0.188 C^3	0.875
	SD	0.258	0.298	0.270
	MIN	0.25	0.00	0.50
	MAX	0.88	0.63	1.13
	N	4	4	4
3	MEAN	0.906	0.688	0.781
	SD	0.188	0.633	0.449
	MIN	0.75	0.25	0.13
	MAX	1.13	1.63	1.13
	N	4	4	4
4	MEAN	0.906	1.063	0.708
	SD	0.483	0.657	0.497
	MIN	0.63	0.50	0.13
	MAX	1.63	1.75	1.33
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 27

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - PUPPIES SUMMARY
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	MEAN	15.55	18.55	20.90	21.68	23.36	24.59	25.36	26.09
	SD	1.27	0.93	1.17	1.17	1.14	0.77	0.67	0.77
	MIN	13.0	16.5	18.5	19.0	21.5	23.0	24.0	24.5
	MAX	18.0	19.5	22.5	23.0	25.0	25.5	26.5	27.0
	N	11	11	10	11	11	11	11	11
2	MEAN	17.64	20.21	21.50	23.21	25.00	25.71	25.93	27.29
	SD	0.48	0.49	0.50	1.50	1.29	1.25	0.93	0.99
	MIN	17.0	19.5	20.5	21.0	23.0	24.0	24.5	26.0
	MAX	18.0	21.0	22.0	25.0	26.5	27.0	27.0	29.0
	N	7	7	7	7	7	7	7	7
3	MEAN	17.17	20.22	21.67	22.21	24.00	25.00	25.56	26.56
	SD	0.90	1.56	1.35	1.22	0.35	0.25	0.68	0.73
	MIN	16.0	18.5	19.5	20.5	23.5	24.5	25.0	26.0
	MAX	18.5	23.5	23.5	24.0	24.5	25.5	27.0	28.0
	N	9	9	9	7	9	9	9	9
4	MEAN	15.61	17.89	20.89	22.67	23.44	24.11	25.44	26.00
	SD	0.93	0.82	0.99	1.94	1.61	1.52	1.07	0.71
	MIN	14.5	16.0	19.0	20.5	21.0	22.0	23.5	25.0
	MAX	17.5	18.5	21.5	26.0	26.0	26.5	27.0	27.0
	N	9	9	9	9	9	9	9	9

TABLE NO. 27

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - PUPPIES SUMMARY
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	MEAN	15.69	18.19	20.58	21.63	22.50	23.44	24.63	25.50
	SD	1.07	1.03	1.11	1.55	1.75	1.45	0.74	0.96
	MIN	14.0	16.5	19.0	20.0	21.0	21.5	23.5	24.0
	MAX	17.0	19.5	22.0	24.0	25.5	25.5	25.5	27.0
	N	8	8	6	8	8	8	8	8
2	MEAN	17.06	19.22	20.72	22.56	24.78	25.28	25.44	25.94
	SD	0.68	0.71	1.06	1.78	1.28	1.00	0.85	0.92
	MIN	16.0	18.5	19.5	20.0	22.0	23.5	24.5	24.5
	MAX	18.0	20.5	22.0	25.5	26.0	27.0	27.0	27.0
	N	9	9	9	9	9	9	9	9
3	MEAN	16.86	20.21	21.50	21.38	23.36	24.14	25.00	25.50
	SD	1.60	2.45	1.55	1.11	0.90	1.03	1.29	1.22
	MIN	14.5	17.0	20.0	20.5	21.5	22.0	23.5	23.5
	MAX	19.0	24.0	24.0	23.0	24.0	25.0	27.0	27.0
	N	7	7	7	4	7	7	7	7
4	MEAN	15.21	17.50	20.14	21.79	22.36	23.57	24.29	25.00
	SD	0.99	0.87	0.80	1.55	1.21	1.24	1.15	0.63
	MIN	14.0	16.5	19.0	20.0	21.5	22.5	22.5	24.0
	MAX	17.0	18.5	21.5	25.0	25.0	26.0	26.0	26.0
	N	7	7	7	7	7	7	7	6

TABLE NO. 28

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - PUPPIES SUMMARY
HEAD CIRCUMFERENCE CHANGE (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 14 to 28	Day 21 to 28	Day 21 to 35	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	3.000	2.450	1.500	0.850	--	1.682	1.227	0.773	0.727
	SD	1.000	0.762	NA	0.669	--	1.383	0.876	0.876	0.410
	MIN	1.00	1.50	1.50	0.00	--	0.50	0.00	0.00	0.00
	MAX	4.00	3.50	1.50	2.00	--	5.00	2.50	2.50	1.50
	N	11	10	1	10	--	11	11	11	11
2	MEAN	2.571	1.286	--	1.714	--	1.786	0.714	0.214	1.357
	SD	0.932	0.699	--	1.113	--	1.035	0.488	0.393	0.556
	MIN	1.50	0.50	--	0 50	--	0.50	0.00	0.00	0.50
	MAX	4.00	2.50	--	3.00	--	3.50	1.50	1.00	2.00
	N	7	7	--	7	--	7	7	7	7
3	MEAN	3.056	1.444	--	1.071	0.250	1.857	1.000	0.556	1.000
	SD	1.530	0.726	--	0.838	0.354	1.345	0.433	0.682	0.750
	MIN	1.00	0.00	--	0.00	0.00	0.00	0.50	0.00	0.00
	MAX	5.50	2.50	--	2 50	0.50	3.50	1.50	2.00	2.50
	N	9	9	--	7	2	7	9	9	9
4	MEAN	2.278	3.000	--	1.778	--	0.778	0.667	1.333	0.556
	SD	0.833	0.829	--	1.839	--	0.618	0.612	0.968	0.527
	MIN	1.00	1.00	--	0.00	--	0.00	0.00	0.50	0.00
	MAX	3.50	4.00	--	4 50	--	2.00	1.50	3.00	1.50
	N	9	9	--	9	--	9	9	9	9

NA - Not applicable

TABLE NO. 28

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - PUPPIES SUMMARY
HEAD CIRCUMFERENCE CHANGE (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 14 to 28	Day 21 to 28	Day 21 to 35	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	2.500	2.750	1.750	1.250	--	0.875	0.938	1.188	0.875
	SD	0.535	0.935	1.061	1.173	--	0.443	1.050	0.961	0.582
	MIN	1.50	1.00	1.00	0.00	--	0.50	0.00	0.00	0.50
	MAX	3.00	3.50	2.50	3.00	--	1.50	3.00	2.50	2.00
	N	8	6	2	6	--	8	8	8	8
2	MEAN	2.167	1.500	--	1.833	--	2.222	0.500	0.167	0.500
	SD	0.750	1.146	--	1.436	--	1.543	0.500	0.354	0.500
	MIN	1.50	0.00	--	0 50	--	0.00	0.00	0.00	0.00
	MAX	3.50	3.00	--	4 50	--	4.50	1.50	1.00	1.50
	N	9	9	--	9	--	9	9	9	9
3	MEAN	3.357	1.286	--	1.000	1.000	1.500	0.786	0.857	0.500
	SD	1.406	1.075	--	1.080	1.000	1.472	0.267	0.852	0.577
	MIN	2.00	0.00	--	0.00	0.00	0.00	0.50	0.00	0.00
	MAX	6.00	3.00	--	2 50	2.00	3.00	1.00	2.00	1.50
	N	7	7	--	4	3	4	7	7	7
4	MEAN	2.286	2.643	--	1.643	--	0.571	1.214	0.714	0.833
	SD	1.286	0.476	--	1.547	--	0.535	0.699	0.906	1.033
	MIN	1.00	2.00	--	0.00	--	0.00	0.00	0.00	0.00
	MAX	4.50	3.00	--	4 50	--	1.50	2.00	2.50	2.50
	N	7	7	--	7	--	7	7	7	6

TABLE NO. 29 (b) (4)

HEIGHT MEASUREMENTS SUMMARY
GROUP LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35
1	MEAN	12.200	15.167	17.100	20.067	21.433
	SD	1.217	1 535	1.557	1.146	0.744
	MIN	10.50	13.50	15.50	18.33	20.50
	MAX	13.50	17.50	19.00	21.00	22.50
	N	5	5	5	5	5
2	MEAN	12.667	15.063	18.500	21.625	22.875 B^3
	SD	0.764	1.638	1.225	1.652	1.493
	MIN	12.00	14.00	17.50	20.00	21.00
	MAX	13.50	17.50	20.00	23.50	24.50
	N	3	4	4	4	4
3	MEAN	12.604	16.229 A^3	17.646	20.417	22.333 B^3
	SD	0.921	1.061	0.591	0.833	0.736
	MIN	11.50	14.67	16.83	19.50	21.33
	MAX	13.75	17.00	18.25	21.50	23.00
	N	4	4	4	4	4
4	MEAN	12.354	14.438	17.063	20.625	22.229
	SD	1.081	0 375	1.087	1.090	0.859
	MIN	11.17	14.25	16.00	19.00	21.67
	MAX	13.75	15.00	18.00	21.25	23.50
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 29 (b) (4)

HEIGHT MEASUREMENTS SUMMARY
GROUP LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 42	Day 49	Day 56
1	MEAN	23.583	25.183	26.300
	SD	1.115	0 560	1.292
	MIN	22.25	24.50	25.25
	MAX	25.00	25.75	28.50
	N	5	5	5
2	MEAN	23.688	25.188	26.000
	SD	0.591	0.688	0.791
	MIN	23.25	24.50	25.25
	MAX	24.50	26.00	27.00
	N	4	4	4
3	MEAN	23.708	25.354	26.417
	SD	0.433	1 137	0.920
	MIN	23.25	24.17	25.67
	MAX	24.25	26.75	27.75
	N	4	4	4
4	MEAN	23.938	24.646	25.167 A^3
	SD	1.560	1.646	1.650
	MIN	22.50	22.75	23.00
	MAX	26.00	26.75	27.00
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 29 (b) (4)

HEIGHT MEASUREMENTS SUMMARY
GROUP LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7	Day 14	Day 21	Day 28	Day 35
1	MEAN	12.750	14.938	17.188	20.063	21.313
	SD	0.612	1.772	1.886	0.473	0.315
	MIN	12.25	13.75	15.00	19.75	21.00
	MAX	13.50	17.50	19.00	20.75	21.75
	N	4	4	4	4	4
2	MEAN	12.306	15.292	17.542	19.875	21.792 B^3
	SD	0.883	1 256	1.479	1.199	0.571
	MIN	11.50	14.50	16.25	18.50	21.00
	MAX	13.25	17.17	19.67	21.00	22.25
	N	3	4	4	4	4
3	MEAN	12.125	15.688 A^3	17.000	20.000	22.250 B^3
	SD	0.661	1 214	1.242	1.369	1.190
	MIN	11.50	15.00	16.00	18.50	21.00
	MAX	13.00	17.50	18.75	21.75	23.50
	N	4	4	4	4	4
4	MEAN	12.188	14.313	16.750	19.563	20.563
	SD	0.688	0.473	1.443	0.515	0.515
	MIN	11.50	14.00	15.50	19.00	20.00
	MAX	13.00	15.00	18.00	20.25	21.25
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 29 (b) (4)

HEIGHT MEASUREMENTS SUMMARY
GROUP LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 42	Day 49	Day 56
1	MEAN	22.625	24.375	25.250
	SD	0.433	0 595	0.866
	MIN	22.00	24.00	24.50
	MAX	23.00	25.25	26.50
	N	4	4	4
2	MEAN	23.042	24.104	25.292
	SD	0.220	0.458	0.846
	MIN	22.75	23.67	24.50
	MAX	23.25	24.50	26.25
	N	4	4	4
3	MEAN	23.750	25.375	25.938
	SD	1.756	2 314	2.183
	MIN	22.00	23.75	24.25
	MAX	25.50	28.75	29.00
	N	4	4	4
4	MEAN	22.938	24.125	24.813 A^3
	SD	1.329	1 199	1.297
	MIN	21.25	22.75	23.25
	MAX	24.00	25.25	26.00
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 29 (b) (4)

HEIGHT MEASUREMENTS SUMMARY
GROUP LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)
PUPS SEX COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7	Day 14	Day 21	Day 28	Day 35
1	MEAN	12.250	14.992	17.025	19.892	21.358
	SD	1.169	1.476	1.587	0.886	0.483
	MIN	10.50	13.63	15.75	18.33	20.88
	MAX	13.50	17.50	19.00	20.50	22.13
	N	5	5	5	5	5
2	MEAN	12.458	15.156	18.000	20.594	22.188 B^3
	SD	0.832	1.397	1.177	1.218	0.582
	MIN	11.75	14.38	17.25	19.25	21.63
	MAX	13.38	17.25	19.75	21.63	22.75
	N	3	4	4	4	4
3	MEAN	12.344	15.938 A^3	17.375	20.313	22.188 B^3
	SD	0.504	1.028	0.669	0.525	0.681
	MIN	11.63	14.75	16.63	19.75	21.63
	MAX	12.75	17.25	18.25	20.88	23.13
	N	4	4	4	4	4
4	MEAN	12.250	14.375	16.906	20.094	21.500
	SD	0.907	0.421	1.264	0.739	0.586
	MIN	11.25	14.13	15.75	19.00	21.13
	MAX	13.38	15.00	18.00	20.63	22.38
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 29 (b) (4)

HEIGHT MEASUREMENTS SUMMARY
GROUP LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)
PUPS SEX COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 42	Day 49	Day 56
1	MEAN	23.108	24.808	25.800
	SD	0.724	0.366	0.971
	MIN	22.13	24.38	25.13
	MAX	24.00	25.38	27.50
	N	5	5	5
2	MEAN	23.281	24.594	25.594
	SD	0.157	0.563	0.739
	MIN	23.13	23.88	24.88
	MAX	23.50	25.25	26.63
	N	4	4	4
3	MEAN	23.656	25.313	26.156
	SD	0.832	1.647	1.498
	MIN	22.63	24.25	25.25
	MAX	24.50	27.75	28.38
	N	4	4	4
4	MEAN	23.375	24.344	24.938 A^3
	SD	1.279	1.336	1.360
	MIN	21.88	22.75	23.13
	MAX	25.00	26.00	26.38
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 30 (b) (4)

HEIGHT MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35
1	MEAN	2 967	1.933	2.967	1.367
	SD	1.719	1.114	0.960	0.944
	MIN	1.25	0.75	2.00	0.25
	MAX	5.50	3.75	4.00	2.83
	N	5	5	5	5
2	MEAN	2.750	3.438 B^3	3.125	1.250
	SD	2.046	0.966	1.652	0.500
	MIN	1.00	2.50	1.00	1.00
	MAX	5.00	4.75	5.00	2.00
	N	3	4	4	4
3	MEAN	3.625 A^3	1.417 A^3	2.771	1.917
	SD	1.493	0.656	0.929	0.920
	MIN	2.00	0.75	1.75	1.17
	MAX	5.50	2.17	3.75	3.25
	N	4	4	4	4
4	MEAN	2.083	2.625	3.563	1.604
	SD	1 379	0.924	1.983	1.021
	MIN	0.50	1.75	1.00	0.50
	MAX	3.83	3.75	5.25	2.67
	N	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 30 (b) (4)

HEIGHT MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)
PUPS SEX: MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	2.150	1.600	1.117
	SD	0.802	1.098	1.063
	MIN	1.50	0.50	0 50
	MAX	3.25	3.25	3.00
	N	5	5	5
2	MEAN	0.813	1 500	0.813
	SD	1.008	1.061	0.239
	MIN	0.00	0.00	0 50
	MAX	2.25	2.25	1.00
	N	4	4	4
3	MEAN	1.375	1.646	1.063
	SD	0.777	1 203	0.427
	MIN	0.75	0.33	0 50
	MAX	2.50	3.25	1 50
	N	4	4	4
4	MEAN	1.708	0.708	0.521
	SD	0.812	0.464	0.315
	MIN	0.75	0.25	0 25
	MAX	2.50	1.33	0.83
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 30 (b) (4)

HEIGHT MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35
1	MEAN	2 188	2.250	2.875	1.250
	SD	2.065	1.137	2.046	0.645
	MIN	0.75	1.25	0.75	0.50
	MAX	5.25	3.75	4.75	2.00
	N	4	4	4	4
2	MEAN	3 166	2.250 B^3	2.333	1.917
	SD	1.876	0.540	1.021	1.264
	MIN	1.25	1.50	1.33	1.00
	MAX	5.00	2.75	3.75	3.75
	N	3	4	4	4
3	MEAN	3.563 A^3	1.313 A^3	3.000	2.250
	SD	1.625	0.315	0.354	1.514
	MIN	2.00	1.00	2.50	1.25
	MAX	5.75	1.75	3.25	4.50
	N	4	4	4	4
4	MEAN	2 125	2.438	2.813	1.000
	SD	1.051	1.125	1.463	0.612
	MIN	1.00	1.50	1.00	0.25
	MAX	3.50	3.75	4.00	1.75
	N	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 30 (b) (4)

HEIGHT MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)
PUPS SEX: FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	1.313	1.750	0.875
	SD	0.515	1.021	0.323
	MIN	0.75	1.00	0 50
	MAX	1.75	3.25	1 25
	N	4	4	4
2	MEAN	1.250	1.063	1.188
	SD	0.677	0 554	0.427
	MIN	0.75	0.50	0.75
	MAX	2.25	1.75	1.75
	N	4	4	4
3	MEAN	1.500	1.625	0.563
	SD	0.577	1 331	0.375
	MIN	1.00	0.00	0 25
	MAX	2.00	3.25	1.00
	N	4	4	4
4	MEAN	2.375	1 188	0.688
	SD	1.362	0 239	0.239
	MIN	0.75	1.00	0 50
	MAX	4.00	1.50	1.00
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 30 (b) (4)

HEIGHT MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)
PUPS SEX COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35
1	MEAN	2.742	2.033	2.867	1.467
	SD	1.792	1.058	1 365	0.891
	MIN	1.25	1.00	1.38	0.63
	MAX	5.38	3.75	4.38	2.83
	N	5	5	5	5
2	MEAN	2.958	2.844 B^3	2 594	1.594
	SD	1.946	0 258	1 243	0.649
	MIN	1.13	2.50	1.63	1.00
	MAX	5.00	3.13	4.38	2.38
	N	3	4	4	4
3	MEAN	3.594 A^3	1.438 A^3	2 938	1.875
	SD	1.501	0 361	0.484	0.489
	MIN	2.00	1.00	2.38	1.38
	MAX	5.63	1.88	3.50	2.50
	N	4	4	4	4
4	MEAN	2.125	2 531	3 188	1.406
	SD	1.250	1.023	1.721	0.838
	MIN	0.75	1.63	1.00	0.63
	MAX	3.75	3.75	4.63	2.25
	N	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 30 (b) (4)

HEIGHT MEASUREMENTS CHANGE SUMMARY
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)
PUPS SEX COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	1.750	1.700	0.992
	SD	0.586	0 971	0.646
	MIN	1.25	0.88	0.50
	MAX	2.50	3.25	2.13
	N	5	5	5
2	MEAN	1.094	1 313	1.000
	SD	0.472	0.681	0.270
	MIN	0.63	0.38	0.75
	MAX	1.50	2.00	1.38
	N	4	4	4
3	MEAN	1.469	1.656	0.844
	SD	0.624	1 231	0.438
	MIN	1.00	0.25	0.38
	MAX	2.38	3.25	1.38
	N	4	4	4
4	MEAN	1.875	0 969	0.594
	SD	0.797	0 213	0.258
	MIN	0.75	0.75	0.38
	MAX	2.63	1.25	0.88
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 31

(b) (4)

HEIGHT MEASUREMENTS (cm) - PUPPIES SUMMARY
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	MEAN	12.05	15.09	17.00	19.91	21.41	23.50	25.14	26.23
	SD	1.47	1.63	1.70	1.59	1.14	1.36	0.84	1.71
	MIN	9.0	12.5	14.0	16.5	19.0	21.0	23.5	24.5
	MAX	14.0	18.0	19.5	22.0	23.0	25.0	26.5	31.0
	N	11	11	11	11	11	11	11	11
2	MEAN	12.70	14.71	18.29	21.36	22.64	23.57	25.29	26.07
	SD	1.10	1.44	1.07	1.52	1.60	0.89	0.81	0.93
	MIN	11.0	13.0	17.0	19.5	21.0	22.0	24.0	24.5
	MAX	14.0	17.5	20.0	23.5	24.5	24.5	26.0	27.5
	N	5	7	7	7	7	7	7	7
3	MEAN	12.61	16.06	17.56	20.39	22.22	23.72	25.22	26.33
	SD	0.89	1.24	0.95	0.86	1.03	0.87	1.23	1.03
	MIN	11.0	14.0	15.5	19.0	20.5	22.0	23.5	25.0
	MAX	14.0	17.0	19.0	22.0	23.5	24.5	27.5	28.0
	N	9	9	9	9	9	9	9	9
4	MEAN	12.22	14.50	17.17	20.44	22.17	23.83	24.61	25.17
	SD	1.35	0.75	1.20	1.29	1.48	1.52	1.56	1.54
	MIN	9.5	13.5	15.0	17.5	19.0	22.0	22.5	23.0
	MAX	14.5	16.0	19.0	21.5	24.0	26.0	27.0	27.0
	N	9	9	9	9	9	9	9	9

TABLE NO. 31

[redacted] (b) (4)

HEIGHT MEASUREMENTS (cm) - PUPPIES SUMMARY
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	MEAN	12.75	14.94	17.19	20.06	21.31	22.63	24.38	25.25
	SD	0.89	1.76	1.79	0.50	0.37	0.83	0.83	0.96
	MIN	11.5	13.0	15.0	19.5	21.0	21.5	23.0	23.5
	MAX	14.5	18.0	19.5	21.0	22.0	24.0	25.5	26.5
	N	8	8	8	8	8	8	8	8
2	MEAN	12.29	15.50	17.78	20.00	21.83	23.06	24.06	25.22
	SD	0.81	1.56	1.50	1.54	1.03	0.58	0.63	0.91
	MIN	11.0	13.0	16.0	17.0	20.0	22.0	23.0	24.0
	MAX	13.5	17.5	20.0	22.5	23.5	24.0	25.0	27.0
	N	7	9	9	9	9	9	9	9
3	MEAN	12.00	15.79	17.14	20.21	22.14	23.57	25.43	25.93
	SD	0.76	1.22	1.28	1.47	1.44	1.81	2.39	2.42
	MIN	11.0	14.5	15.5	18.5	20.0	21.0	23.0	23.0
	MAX	13.0	17.5	19.0	22.5	24.0	26.0	29.5	30.0
	N	7	7	7	7	7	7	7	7
4	MEAN	12.29	14.21	16.57	19.64	20.64	22.79	24.00	24.64
	SD	0.76	0.39	1.51	0.63	0.80	1.78	1.38	1.35
	MIN	11.0	14.0	15.0	19.0	19.5	20.5	22.5	22.5
	MAX	13.0	15.0	19.0	20.5	21.5	26.0	26.5	26.5
	N	7	7	7	7	7	7	7	7

TABLE NO. 32

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES- PUPPIES SUMMARY
HEIGHT CHANGE (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	3.045	1.909	2 909	1.500	2.091	1.636	1.091
	SD	1.665	1.200	1.091	1.049	0.944	1.120	1 200
	MIN	0.50	0 50	1.50	0.00	1.00	0.50	0.50
	MAX	5.50	5.00	5.00	3.50	4.00	3.50	4.50
	N	11	11	11	11	11	11	11
2	MEAN	2.300	3.571	3.071	1.286	0.929	1.714	0.786
	SD	1.681	1.170	1.790	0.809	0.976	0.906	0 393
	MIN	0.50	2 50	0.50	0.50	0.00	0.00	0.50
	MAX	5.00	5 50	5.50	3.00	2.50	2.50	1.50
	N	5	7	7	7	7	7	7
3	MEAN	3.444	1.500	2.833	1.833	1.500	1.500	1 111
	SD	1.530	0.791	1.000	1.146	0.791	1.199	0.697
	MIN	1.00	0 50	1.50	0.50	0.50	0.00	0.50
	MAX	6.00	3.00	4.00	4.00	2.50	3.50	2.50
	N	9	9	9	9	9	9	9
4	MEAN	2.278	2.667	3 278	1.722	1.667	0.778	0 556
	SD	1.502	1.090	2.033	1.149	1.250	0.755	0 391
	MIN	0.50	1 50	0.00	0.50	0.00	0.00	0.00
	MAX	4.50	4.00	6.00	4.00	3.50	2.50	1.00
	N	9	9	9	9	9	9	9

TABLE NO. 32

(b) (4)

HEIGHT MEASUREMENT CHANGES- PUPPIES SUMMARY
HEIGHT CHANGE (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	MEAN	2.188	2.250	2.875	1.250	1.313	1.750	0.875
	SD	1.926	1.102	1 923	0.598	0.799	1.165	0.443
	MIN	0.50	1.00	0.50	0.50	0.50	0.50	0.50
	MAX	5.50	4.00	5.00	2.00	2.50	4.00	1.50
	N	8	8	8	8	8	8	8
2	MEAN	3.429	2.278	2 222	1.833	1.222	1.000	1 167
	SD	1.835	1.003	1 302	1.250	0.905	0.791	0.866
	MIN	1.00	0.00	0.50	0.50	0.50	0.00	0.50
	MAX	5.00	3 50	4.50	4.00	3.50	2.50	3.00
	N	7	9	9	9	9	9	9
3	MEAN	3.786	1.357	3.071	1.929	1.429	1.857	0 500
	SD	1.551	0.378	0.673	1.170	0.607	1.180	0 577
	MIN	2.00	1.00	2.00	1.00	0.50	0.00	0.00
	MAX	6.50	2.00	4.00	4.50	2.00	3.50	1.50
	N	7	7	7	7	7	7	7
4	MEAN	1.929	2.357	3.071	1.000	2.143	1.214	0.643
	SD	0.976	1.376	1.427	0.816	1.749	0.567	0.476
	MIN	1.00	1.00	1.00	0.00	0.50	0.50	0.00
	MAX	3.50	5.00	4.00	2.50	5.00	2.00	1.00
	N	7	7	7	7	7	7	7

SUMMARY TABLES
F1 PUPPIES POST-WEANING

TABLE NO. 33

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
MALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Discharge, Brown	Number of Animal-Days	6	0	0	3
	Number of Animals	1	0	0	2
	Days from - to	91 to 231	NA	NA	203 to 238
Discharge, Clear	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	119 to 119
Discharge, Yellow	Number of Animal-Days	1	0	0	1
	Number of Animals	1	0	0	1
	Days from - to	175 to 175	NA	NA	175 to 175
Fur Thin	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	175 to 175
Feces Red	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	143 to 143	NA	NA
Feces Soft	Number of Animal-Days	19	22	6	20
	Number of Animals	4	4	3	4
	Days from - to	77 to 210	83 to 203	120 to 205	92 to 228

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
MALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Feces Loose	Number of Animal-Days	20	41	13	30
	Number of Animals	4	4	4	4
	Days from - to	72 to 199	92 to 227	105 to 206	81 to 237
Feces Liquid	Number of Animal-Days	1	5	0	1
	Number of Animals	1	1	0	1
	Days from - to	119 to 119	95 to 170	NA	136 to 136
Feces Soft (Group Housed)	Number of Animal-Days	38	42	41	57
	Number of Animals	4	4	4	4
	Days from - to	72 to 227	75 to 225	63 to 227	72 to 233
Feces Loose (Group Housed)	Number of Animal-Days	113	156	103	121
	Number of Animals	4	4	4	4
	Days from - to	62 to 229	62 to 235	66 to 235	62 to 231
Feces Liquid (Group Housed)	Number of Animal-Days	0	6	4	4
	Number of Animals	0	2	2	4
	Days from - to	NA	117 to 200	100 to 159	118 to 162
Material Mucoid Brown	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	196 to 196	NA	NA
Material Mucoid Red	Number of Animal-Days	0	2	0	0
	Number of Animals	0	2	0	0
	Days from - to	NA	142 to 143	NA	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
MALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Material Mucoid Yellow	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	144 to 144	NA	NA
Material Undigested Food	Number of Animal-Days	0	2	1	1
	Number of Animals	0	2	1	1
	Days from - to	NA	70 to 78	82 to 82	133 to 133
Material Dry Brown (Group Housed)	Number of Animal-Days	0	2	4	1
	Number of Animals	0	2	2	1
	Days from - to	NA	212 to 219	179 to 203	64 to 64
Material Frothy Beige (Group Housed)	Number of Animal-Days	0	0	2	0
	Number of Animals	0	0	2	0
	Days from - to	NA	NA	204 to 204	NA
Material Frothy Brown (Group Housed)	Number of Animal-Days	0	0	2	0
	Number of Animals	0	0	2	0
	Days from - to	NA	NA	84 to 85	NA
Material Frothy Clear (Group Housed)	Number of Animal-Days	0	0	2	0
	Number of Animals	0	0	2	0
	Days from - to	NA	NA	204 to 204	NA
Material Liquid Beige (Group Housed)	Number of Animal-Days	2	0	4	0
	Number of Animals	2	0	2	0
	Days from - to	167 to 169	NA	176 to 205	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
MALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Material Liquid Brown (Group Housed)	Number of Animal-Days	4	0	0	0
	Number of Animals	2	0	0	0
	Days from - to	166 to 203	NA	NA	NA
Undigested Food (Group Housed)	Number of Animal-Days	2	4	0	1
	Number of Animals	2	2	0	1
	Days from - to	201 to 203	144 to 184	NA	68 to 68
Broken Nail/Claw	Number of Animal-Days	0	0	3	0
	Number of Animals	0	0	2	0
	Days from - to	NA	NA	147 to 238	NA
Limited Usage	Number of Animal-Days	0	4	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	161 to 231	NA	NA
Tail Kinked	Number of Animal-Days	0	0	0	5
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	147 to 238
Skin, Blue	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	231 to 231	NA
Skin Dry	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	91 to 91

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
MALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Skin Red	Number of Animal-Days	7	0	7	2
	Number of Animals	2	0	2	1
	Days from - to	91 to 203	NA	147 to 238	63 to 91
Skin Scab	Number of Animal-Days	3	0	2	4
	Number of Animals	1	0	1	4
	Days from - to	63 to 119	NA	231 to 238	63 to 91
Swelling Firm	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	231 to 231	NA
Skin Wound with Discharge	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	217 to 217	NA
Teeth Broken	Number of Animal-Days	0	1	1	0
	Number of Animals	0	1	1	0
	Days from - to	NA	238 to 238	119 to 119	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
FEMALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Discharge, Brown	Number of Animal-Days	4	1	0	4
	Number of Animals	2	1	0	1
	Days from - to	147 to 203	238 to 238	NA	91 to 175
Discharge, Green	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	238 to 238	NA	NA
Discharge, Yellow	Number of Animal-Days	1	0	0	0
	Number of Animals	1	0	0	0
	Days from - to	175 to 175	NA	NA	NA
Fur Thin	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	91 to 91
Feces Soft	Number of Animal-Days	2	12	4	5
	Number of Animals	2	3	2	4
	Days from - to	103 to 131	117 to 220	113 to 206	114 to 204
Feces Loose	Number of Animal-Days	12	43	13	22
	Number of Animals	3	4	3	4
	Days from - to	79 to 160	81 to 234	91 to 218	100 to 235

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
FEMALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Feces Liquid	Number of Animal-Days	0	6	0	3
	Number of Animals	0	4	0	1
	Days from - to	NA	149 to 206	NA	210 to 234
Feces, Output	Number of Animal-Days	1	0	0	0
	Number of Animals	1	0	0	0
	Days from - to	123 to 123	NA	NA	NA
Feces Red (Group Housed)	Number of Animal-Days	0	0	4	2
	Number of Animals	0	0	4	2
	Days from - to	NA	NA	142 to 146	144 to 146
Feces Soft (Group Housed)	Number of Animal-Days	14	34	33	33
	Number of Animals	4	4	4	4
	Days from - to	87 to 181	96 to 220	63 to 233	72 to 223
Feces Loose (Group Housed)	Number of Animal-Days	50	79	128	84
	Number of Animals	4	4	4	4
	Days from - to	62 to 196	62 to 226	66 to 232	62 to 237
Feces Liquid (Group Housed)	Number of Animal-Days	2	6	4	2
	Number of Animals	2	4	4	2
	Days from - to	192 to 194	100 to 201	198 to 233	101 to 103
Material Frothy Green	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	238 to 238

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
FEMALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Material Liquid Beige	Number of Animal-Days	0	0	1	0
	Number of Animals	0	0	1	0
	Days from - to	NA	NA	152 to 152	NA
Material Liquid Green	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	238 to 238
Material Liquid Red	Number of Animal-Days	1	1	0	0
	Number of Animals	1	1	0	0
	Days from - to	137 to 137	140 to 140	NA	NA
Material Liquid Yellow	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	105 to 105
Material Mucoid Red	Number of Animal-Days	0	1	1	0
	Number of Animals	0	1	1	0
	Days from - to	NA	111 to 111	146 to 146	NA
Material Mucoid Yellow	Number of Animal-Days	0	0	1	1
	Number of Animals	0	0	1	1
	Days from - to	NA	NA	170 to 170	210 to 210
Material Undigested Food	Number of Animal-Days	2	2	1	1
	Number of Animals	1	2	1	1
	Days from - to	122 to 129	108 to 169	238 to 238	198 to 198

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
FEMALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Material Dry Brown (Group Housed)	Number of Animal-Days	0	0	0	1
	Number of Animals	0	0	0	1
	Days from - to	NA	NA	NA	64 to 64
Material Frothy Yellow (Group Housed)	Number of Animal-Days	2	2	6	0
	Number of Animals	2	2	2	0
	Days from - to	182 to 184	182 to 189	147 to 165	NA
Material Liquid Beige (Group Housed)	Number of Animal-Days	0	2	0	0
	Number of Animals	0	2	0	0
	Days from - to	NA	172 to 173	NA	NA
Material Liquid Red (Group Housed)	Number of Animal-Days	0	0	2	0
	Number of Animals	0	0	2	0
	Days from - to	NA	NA	147 to 148	NA
Material Liquid Yellow (Group Housed)	Number of Animal-Days	0	2	0	0
	Number of Animals	0	2	0	0
	Days from - to	NA	221 to 228	NA	NA
Material Mucoid Brown (Group Housed)	Number of Animal-Days	2	0	2	0
	Number of Animals	2	0	2	0
	Days from - to	166 to 168	NA	198 to 198	NA
Material Mucoid Red (Group Housed)	Number of Animal-Days	0	4	2	2
	Number of Animals	0	2	2	2
	Days from - to	NA	140 to 142	145 to 146	144 to 146

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

[redacted] (b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
FEMALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Material Mucoid Yellow (Group Housed)	Number of Animal-Days	0	2	2	2
	Number of Animals	0	2	2	2
	Days from - to	NA	221 to 228	144 to 144	101 to 103
Undigested Food (Group Housed)	Number of Animal-Days	0	4	0	3
	Number of Animals	0	2	0	2
	Days from - to	NA	87 to 95	NA	68 to 229
Broken Nail/Claw	Number of Animal-Days	2	0	0	3
	Number of Animals	1	0	0	1
	Days from - to	81 to 119	NA	NA	90 to 119
Skin Dry	Number of Animal-Days	2	0	2	0
	Number of Animals	1	0	1	0
	Days from - to	231 to 238	NA	63 to 91	NA
Skin Lump	Number of Animal-Days	0	1	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	238 to 238	NA	NA
Skin Red	Number of Animal-Days	8	3	5	3
	Number of Animals	4	1	2	1
	Days from - to	91 to 238	175 to 231	175 to 238	119 to 175

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 33

(b) (4)

SUMMARY OF CLINICAL OBSERVATIONS
FEMALES
F1 GENENRATION - PUPPIES - POST WEANING

See Appendix No. 3 Experimental Design for group definition

CLINICAL SIGN		GROUP NO. 1 N= 4	2 N= 4	3 N= 4	4 N= 4
Skin Scab	Number of Animal-Days	0	2	1	2
	Number of Animals	0	2	1	2
	Days from - to	NA	175 to 175	238 to 238	63 to 91
Swelling Firm	Number of Animal-Days	0	3	0	0
	Number of Animals	0	1	0	0
	Days from - to	NA	175 to 231	NA	NA
Swelling Soft	Number of Animal-Days	4	0	0	0
	Number of Animals	2	0	0	0
	Days from - to	91 to 147	NA	NA	NA
Skin Wound with Discharge	Number of Animal-Days	1	0	0	1
	Number of Animals	1	0	0	1
	Days from - to	81 to 81	NA	NA	90 to 90
Malocclusion	Number of Animal-Days	4	0	0	0
	Number of Animals	1	0	0	0
	Days from - to	175 to 238	NA	NA	NA

Number of Animal-Days: Total number of occurrences across animals and days combination (an animal is counted more than once if its symptom is observed on many days).
Number of Animals: Total number of animals having the symptom observed at least once (an animal is counted only once even if its symptom is observed on many days).
N: Number of Animals per Group, NA: Not Applicable.

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	Day 63	Day 70	Day 77	Day 84	Day 91	Day 98	Day 105	Day 112	Day 119
1	MEAN	2.734	3.210	3.590	3.870	4.265	4.830	5.525	5.845	6.090	6.720
	SD	0.165	0.212	0.251	0.313	0.390	0.422	0.624	0.589	0.608	0.659
	MIN	2 54	3.02	3.38	3.58	3.92	4.42	4.90	5.26	5.46	6.06
	MAX	2 91	3.44	3.94	4.28	4.66	5.26	6.20	6.58	6.74	7.40
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	2.953	3.360	3.790	4.135	4.440	4.920	5.565	6.145	6.330	6.900
	SD	0.199	0.236	0.270	0.328	0.399	0.483	0.706	0.764	0.797	1.009
	MIN	2.70	3.02	3.56	3.76	3.94	4.36	4.84	5.46	5.52	5.92
	MAX	3 15	3.56	4.18	4.56	4.80	5.44	6.36	7.14	7.12	7.80
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	2.820	3.285	3.750	4.095	4.360	4.770	5.290	5.920	6.025	6.440
	SD	0.238	0.230	0.232	0.298	0.215	0.414	0.493	0.808	0.527	0.574
	MIN	2.47	2.96	3.42	3.70	4.04	4.24	4.74	5.16	5.46	5.84
	MAX	3.01	3.50	3.94	4.40	4.50	5.18	5.84	6.76	6.64	7.10
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	2.789	3.275	3.635	3.915	4.240	4.650	5.205	5.730	5.990	6.350
	SD	0.290	0.264	0.357	0.330	0.347	0.441	0.505	0.713	0.580	0.679
	MIN	2 50	3.00	3.26	3.60	3.84	4.10	4.60	4.98	5.40	5.54
	MAX	3.08	3.52	3.94	4.20	4.54	5.08	5.66	6.52	6.60	6.94
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 34

(b) (4)2

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126	Day 133	Day 140	Day 147	Day 154	Day 161	Day 168	Day 175	Day 182	Day 189
1	MEAN	7.110	7.500	7.870	8.248	8.570	9.080	9.515	9.580	9.755	10.080
	SD	0.587	0.631	0.661	0.743	0.776	0.846	0.892	0.909	0.911	0.914
	MIN	6.52	6.86	7.22	7.45	7.68	8.00	8.34	8.58	8.80	9.10
	MAX	7.70	8.18	8.44	8.92	9.36	9.94	10.40	10.38	10.64	11.00
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	7.495	7.775	8.110	8.445	8.930	9.160	9.530	9.970	10.360 A^3	10.500 A^3
	SD	1.019	1.067	1.052	1.236	1.124	1.078	1.149	1.152	1.283	1.312
	MIN	6.56	6.84	7.16	7.24	7.78	8.08	8.26	8.70	8.98	9.10
	MAX	8.72	8.94	9.20	9.58	10.25	10.24	10.60	11.16	11.72	12.00
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	7.000	7.160	7.390	7.800	8.270	8.425	8.740	9.145	9.240	9.430
	SD	0.882	0.768	0.724	0.862	1.033	0.843	0.906	0.916	1.220	1.037
	MIN	6.14	6.36	6.64	6.84	7.22	7.44	7.84	8.26	7.90	8.22
	MAX	7.92	8.04	8.20	8.72	9.30	9.34	9.78	10.18	10.58	10.56
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	6.850	7.255	7.585	7.995	8.415	8.780	9.190	9.400	9.765	10.160
	SD	0.881	0.858	1.064	0.945	1.048	1.263	1.342	1.409	1.439	1.427
	MIN	5.90	6.30	6.38	6.98	7.28	7.50	7.76	8.12	8.28	8.80
	MAX	7.60	8.00	8.48	8.82	9.44	10.00	10.46	10.82	11.18	11.62
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196	Day 203	Day 210	Day 217	Day 224	Day 231	Day 238
1	MEAN	10.270	10.720	10.660	10.740	11.005	11.195	10.890
	SD	0.843	0.816	0.837	0.796	0.919	0.869	0.899
	MIN	9.30	9.60	9.72	9.88	9.84	10.12	9.74
	MAX	11.22	11.46	11.54	11.54	11.76	12.12	11.80
	N	4	4	4	4	4	4	4
2	MEAN	10.615	11.000	11.100	11.255 A^3	11.570 A^3	11.885 B^3	11.385 A^3
	SD	1 113	1.166	1.177	1.246	1.252	1.284	1.286
	MIN	9.46	9.82	10.02	10.10	10.40	10.72	10.26
	MAX	11.80	12.20	12.42	12.74	13.06	13.48	12.94
	N	4	4	4	4	4	4	4
3	MEAN	9.655	9.780	9.945	10.170	10.370	10.375	10.300
	SD	1.036	1.001	0.855	1.145	1.229	1.187	1.264
	MIN	8.46	8.50	9.04	8.72	8.74	8.88	8.54
	MAX	10.88	10.82	11.02	11.44	11.68	11.68	11.54
	N	4	4	4	4	4	4	4
4	MEAN	10.400	10.880	11.055	11.270 A^3	11.560 A^3	11.810 A^3	11.450 A^3
	SD	1 524	1.599	1.616	1.629	1.693	1.961	1.745
	MIN	8.96	9.34	9.60	9.70	10.02	9.98	9.82
	MAX	11.90	12.26	12.60	13.02	13.38	14.00	13.54
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	Day 63	Day 70	Day 77	Day 84	Day 91	Day 98	Day 105	Day 112	Day 119
1	MEAN	2.621	2.770	3.005	3.310	3.580	4.135	4.645	4.905	5.195	5.595
	SD	0.290	0.265	0.242	0.300	0.301	0.382	0.597	0.442	0.545	0.618
	MIN	2 29	2.44	2.66	2.88	3.18	3.60	3.84	4.26	4.42	4.76
	MAX	3.00	3.06	3.20	3.56	3.84	4.42	5.24	5.22	5.70	6.20
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	2.535	2.875	3.360	3.575	3.920	4.390	5.035	5.485	5.585	6.110
	SD	0.394	0.428	0.456	0.480	0.388	0.416	0.425	0.715	0.608	0.709
	MIN	2 17	2.46	2.92	3.06	3.52	4.04	4.50	4.82	5.02	5.30
	MAX	2.88	3.32	3.88	4.14	4.36	4.90	5.54	6.50	6.42	7.02
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	2.685	2.970	3.350	3.540	3.775	4.085	4.545	5.150	5.295	5.555
	SD	0.392	0.420	0.391	0.422	0.437	0.380	0.443	0.299	0.621	0.621
	MIN	2 39	2.58	2.92	3.14	3.36	3.76	4.14	4.90	4.76	5.04
	MAX	3 26	3.56	3.86	4.06	4.36	4.60	5.10	5.56	6.06	6.32
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	2.503	2.910	3.210	3.470	3.770	4.135	4.590	5.060	5.435	5.790
	SD	0.224	0.258	0.295	0.317	0.322	0.381	0.461	0.590	0.649	0.586
	MIN	2 23	2.62	2.86	3.08	3.42	3.70	4.06	4.44	4.68	5.14
	MAX	2.78	3.22	3.54	3.80	4.14	4.60	5.18	5.84	6.24	6.54
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126	Day 133	Day 140	Day 147	Day 154	Day 161	Day 168	Day 175	Day 182	Day 189
1	MEAN	5.890	6.180	6.450	6.720	6.980	7.365	7.780	7.710	7.945	8.040
	SD	0.510	0.475	0.476	0.603	0.576	0.589	0.592	0.471	0.500	0.444
	MIN	5.16	5.56	5.82	5.90	6.24	6.62	7.04	7.20	7.34	7.52
	MAX	6.34	6.70	6.96	7.28	7.62	8.06	8.48	8.28	8.48	8.56
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	6.705	6.870	7.160	7.445	7.780	7.955	8.175	8.525	8.815 A^3	9.035 A^3
	SD	0.920	0.879	0.820	0.906	0.972	0.973	1.024	1.066	1.147	1.205
	MIN	6.12	5.98	6.32	6.54	7.00	7.02	7.16	7.46	7.86	8.08
	MAX	8.06	8.06	8.24	8.70	9.20	9.32	9.60	10.00	10.46	10.80
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	6.115	6.200	6.370	6.650	6.953	7.090	7.425	7.730	7.775	7.965
	SD	0.492	0.712	0.712	0.833	0.795	0.914	0.901	0.976	0.766	1.047
	MIN	5.74	5.58	5.74	5.88	6.30	6.18	6.66	6.86	7.12	7.08
	MAX	6.82	7.10	7.24	7.66	7.98	8.16	8.46	8.78	8.78	9.32
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	6.205	6.560	6.920	7.143	7.535	7.938	8.280	8.385	8.580	8.865
	SD	0.656	0.634	0.770	0.805	0.785	0.989	1.115	0.920	0.924	0.958
	MIN	5.42	5.82	5.94	6.15	6.60	6.91	7.24	7.34	7.64	7.90
	MAX	7.02	7.36	7.82	8.12	8.52	9.28	9.86	9.58	9.84	10.18
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196	Day 203	Day 210	Day 217	Day 224	Day 231	Day 238
1	MEAN	8.155	8.595	8.440	8.475	8.530	8.630	8.425
	SD	0.557	0.662	0.557	0.471	0.612	0.542	0.543
	MIN	7.50	7.80	7.76	8.00	7.86	7.94	7.78
	MAX	8.86	9.42	9.12	9.10	9.24	9.26	9.00
	N	4	4	4	4	4	4	4
2	MEAN	8.985	9.170	9.260	9.455 A^3	9.650 A^3	9.930 B^3	9.555 A^3
	SD	1.205	1.193	1.159	1.219	1.267	1.329	1.401
	MIN	7.88	8.02	8.10	8.32	8.50	8.66	8.42
	MAX	10.70	10.84	10.86	11.18	11.44	11.80	11.60
	N	4	4	4	4	4	4	4
3	MEAN	8.055	8.120	8.325	8.340	8.460	8.580	8.285
	SD	1.155	1.215	1.346	1.127	1.052	1.180	1.105
	MIN	7.10	7.08	7.16	7.38	7.60	7.60	7.32
	MAX	9.56	9.64	9.78	9.72	9.80	10.16	9.68
	N	4	4	4	4	4	4	4
4	MEAN	9.015	9.285	9.375	9.425 A^3	9.660 A^3	9.895 A^3	9.570 A^3
	SD	0.945	1.245	1.181	1.126	1.180	1.120	1.002
	MIN	8.10	8.16	8.30	8.46	8.54	8.76	8.44
	MAX	10.34	11.06	11.06	11.04	11.32	11.32	10.86
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	Day 63	Day 70	Day 77	Day 84	Day 91	Day 98	Day 105	Day 112	Day 119
1	MEAN	2.677	2.990	3.298	3.590	3.923	4.483	5.085	5.375	5.643	6.158
	SD	0.227	0.323	0.387	0.413	0.488	0.526	0.735	0.696	0.717	0.844
	MIN	2 29	2.44	2.66	2.88	3.18	3.60	3.84	4.26	4.42	4.76
	MAX	3.00	3.44	3.94	4.28	4.66	5.26	6.20	6.58	6.74	7.40
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	2.744	3.118	3.575	3.855	4.180	4.655	5.300	5.815	5.958	6.505
	SD	0.366	0.412	0.416	0.484	0.458	0.505	0.609	0.771	0.768	0.911
	MIN	2 17	2.46	2.92	3.06	3.52	4.04	4.50	4.82	5.02	5.30
	MAX	3 15	3.56	4.18	4.56	4.80	5.44	6.36	7.14	7.12	7.80
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	2.753	3.128	3.550	3.818	4.068	4.428	4.918	5.535	5.660	5.998
	SD	0.309	0.356	0.366	0.450	0.447	0.519	0.589	0.698	0.661	0.728
	MIN	2 39	2.58	2.92	3.14	3.36	3.76	4.14	4.90	4.76	5.04
	MAX	3 26	3.56	3.94	4.40	4.50	5.18	5.84	6.76	6.64	7.10
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	2.646	3.093	3.423	3.693	4.005	4.393	4.898	5.395	5.713	6.070
	SD	0.284	0.311	0.379	0.383	0.399	0.470	0.555	0.704	0.642	0.659
	MIN	2 23	2.62	2.86	3.08	3.42	3.70	4.06	4.44	4.68	5.14
	MAX	3.08	3.52	3.94	4.20	4.54	5.08	5.66	6.52	6.60	6.94
	N	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126	Day 133	Day 140	Day 147	Day 154	Day 161	Day 168	Day 175	Day 182	Day 189
1	MEAN	6.500	6.840	7.160	7.484	7.775	8.223	8.648	8.645	8.850	9.060
	SD	0.827	0.875	0.928	1.029	1.060	1.138	1.162	1.204	1.183	1.277
	MIN	5.16	5.56	5.82	5.90	6.24	6.62	7.04	7.20	7.34	7.52
	MAX	7.70	8.18	8.44	8.92	9.36	9.94	10.40	10.38	10.64	11.00
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	7.100	7.323	7.635	7.945	8.355	8.558	8.853	9.248	9.588 A^3	9.768 A^3
	SD	0.993	1.026	1.010	1.137	1.151	1.149	1.241	1.285	1.397	1.405
	MIN	6.12	5.98	6.32	6.54	7.00	7.02	7.16	7.46	7.86	8.08
	MAX	8.72	8.94	9.20	9.58	10.25	10.24	10.60	11.16	11.72	12.00
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	6.558	6.680	6.880	7.225	7.611	7.758	8.083	8.438	8.508	8.698
	SD	0.813	0.857	0.860	0.997	1.106	1.082	1.093	1.157	1.226	1.243
	MIN	5.74	5.58	5.74	5.88	6.30	6.18	6.66	6.86	7.12	7.08
	MAX	7.92	8.04	8.20	8.72	9.30	9.34	9.78	10.18	10.58	10.56
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	6.528	6.908	7.253	7.569	7.975	8.359	8.735	8.893	9.173	9.513
	SD	0.798	0.791	0.931	0.932	0.978	1.143	1.241	1.228	1.286	1.321
	MIN	5.42	5.82	5.94	6.15	6.60	6.91	7.24	7.34	7.64	7.90
	MAX	7.60	8.00	8.48	8.82	9.44	10.00	10.46	10.82	11.18	11.62
	N	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 34 (b) (4)

BODY WEIGHT (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196	Day 203	Day 210	Day 217	Day 224	Day 231	Day 238
1	MEAN	9.213	9.658	9.550	9.608	9.768	9.913	9.658
	SD	1.310	1.328	1.357	1.354	1.507	1.526	1.486
	MIN	7.50	7.80	7.76	8.00	7.86	7.94	7.78
	MAX	11.22	11.46	11.54	11.54	11.76	12.12	11.80
	N	8	8	8	8	8	8	8
2	MEAN	9.800	10.085	10.180	10.355 A^3	10.610 A^3	10.908 B^3	10.470 A^3
	SD	1.383	1.466	1.462	1.493	1.554	1.598	1.583
	MIN	7.88	8.02	8.10	8.32	8.50	8.66	8.42
	MAX	11.80	12.20	12.42	12.74	13.06	13.48	12.94
	N	8	8	8	8	8	8	8
3	MEAN	8.855	8.950	9.135	9.255	9.415	9.478	9.293
	SD	1.328	1.360	1.356	1.437	1.471	1.457	1.539
	MIN	7.10	7.08	7.16	7.38	7.60	7.60	7.32
	MAX	10.88	10.82	11.02	11.44	11.68	11.68	11.54
	N	8	8	8	8	8	8	8
4	MEAN	9.708	10.083	10.215	10.348 A^3	10.610 A^3	10.853 A^3	10.510 A^3
	SD	1.388	1.577	1.589	1.629	1.690	1.798	1.657
	MIN	8.10	8 16	8.30	8.46	8.54	8.76	8.44
	MAX	11.90	12.26	12.60	13.02	13.38	14.00	13.54
	N	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112
1	MEAN	0.476	0.380	0.280	0.395	0.565	0.695	0.320	0.245
	SD	0.069	0.103	0.071	0.150	0.057	0.265	0.350	0.118
	MIN	0.38	0.26	0 20	0.24	0.48	0.48	-0.16	0.16
	MAX	0.53	0.50	0 34	0.60	0.60	1.08	0.68	0.42
	N	4	4	4	4	4	4	4	4
2	MEAN	0.407	0.430 B^3	0.345	0.305	0.480	0.645	0.580	0.185
	SD	0.075	0.179	0.097	0.251	0.110	0.236	0.532	0.313
	MIN	0.32	0.24	0 20	0.16	0.40	0.42	-0.02	-0.12
	MAX	0.50	0.62	0.40	0.68	0.64	0.92	1.20	0.56
	N	4	4	4	4	4	4	4	4
3	MEAN	0.465	0.465 A^3	0.345	0.265	0.410 C^3	0.520	0.630	0.105
	SD	0.031	0.146	0.081	0.158	0.262	0.115	0.341	0.313
	MIN	0.44	0.26	0 28	0.04	0.20	0.38	0.26	-0.20
	MAX	0.50	0.58	0.46	0.40	0.74	0.66	0.92	0.44
	N	4	4	4	4	4	4	4	4
4	MEAN	0.486	0.360	0.280	0.325	0.410 B^3	0.555	0.525	0.260
	SD	0.079	0.095	0.040	0.115	0.125	0.082	0.242	0.141
	MIN	0.42	0.26	0 26	0.18	0.26	0.48	0.32	0.08
	MAX	0.60	0.46	0 34	0.46	0.56	0.66	0.86	0.42
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 112 to 119	Day 119 to 126	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168
1	MEAN	0.630	0.390	0.390	0.370	0.378	0.323	0.510	0.435
	SD	0.221	0.185	0.062	0.133	0.105	0.170	0.155	0.068
	MIN	0.42	0.12	0.34	0.26	0.23	0.14	0.32	0.34
	MAX	0.94	0.54	0.48	0.56	0.48	0.52	0.68	0.50
	N	4	4	4	4	4	4	4	4
2	MEAN	0.570	0.595	0.280	0.335	0.335	0.485	0.230 B^3	0.370
	SD	0.248	0.386	0.170	0.060	0.265	0.333	0.209	0.137
	MIN	0.36	0.14	0.08	0.26	-0.02	0.00	-0.01	0.18
	MAX	0.90	0.98	0.48	0.40	0.62	0.73	0.48	0.48
	N	4	4	4	4	4	4	4	4
3	MEAN	0.415	0.560	0 160 B^3	0.230	0.410	0.470	0.155 B^3	0.315
	SD	0.053	0.324	0.161	0.050	0.151	0.213	0.273	0.162
	MIN	0.36	0.26	-0.04	0.16	0.20	0.22	-0.14	0.08
	MAX	0.46	0.86	0.34	0.28	0.52	0.70	0.50	0.44
	N	4	4	4	4	4	4	4	4
4	MEAN	0.360	0.500	0.405	0.330	0.410	0.420	0.365	0.410
	SD	0.164	0.224	0.041	0.208	0.133	0.163	0.323	0.101
	MIN	0.14	0.26	0.36	0.08	0.30	0.30	0.12	0.26
	MAX	0.52	0.72	0.46	0.52	0.60	0.66	0.84	0.48
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224
1	MEAN	0.065	0.175	0.325	0.190	0.450	-0.060	0.080	0.265
	SD	0.330	0.122	0.041	0.173	0.235	0.258	0.073	0.228
	MIN	-0.32	0.04	0.28	-0.04	0.24	-0.44	0.00	-0.04
	MAX	0.42	0.32	0.36	0.38	0.76	0.12	0.16	0.44
	N	4	4	4	4	4	4	4	4
2	MEAN	0.440 C^3	0.390	0.140	0.115	0.385 A^3	0.100 B^3	0.155	0.315
	SD	0.107	0.136	0.115	0.232	0.075	0.128	0.118	0.010
	MIN	0.30	0.28	0.00	-0.20	0.30	-0.02	0.06	0.30
	MAX	0.56	0.56	0.28	0.36	0.48	0.22	0.32	0.32
	N	4	4	4	4	4	4	4	4
3	MEAN	0.405 C^3	0.095	0.190	0.225	0.125 C^3	0.165 C^3	0.225	0.200
	SD	0.034	0.330	0.202	0.115	0.162	0.276	0.363	0.141
	MIN	0.36	-0.36	-0.02	0.06	-0.06	-0.08	-0.32	0.02
	MAX	0.44	0.40	0.40	0.32	0.28	0.54	0.42	0.36
	N	4	4	4	4	4	4	4	4
4	MEAN	0.210	0.365	0.395	0.240	0.480	0.175 B^3	0.215	0.290
	SD	0.340	0.157	0.106	0.112	0.177	0.218	0.209	0.101
	MIN	-0.08	0.16	0.28	0.14	0.36	-0.06	-0.02	0.14
	MAX	0.62	0.54	0.52	0.38	0.74	0.38	0.42	0.36
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 224 to 231	Day 231 to 238
1	MEAN	0.190	-0.305
	SD	0.202	0.057
	MIN	-0.10	-0.38
	MAX	0.36	-0.26
	N	4	4
2	MEAN	0.315	-0.500
	SD	0.235	0.172
	MIN	0.04	-0.72
	MAX	0.58	-0.32
	N	4	4
3	MEAN	0.005	-0.075
	SD	0.148	0.303
	MIN	-0.20	-0.34
	MAX	0.14	0.36
	N	4	4
4	MEAN	0.250	-0.360
	SD	0.283	0.273
	MIN	-0.04	-0.70
	MAX	0.62	-0.12
	N	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112
1	MEAN	0.149	0.235	0.305	0.270	0.555	0.510	0.260	0.290
	SD	0.479	0.114	0.060	0.089	0.096	0.247	0.360	0.158
	MIN	-0.56	0.08	0 22	0.18	0.42	0.24	-0.26	0.16
	MAX	0.47	0.32	0 36	0.38	0.64	0.84	0.56	0.48
	N	4	4	4	4	4	4	4	4
2	MEAN	0.341	0.485 **B**[3]	0.215	0.345	0.470	0.645	0.450	0.100
	SD	0.069	0.053	0.066	0.098	0.074	0.251	0.531	0.329
	MIN	0.29	0.44	0 14	0.22	0.38	0.44	-0.22	-0.26
	MAX	0.44	0.56	0 28	0.46	0.54	1.00	0.96	0.46
	N	4	4	4	4	4	4	4	4
3	MEAN	0.285	0 380 **A**[3]	0.190	0.235	0.310 **C**[3]	0.460	0.605	0.145
	SD	0.094	0.071	0.125	0.072	0.066	0.085	0.157	0.338
	MIN	0.19	0.30	0.02	0.14	0.24	0.38	0.46	-0.20
	MAX	0.41	0.44	0 32	0.30	0.40	0.56	0.76	0.50
	N	4	4	4	4	4	4	4	4
4	MEAN	0.407	0.300	0.260	0.300	0.365 **B**[3]	0.455	0.470	0.375
	SD	0.103	0.043	0.033	0.049	0.081	0.104	0.144	0.091
	MIN	0.28	0.24	0 22	0.24	0.28	0.36	0.34	0.24
	MAX	0.52	0.34	0 30	0.34	0.46	0.58	0.66	0.44
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 112 to 119	Day 119 to 126	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168
1	MEAN	0.400	0.295	0.290	0.270	0.270	0.260	0.385	0.415
	SD	0.314	0.348	0.155	0.012	0.151	0.105	0.120	0.057
	MIN	0.18	-0.22	0.06	0.26	0.08	0.12	0.22	0.34
	MAX	0.86	0.54	0.40	0.28	0.44	0.34	0.50	0.48
	N	4	4	4	4	4	4	4	4
2	MEAN	0.525	0.595	0.165	0.290	0.285	0.335	0.175 B^3	0.220
	SD	0.274	0.471	0.290	0.089	0.194	0.168	0.129	0.094
	MIN	0.28	-0.04	-0.16	0.18	0.04	0.18	0.02	0.14
	MAX	0.88	1.04	0.42	0.38	0.46	0.50	0.30	0.32
	N	4	4	4	4	4	4	4	4
3	MEAN	0.260	0.560	0.085 B^3	0.170	0.280	0.303	0.138 B^3	0.335
	SD	0.033	0.220	0.273	0.035	0.124	0.099	0.191	0.143
	MIN	0.22	0.28	-0.16	0.14	0.14	0.18	-0.12	0.16
	MAX	0.30	0.78	0.36	0.22	0.42	0.42	0.34	0.50
	N	4	4	4	4	4	4	4	4
4	MEAN	0.355	0.415	0.355	0.360	0.223	0.393	0.403	0.343
	SD	0.072	0.108	0.034	0.202	0.104	0.078	0.250	0.175
	MIN	0.30	0.28	0.32	0.12	0.08	0.28	0.18	0.16
	MAX	0.46	0.52	0.40	0.58	0.30	0.45	0.76	0.58
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224
1	MEAN	-0.070	0.235	0.095	0.115	0.440	-0.155	0.035	0.055
	SD	0.278	0.081	0.075	0.205	0.114	0.112	0.152	0.179
	MIN	-0.40	0.14	0.00	-0.10	0.30	-0.30	-0.12	-0.14
	MAX	0.16	0.32	0.18	0.30	0.56	-0.04	0.24	0.26
	N	4	4	4	4	4	4	4	4
2	MEAN	0.350 C^3	0.290	0.220	-0.050	0.185 A^3	0.090 B^3	0.195	0.195
	SD	0.084	0.288	0.214	0.125	0.148	0.053	0.097	0.100
	MIN	0.26	-0.14	-0.08	-0.20	0.06	0.02	0.10	0.06
	MAX	0.44	0.46	0.40	0.08	0.40	0.14	0.32	0.28
	N	4	4	4	4	4	4	4	4
3	MEAN	0.305 C^3	0.045	0.190	0.090	0.065 C^3	0.205 C^3	0.015	0.120
	SD	0.108	0.313	0.283	0.109	0.134	0.275	0.288	0.099
	MIN	0.18	-0.38	-0.04	0.00	-0.12	-0.04	-0.36	0.00
	MAX	0.44	0.30	0.54	0.24	0.20	0.60	0.26	0.22
	N	4	4	4	4	4	4	4	4
4	MEAN	0.105	0.195	0.285	0.150	0.270	0.090 B^3	0.050	0.235
	SD	0.274	0.115	0.038	0.076	0.306	0.123	0.173	0.111
	MIN	-0.28	0.04	0.26	0.04	0.06	-0.02	-0.16	0.08
	MAX	0.32	0.30	0.34	0.20	0.72	0.24	0.22	0.34
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 224 to 231	Day 231 to 238
1	MEAN	0.100	-0.205
	SD	0.198	0.168
	MIN	-0.08	-0.40
	MAX	0.38	0.00
	N	4	4
2	MEAN	0.280	-0.375
	SD	0.156	0.180
	MIN	0.14	-0.54
	MAX	0.46	-0.20
	N	4	4
3	MEAN	0.120	-0.295
	SD	0.170	0.140
	MIN	0.00	-0.48
	MAX	0.36	-0.14
	N	4	4
4	MEAN	0.235	-0.325
	SD	0.326	0.515
	MIN	0.00	-0.88
	MAX	0.70	0.36
	N	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112
1	MEAN	0.313	0.308	0.293	0.333	0.560	0.603	0.290	0.268
	SD	0.362	0.127	0.062	0.132	0.073	0.257	0.331	0.131
	MIN	-0.56	0.08	0 20	0.18	0.42	0.24	-0.26	0.16
	MAX	0.53	0.50	0 36	0.60	0.64	1.08	0.68	0.48
	N	8	8	8	8	8	8	8	8
2	MEAN	0.374	0.458 **B**[3]	0.280	0.325	0.475	0.645	0.515	0.143
	SD	0.075	0.126	0.104	0.178	0.087	0.225	0.497	0.301
	MIN	0.29	0.24	0 14	0.16	0.38	0.42	-0.22	-0.26
	MAX	0.50	0.62	0.40	0.68	0.64	1.00	1.20	0.56
	N	8	8	8	8	8	8	8	8
3	MEAN	0.375	0.423 **A**[3]	0.268	0.250	0.360 **C**[3]	0.490	0.618	0.125
	SD	0.116	0.116	0.128	0.115	0.185	0.099	0.246	0.302
	MIN	0.19	0.26	0.02	0.04	0.20	0.38	0.26	-0.20
	MAX	0.50	0.58	0.46	0.40	0.74	0.66	0.92	0.50
	N	8	8	8	8	8	8	8	8
4	MEAN	0.446	0.330	0.270	0.313	0.388 **B**[3]	0.505	0.498	0.318
	SD	0.095	0.076	0.035	0.083	0.100	0.102	0.187	0.126
	MIN	0.28	0.24	0 22	0.18	0.26	0.36	0.32	0.08
	MAX	0.60	0.46	0 34	0.46	0.56	0.66	0.86	0.44
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 112 to 119	Day 119 to 126	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168
1	MEAN	0.515	0.343	0.340	0.320	0.324	0.291	0.448	0.425
	SD	0.280	0.263	0.122	0.103	0.134	0.135	0.145	0.059
	MIN	0.18	-0.22	0.06	0.26	0.08	0.12	0.22	0.34
	MAX	0.94	0.54	0.48	0.56	0.48	0.52	0.68	0.50
	N	8	8	8	8	8	8	8	8
2	MEAN	0.548	0.595	0.223	0.313	0.310	0.410	0.203 B^3	0.295
	SD	0.243	0.398	0.229	0.074	0.216	0.257	0.164	0.135
	MIN	0.28	-0.04	-0.16	0.18	-0.02	0.00	-0.01	0.14
	MAX	0.90	1.04	0.48	0.40	0.62	0.73	0.48	0.48
	N	8	8	8	8	8	8	8	8
3	MEAN	0.338	0.560	0 123 B^3	0.200	0.345	0.386	0.146 B^3	0.325
	SD	0.092	0.256	0.212	0.051	0.146	0.178	0.218	0.142
	MIN	0.22	0.26	-0.16	0.14	0.14	0.18	-0.14	0.08
	MAX	0.46	0.86	0.36	0.28	0.52	0.70	0.50	0.50
	N	8	8	8	8	8	8	8	8
4	MEAN	0.358	0.458	0.380	0.345	0.316	0.406	0.384	0.376
	SD	0.117	0.169	0.044	0.190	0.149	0.119	0.268	0.137
	MIN	0.14	0.26	0.32	0.08	0.08	0.28	0.12	0.16
	MAX	0.52	0.72	0.46	0.58	0.60	0.66	0.84	0.58
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224
1	MEAN	-0.003	0.205	0.210	0.153	0.445	-0.108	0.058	0.160
	SD	0.291	0.101	0.135	0.180	0.171	0.191	0.113	0.221
	MIN	-0.40	0.04	0.00	-0.10	0.24	-0.44	-0.12	-0.14
	MAX	0.42	0.32	0.36	0.38	0.76	0.12	0.24	0.44
	N	8	8	8	8	8	8	8	8
2	MEAN	0.395 C^3	0.340	0.180	0.033	0.285 A^3	0.095 B^3	0.175	0.255
	SD	0.101	0.215	0.165	0.194	0.153	0.091	0.102	0.092
	MIN	0.26	-0.14	-0.08	-0.20	0.06	-0.02	0.06	0.06
	MAX	0.56	0.56	0.40	0.36	0.48	0.22	0.32	0.32
	N	8	8	8	8	8	8	8	8
3	MEAN	0.355 C^3	0.070	0.190	0.158	0.095 C^3	0.185 C^3	0.120	0.160
	SD	0.091	0.299	0.228	0.126	0.141	0.256	0.324	0.121
	MIN	0.18	-0.38	-0.04	0.00	-0.12	-0.08	-0.36	0.00
	MAX	0.44	0.40	0.54	0.32	0.28	0.60	0.42	0.36
	N	8	8	8	8	8	8	8	8
4	MEAN	0.158	0.280	0.340	0.195	0.375	0.133 B^3	0.133	0.263
	SD	0.291	0.156	0.094	0.101	0.257	0.170	0.199	0.103
	MIN	-0.28	0.04	0.26	0.04	0.06	-0.06	-0.16	0.08
	MAX	0.62	0.54	0.52	0.38	0.74	0.38	0.42	0.36
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 35 (b) (4)

BODY WEIGHT CHANGE (kg) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 224 to 231	Day 231 to 238
1	MEAN	0.145	-0.255
	SD	0.191	0.128
	MIN	-0.10	-0.40
	MAX	0.38	0.00
	N	8	8
2	MEAN	0.298	-0.438
	SD	0.186	0.176
	MIN	0.04	-0.72
	MAX	0.58	-0.20
	N	8	8
3	MEAN	0.063	-0.185
	SD	0.160	0.248
	MIN	-0.20	-0.48
	MAX	0.36	0.36
	N	8	8
4	MEAN	0.243	-0.343
	SD	0.283	0.382
	MIN	-0.04	-0.88
	MAX	0.70	0.36
	N	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	MEAN	26.25	27.63	27.88	28.13	29.00	29.00	28.75	29.13	29.50	30.25	31.50
	SD	0.65	0.48	0 25	0.25	1.00	1.00	0.29	0.25	0.41	0.65	0.91
	MIN	25.5	27.0	27.5	28.0	28.5	28.5	28.5	29.0	29.0	29.5	30.5
	MAX	27.0	28.0	28.0	28.5	30.5	30.5	29.0	29.5	30.0	31.0	32.5
	N	4	4	4	4	4	4	4	4	4	4	4
2	MEAN	27.00	26.50	26.88	27.38	29.00	29.38	29.75 C^3	30.00 B^3	30.13	30.88	31.88
	SD	0.91	0.91	1 11	0.75	0.71	0.48	0.50	0.00	0.25	0.25	0.85
	MIN	26.0	25.5	25.5	26.5	28.0	29.0	29.0	30.0	30.0	30.5	31.0
	MAX	28.0	27.5	28.0	28.0	29.5	30.0	30.0	30.0	30.5	31.0	33.0
	N	4	4	4	4	4	4	4	4	4	4	4
3	MEAN	26.75	27.00	28.75	28.75	29.25	29.25	29.63 B^3	29.63	29.88	31.00	30.88
	SD	0.96	1.22	1.04	1.04	0 50	0.29	0.48	0.48	0.25	1.22	0.85
	MIN	26.0	26.0	27.5	27.5	29.0	29.0	29.0	29.0	29.5	29.5	30.0
	MAX	28.0	28.5	30.0	30.0	30.0	29.5	30.0	30.0	30.0	32.0	32.0
	N	4	4	4	4	4	4	4	4	4	4	4
4	MEAN	26.00	26.25	28.38	28.00	28.25	28.38	29.13	29.25	29.63	30.63	30.75
	SD	0.82	1.26	1.44	1.22	1.04	0.85	0.75	0.87	0.75	1.11	1.32
	MIN	25.0	25.0	26.5	26.5	27.0	27.5	28.5	28.5	29.0	29.0	29.0
	MAX	27.0	28.0	29.5	29.5	29.5	29.5	30.0	30.0	30.5	31.5	32.0
	N	4	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	MEAN	31.13	31.75	32.13	33.00	33.13	33.50	33.75	34.13	34.25	34.38
	SD	0.85	0.29	0.48	1.15	1.03	1 15	1.19	1.11	0.87	0.63
	MIN	30.0	31.5	31.5	32.0	32.0	32.5	32.5	32.5	33.0	33.5
	MAX	32.0	32.0	32.5	34.0	34.0	34.5	35.0	35.0	35.0	35.0
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	32.50	31.75	32.00	32.25	32.38	32.88	33.13	34.38	34.50	34.75
	SD	1.87	1.32	1.29	1.32	1.11	1.03	0.85	1.11	1.00	1.19
	MIN	30.5	30.0	30.5	30.5	31.0	31.5	32.0	33.5	34.0	34.0
	MAX	35.0	33.0	33.5	33.5	33.5	34.0	34.0	36.0	36.0	36.5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	32.38	31.75	32.13	32.25	32.88	32.88	33.38	33.75	33.75	34.00
	SD	1.93	1.26	1.31	1.32	1.18	1 18	0.85	1.32	1.32	1.58
	MIN	30.5	30.5	31.0	31.0	32.0	32.0	32.5	32.5	32.5	32.5
	MAX	34.5	33.5	34.0	34.0	34.5	34.5	34.5	35.5	35.5	36.0
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	31.25	31.63	32.00	32.63	33.00	33.00	33.38	33.38	33.63	34.00
	SD	1.55	1.60	1.47	1.97	1.83	1.83	1.89	1.89	1.70	1.47
	MIN	29.5	30.0	30.5	31.0	31.0	31.0	31.5	31.5	31.5	32.5
	MAX	33.0	33.0	33.5	35.0	35.0	35.0	35.0	35.0	35.0	35.5
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	MEAN	34.38	34.75	34.50	34.88	34.88	35.13
	SD	0.63	1.04	0.71	0.48	0.48	0.48
	MIN	33.5	33.5	33.5	34.5	34.5	34.5
	MAX	35.0	36.0	35.0	35.5	35.5	35.5
	N	4	4	4	4	4	4
2	MEAN	34.88	34.88	35.13	35.38	35.88 A^3	36.25
	SD	1.11	1.11	1.11	1.03	0.85	0.96
	MIN	34.0	34.0	34.0	34.0	35.0	35.0
	MAX	36.5	36.5	36.5	36.5	37.0	37.0
	N	4	4	4	4	4	4
3	MEAN	34.13	34.38	34.63	34.38	34.63	34.63 A^3
	SD	1.49	1.38	1.11	1.38	1.60	1.60
	MIN	32.5	33.0	33.5	33.0	33.0	33.0
	MAX	36.0	36.0	36.0	36.0	36.0	36.0
	N	4	4	4	4	4	4
4	MEAN	34.13	33.75	33.63	33.75	33.75	33.75 A^3
	SD	1.31	1.19	1.70	1.66	1.66	1.66
	MIN	33.0	33.0	32.0	32.0	32.0	32.0
	MAX	35.5	35.5	36.0	36.0	36.0	36.0
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	MEAN	25.88	26.88	26.13	26.88	26.88	27.13	27.13	27.63	28.50	29.13	29.88
	SD	0.85	1.44	0.48	0.48	0.48	0.48	0.48	0.48	1.15	1.11	0.25
	MIN	25.0	25.0	25.5	26.5	26.5	26.5	26.5	27.0	27.5	27.5	29.5
	MAX	27.0	28.0	26.5	27.5	27.5	27.5	27.5	28.0	29.5	30.0	30.0
	N	4	4	4	4	4	4	4	4	4	4	4
2	MEAN	25.50	25.75	25.88	26.63	27.38	28.13	28.38 C^3	28.50 B^3	28.63	28.88	29.88
	SD	0.91	1.50	1.44	1.03	1 25	1.11	1.03	0.82	0.85	0.48	0.48
	MIN	24.5	25.0	25.0	25.5	26.0	27.0	27.0	27.5	27.5	28.5	29.5
	MAX	26.5	28.0	28.0	28.0	29.0	29.5	29.5	29.5	29.5	29.5	30.5
	N	4	4	4	4	4	4	4	4	4	4	4
3	MEAN	25.75	25.88	27.75	26.75	26.88	27.25	27.88 B^3	27.88	28.13	29.00	29.50
	SD	0.87	0.25	2 36	1.19	1 18	0.96	0.75	0.75	0.75	1.08	0.71
	MIN	25.0	25.5	26.0	26.0	26.0	26.5	27.0	27.0	27.5	27.5	29.0
	MAX	27.0	26.0	31.0	28.5	28.5	28.5	28.5	28.5	29.0	30.0	30.5
	N	4	4	4	4	4	4	4	4	4	4	4
4	MEAN	25.00	25.00	27.00	27.00	27.13	27.25	27.38	27.50	27.88	28.63	29.13
	SD	1.00	1.08	1 91	0.58	0.75	0.65	0.48	0.71	0.48	0.48	0.48
	MIN	24.0	24.0	25.5	26.5	26.5	26.5	27.0	27.0	27.5	28.0	28.5
	MAX	26.0	26.5	29.5	27.5	28.0	28.0	28.0	28.5	28.5	29.0	29.5
	N	3	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	MEAN	29.63	30.00	30.50	31.00	31.00	31.25	31.75	32.00	32.13	32.25
	SD	1.11	0.41	0.58	0.71	0.71	1 19	1.04	0.91	0.75	0.65
	MIN	28.0	29.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5	31.5
	MAX	30.5	30.5	31.0	32.0	32.0	33.0	33.0	33.0	33.0	33.0
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	30.63	30.50	31.00	31.13	31.13	31.13	32.00	32.38	32.50	32.75
	SD	1.89	0.41	0.71	0.63	0.63	0.63	1.41	1.11	1.00	1.50
	MIN	28.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5	32.0	32.0
	MAX	33.0	31.0	32.0	32.0	32.0	32.0	34.0	34.0	34.0	35.0
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	30.13	30.25	30.38	30.63	30.88	30.88	31.25	31.63	31.63	32.13
	SD	0.63	0.65	0.63	0.48	0.48	0.48	0.87	1.11	1.11	1.38
	MIN	29.5	29.5	29.5	30.0	30.5	30.5	30.5	30.5	30.5	30.5
	MAX	31.0	31.0	31.0	31.0	31.5	31.5	32.0	33.0	33.0	33.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	29.75	30.50	30.50	31.00	31.00	31.38	32.00	32.13	32.38	32.88
	SD	0.50	0.71	0.71	0.82	0.82	1.49	1.08	0.95	1.11	1.18
	MIN	29.5	29.5	29.5	30.0	30.0	30.0	31.0	31.5	31.5	32.0
	MAX	30.5	31.0	31.0	32.0	32.0	33.5	33.5	33.5	34.0	34.5
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	MEAN	32.25	33.63	33.00	33.25	33.25	33.75
	SD	0.65	2.02	1.22	1.04	1.04	0.87
	MIN	31.5	31.5	31.5	32.0	32.0	33.0
	MAX	33.0	36.0	34.5	34.5	34.5	34.5
	N	4	4	4	4	4	4
2	MEAN	32.75	32.75	33.25	33.25	34.00 A^3	34.00
	SD	1.50	1.50	1.32	1.32	1.47	1.47
	MIN	32.0	32.0	32.0	32.0	32.5	32.5
	MAX	35.0	35.0	35.0	35.0	36.0	36.0
	N	4	4	4	4	4	4
3	MEAN	32.25	32.38	32.88	32.38	32.38	32.50 A^3
	SD	1.19	1.11	1.75	1.11	1.11	0.91
	MIN	31.0	31.0	31.0	31.0	31.0	31.5
	MAX	33.5	33.5	35.0	33.5	33.5	33.5
	N	4	4	4	4	4	4
4	MEAN	32.88	33.50	33.25	33.25	33.25	33.38 A^3
	SD	1.18	1.73	1.04	1.04	1.04	1.03
	MIN	32.0	32.0	32.0	32.0	32.0	32.0
	MAX	34.5	36.0	34.5	34.5	34.5	34.5
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	MEAN	26.06	27.25	27.00	27.50	27.94	28.06	27.94	28.38	29.00	29.69	30.69
	SD	0.73	1.07	1.00	0.76	1.35	1.24	0.94	0.88	0.96	1.03	1.07
	MIN	25.0	25.0	25.5	26.5	26.5	26.5	26.5	27.0	27.5	27.5	29.5
	MAX	27.0	28.0	28.0	28.5	30.5	30.5	29.0	29.5	30.0	31.0	32.5
	N	8	8	8	8	8	8	8	8	8	8	8
2	MEAN	26.25	26.13	26.38	27.00	28.19	28.75	29.06 C^3	29.25 B^3	29.38	29.88	30.88
	SD	1 16	1.22	1.30	0.93	1.28	1.04	1.05	0.96	0.99	1.13	1.25
	MIN	24.5	25.0	25.0	25.5	26.0	27.0	27.0	27.5	27.5	28.5	29.5
	MAX	28.0	28.0	28.0	28.0	29.5	30.0	30.0	30.0	30.5	31.0	33.0
	N	8	8	8	8	8	8	8	8	8	8	8
3	MEAN	26.25	26.44	28.25	27.75	28.06	28.25	28.75 B^3	28.75	29.00	30.00	30.19
	SD	1.00	1.02	1.77	1.49	1.52	1.25	1.10	1.10	1.07	1.51	1.03
	MIN	25.0	25.5	26.0	26.0	26.0	26.5	27.0	27.0	27.5	27.5	29.0
	MAX	28.0	28.5	31.0	30.0	30.0	29.5	30.0	30.0	30.0	32.0	32.0
	N	8	8	8	8	8	8	8	8	8	8	8
4	MEAN	25.57	25.63	27.69	27.50	27.69	27.81	28.25	28.38	28.75	29.63	29.94
	SD	0 98	1.27	1.73	1.04	1.03	0.92	1.10	1.19	1.10	1.33	1.27
	MIN	24.0	24.0	25.5	26.5	26.5	26.5	27.0	27.0	27.5	28.0	28.5
	MAX	27.0	28.0	29.5	29.5	29.5	29.5	30.0	30.0	30.5	31.5	32.0
	N	7	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	MEAN	30.38	30.88	31.31	32.00	32.06	32.38	32.75	33.06	33.19	33.31
	SD	1.22	0.99	1.00	1.39	1.40	1.62	1.49	1.47	1.36	1.28
	MIN	28.0	29.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5	31.5
	MAX	32.0	32.0	32.5	34.0	34.0	34.5	35.0	35.0	35.0	35.0
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	31.56	31.13	31.50	31.69	31.75	32.00	32.56	33.38	33.50	33.75
	SD	2.01	1.13	1.10	1.13	1.07	1 22	1.24	1.48	1.41	1.65
	MIN	28.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5	32.0	32.0
	MAX	35.0	33.0	33.5	33.5	33.5	34.0	34.0	36.0	36.0	36.5
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	31.25	31.00	31.25	31.44	31.88	31.88	32.31	32.69	32.69	33.06
	SD	1.79	1.22	1.34	1.27	1.36	1 36	1.39	1.60	1.60	1.70
	MIN	29.5	29.5	29.5	30.0	30.5	30.5	30.5	30.5	30.5	30.5
	MAX	34.5	33.5	34.0	34.0	34.5	34.5	34.5	35.5	35.5	36.0
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	30.50	31.06	31.25	31.81	32.00	32.19	32.69	32.75	33.00	33.44
	SD	1.34	1.29	1.34	1.65	1.69	1.77	1.60	1.54	1.49	1.37
	MIN	29.5	29.5	29.5	30.0	30.0	30.0	31.0	31.5	31.5	32.0
	MAX	33.0	33.0	33.5	35.0	35.0	35.0	35.0	35.0	35.0	35.5
	N	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	MEAN	33.31	34.19	33.75	34.06	34.06	34.44
	SD	1.28	1.60	1.22	1.15	1.15	0.98
	MIN	31.5	31.5	31.5	32.0	32.0	33.0
	MAX	35.0	36.0	35.0	35.5	35.5	35.5
	N	8	8	8	8	8	8
2	MEAN	33.81	33.81	34.19	34.31	34.94 A^3	35.13
	SD	1.67	1.67	1.51	1.58	1.50	1.66
	MIN	32.0	32.0	32.0	32.0	32.5	32.5
	MAX	36.5	36.5	36.5	36.5	37.0	37.0
	N	8	8	8	8	8	8
3	MEAN	33.19	33.38	33.75	33.38	33.50	33.56 A^3
	SD	1.60	1.58	1.65	1.58	1.75	1.66
	MIN	31.0	31.0	31.0	31.0	31.0	31.5
	MAX	36.0	36.0	36.0	36.0	36.0	36.0
	N	8	8	8	8	8	8
4	MEAN	33.50	33.63	33.44	33.50	33.50	33.56 A^3
	SD	1.34	1.38	1.32	1.31	1.31	1.29
	MIN	32.0	32.0	32.0	32.0	32.0	32.0
	MAX	35.5	36.0	36.0	36.0	36.0	36.0
	N	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	1.38	0 25	0.25	0.88	0.00	-0.25	0.38	0.38	0.75	1.25
	SD	1.03	0 50	0.29	0.75	0.00	0.87	0.25	0.48	0.65	1.04
	MIN	0.0	0.0	0.0	0.5	0.0	-1.5	0.0	0.0	0.0	0.0
	MAX	2.5	1.0	0.5	2.0	0.0	0.5	0.5	1.0	1.5	2.5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	-0.50 B^3	0 38	0.50	1.63 C^3	0.38	0.38	0.25	0.13	0.75	1.00
	SD	0.58	0.75	0.41	0.63	0.48	0.48	0.50	0.25	0.29	1.08
	MIN	-1.0	-0.5	0.0	1.0	0.0	0.0	0.0	0.0	0.5	0.0
	MAX	0.0	1.0	1.0	2.5	1.0	1.0	1.0	0.5	1.0	2.5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	0.25 A^3	1.75 C^3	0.00	0 50	0.00	0.38	0.00	0.25	1.13	-0.13
	SD	1.04	2.06	0.00	0.71	0.41	0.48	0.00	0.29	1.03	0.95
	MIN	-1.0	0.0	0.0	0.0	-0.5	0.0	0.0	0.0	0.0	-1.5
	MAX	1.5	4.0	0.0	1.5	0.5	1.0	0.0	0.5	2.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	0.25 B^3	2.13 C^3	-0.38	0 25	0.13	0.75	0.13	0.38	1.00	0.13
	SD	1.26	1.70	1.89	0 29	0.25	0.65	0.25	0.25	1.08	0.85
	MIN	-1.0	0.5	-3.0	0.0	0.0	0.0	0.0	0.0	0.0	-1.0
	MAX	2.0	4.5	1.5	0.5	0.5	1.5	0.5	0.5	2.5	1.0
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	-0.38	0.63	0.38	0.88	0.13	0.38	0.25	0 38	0.13	0.13
	SD	1.49	0.75	0.48	0.75	0.25	0.25	0.29	0.75	0.25	0.25
	MIN	-2.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	1.0	1.5	0.5	0.5	0.5	1 5	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	0.63	-0.75 B^3	0.25	0.25	0.13	0.50	0.25	1 25	0.13	0.25
	SD	2.46	1.50	0.29	0.29	0.25	0.41	0.29	0.87	0.25	0.29
	MIN	-2.5	-2.0	0.0	0.0	0.0	0.0	0.0	0 5	0.0	0.0
	MAX	3.5	1.0	0.5	0.5	0.5	1.0	0.5	2.0	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	1.50	-0.63	0.38	0.13	0.63 C^3	0.00	0.50	0 38	0.00	0.25
	SD	1.15	1.11	0.25	0.25	0.25	0.00	0.41	0.48	0.00	0.29
	MIN	0.5	-2.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	0.5	0.5	1.0	0.0	1.0	1.0	0.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	0.50	0.38	0.38	0.63	0.38	0.00	0.38	0.00	0.25	0.38
	SD	0.41	0.48	0.48	0.63	0.48	0.00	0.48	0.00	0.50	0.48
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.0	1.0	1.5	1.0	0.0	1.0	0.0	1.0	1.0
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238
1	MEAN	0.00	0.38	-0.25	0.38	0.00	0.25
	SD	0.00	0.75	0.50	0.48	0.00	0.50
	MIN	0.0	0.0	-1.0	0.0	0.0	0.0
	MAX	0.0	1.5	0.0	1.0	0.0	1.0
	N	4	4	4	4	4	4
2	MEAN	0.13	0.00	0.25 B^3	0.25	0.50 C^3	0.38
	SD	0.25	0.00	0.50	0.50	0.41	0.75
	MIN	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	0.5	0.0	1.0	1.0	1.0	1.5
	N	4	4	4	4	4	4
3	MEAN	0.13	0.25	0.25 B^3	-0.25 C^3	0.25	0.00
	SD	0.25	0.29	0.50	0.50	0.50	0.00
	MIN	0.0	0.0	0.0	-1.0	0.0	0.0
	MAX	0.5	0.5	1.0	0.0	1.0	0.0
	N	4	4	4	4	4	4
4	MEAN	0.13	-0.38	-0.13	0.13	0.00	0.00
	SD	0.25	1.11	0.63	0.25	0.00	0.00
	MIN	0.0	-2.0	-1.0	0.0	0.0	0.0
	MAX	0.5	0.5	0.5	0.5	0.0	0.0
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	1.00	-0.75	0.75	0.00	0.25	0.00	0.50	0.88	0.63	0.75
	SD	1.47	1 19	0.65	0.00	0.50	0.00	0.71	0.75	1.25	1.19
	MIN	-0.5	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	3.0	0.5	1.5	0.0	1.0	0.0	1.5	1.5	2.5	2.5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	0.25 B^3	0 13	0.75	0.75 C^3	0.75	0.25	0.13	0.13	0.25	1.00
	SD	1.04	0 25	0.65	0 29	1.19	0.50	0.25	0.25	0.50	0.91
	MIN	-1.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.5	0.5	1.5	1.0	2.5	1.0	0.5	0.5	1.0	2.0
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	0.13 A^3	1.88 C^3	-1.00	0 13	0.38	0.63	0.00	0.25	0.88	0.50
	SD	0.75	2 25	2.35	0 25	0.25	0.48	0.00	0.29	0.75	0.71
	MIN	-1.0	0.0	-4.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	0.5	5.0	0.5	0.5	0.5	1.0	0.0	0.5	1.5	1.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	0.00 B^3	2.00 C^3	0.00	0 13	0.13	0.13	0.13	0.38	0.75	0.50
	SD	1.80	1.68	2.16	0 25	0.25	0.25	0.25	0.48	0.29	0.41
	MIN	-2.0	1.0	-3.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0
	MAX	1.5	4.5	2.0	0.5	0.5	0.5	0.5	1.0	1.0	1.0
	N	3	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 37

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	-0.25	0.38	0.50	0.50	0.00	0.25	0.50	0 25	0.13	0.13
	SD	1.19	0.75	0.41	0.41	0.00	0.50	0.71	0 29	0.25	0.25
	MIN	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	0.5	1.5	1.0	1.0	0.0	1.0	1.5	0 5	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	0.75	-0.13 B^3	0.50	0.13	0.00	0.00	0.88	0 38	0.13	0.25
	SD	2.33	1.75	0.58	0.25	0.00	0.00	1.75	1.70	0.25	0.50
	MIN	-2.0	-2.0	0.0	0.0	0.0	0.0	0.0	-2.0	0.0	0.0
	MAX	3.5	2.0	1.0	0.5	0.0	0.0	3.5	2.0	0.5	1.0
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	0.63	0.13	0.13	0.25	0.25 C^3	0.00	0.38	0 38	0.00	0.50
	SD	0.25	0.25	0.25	0.29	0.29	0.00	0.48	0.48	0.00	0.41
	MIN	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	0.5	0.5	0.5	0.5	0.0	1.0	1.0	0.0	1.0
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	0.63	0.75	0.00	0.50	0.00	0.38	0.63	0 13	0.25	0.50
	SD	0.48	0.87	0.00	0.71	0.00	0.75	0.48	0 25	0.29	0.41
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	0.0	1.5	0.0	1.5	1.0	0 5	0.5	1.0
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238
1	MEAN	0.00	1.38	-0.63	0.25	0.00	0.50
	SD	0.00	1.60	1.03	0.29	0.00	0.58
	MIN	0.0	0.0	-1.5	0.0	0.0	0.0
	MAX	0.0	3.0	0.5	0.5	0.0	1.0
	N	4	4	4	4	4	4
2	MEAN	0.00	0.00	0.50 B^3	0.00	0.75 C^3	0.00
	SD	0.00	0.00	0.71	0.41	0.65	0.00
	MIN	0.0	0.0	0.0	-0.5	0.0	0.0
	MAX	0.0	0.0	1.5	0.5	1.5	0.0
	N	4	4	4	4	4	4
3	MEAN	0.13	0.13	0.50 B^3	-0.50 C^3	0.00	0.13
	SD	0.48	0.25	1.00	1.00	0.00	0.25
	MIN	-0.5	0.0	0.0	-2.0	0.0	0.0
	MAX	0.5	0.5	2.0	0.0	0.0	0.5
	N	4	4	4	4	4	4
4	MEAN	0.00	0.63	-0.25	0.00	0.00	0.13
	SD	0.00	0.75	0.87	0.00	0.00	0.25
	MIN	0.0	0.0	-1.5	0.0	0.0	0.0
	MAX	0.0	1.5	0.5	0.0	0.0	0.5
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	1.19	-0.25	0.50	0.44	0.13	-0.13	0.44	0.63	0.69	1.00
	SD	1.19	1.00	0.53	0.68	0.35	0.58	0.50	0.64	0.92	1.07
	MIN	-0.5	-2.0	0.0	0.0	0.0	-1.5	0.0	0.0	0.0	0.0
	MAX	3.0	1.0	1.5	2.0	1.0	0.5	1.5	1.5	2.5	2.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	-0.13 B^3	0 25	0.63	1 19 C^3	0.56	0.31	0.19	0.13	0.50	1.00
	SD	0.88	0 53	0.52	0.65	0.86	0.46	0.37	0.23	0.46	0.93
	MIN	-1.0	-0.5	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.5	1.0	1.5	2.5	2.5	1.0	1.0	0.5	1.0	2.5
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	0.19 A^3	1.81 C^3	-0.50	0 31	0.19	0.50	0.00	0.25	1.00	0.19
	SD	0.84	2.00	1.63	0 53	0.37	0.46	0.00	0.27	0.85	0.84
	MIN	-1.0	0.0	-4.5	0.0	-0.5	0.0	0.0	0.0	0.0	-1.5
	MAX	1.5	5.0	0.5	1.5	0.5	1.0	0.0	0.5	2.0	1.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.14 B^3	2.06 C^3	-0.19	0 19	0.13	0.44	0.13	0.38	0.88	0.31
	SD	1.38	1 57	1.89	0 26	0.23	0.56	0.23	0.35	0.74	0.65
	MIN	-2.0	0.5	-3.0	0.0	0.0	0.0	0.0	0.0	0.0	-1.0
	MAX	2.0	4.5	2.0	0.5	0.5	1.5	0.5	1.0	2.5	1.0
	N	7	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	-0.31	0.50	0.44	0.69	0.06	0.31	0.38	0 31	0.13	0.13
	SD	1.25	0.71	0.42	0.59	0.18	0.37	0.52	0 53	0.23	0.23
	MIN	-2.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	1.0	1.5	0.5	1.0	1.5	1 5	0.5	0.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	0.69	-0.44 B^3	0.38	0.19	0.06	0.25	0.56	0.81	0.13	0.25
	SD	2.22	1.55	0.44	0.26	0.18	0.38	1.21	1 33	0.23	0.38
	MIN	-2.5	-2.0	0.0	0.0	0.0	0.0	0.0	-2.0	0.0	0.0
	MAX	3.5	2.0	1.0	0.5	0.5	1.0	3.5	2.0	0.5	1.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	1.06	-0.25	0.25	0.19	0.44 C^3	0.00	0.44	0 38	0.00	0.38
	SD	0.90	0.85	0.27	0.26	0.32	0.00	0.42	0.44	0.00	0.35
	MIN	0.5	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	0.5	0.5	1.0	0.0	1.0	1.0	0.0	1.0
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.56	0.56	0.19	0.56	0.19	0.19	0.50	0.06	0.25	0.44
	SD	0.42	0.68	0.37	0.62	0.37	0.53	0.46	0 18	0.38	0.42
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	1.0	1.5	1.0	1.5	1.0	0 5	1.0	1.0
	N	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 37

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238
1	MEAN	0.00	0.88	-0.44	0.31	0.00	0.38
	SD	0.00	1.27	0.78	0.37	0.00	0.52
	MIN	0.0	0.0	-1.5	0.0	0.0	0.0
	MAX	0.0	3.0	0.5	1.0	0.0	1.0
	N	8	8	8	8	8	8
2	MEAN	0.06	0.00	0.38 B^3	0.13	0.63 C^3	0.19
	SD	0.18	0.00	0.58	0.44	0.52	0.53
	MIN	0.0	0.0	0.0	-0.5	0.0	0.0
	MAX	0.5	0.0	1.5	1.0	1.5	1.5
	N	8	8	8	8	8	8
3	MEAN	0.13	0.19	0.38 B^3	-0.38 C^3	0.13	0.06
	SD	0.35	0.26	0.74	0.74	0.35	0.18
	MIN	-0.5	0.0	0.0	-2.0	0.0	0.0
	MAX	0.5	0.5	2.0	0.0	1.0	0.5
	N	8	8	8	8	8	8
4	MEAN	0.06	0.13	-0.19	0.06	0.00	0.06
	SD	0.18	1.03	0.70	0.18	0.00	0.18
	MIN	0.0	-2.0	-1.5	0.0	0.0	0.0
	MAX	0.5	1.5	0.5	0.5	0.0	0.5
	N	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	MEAN	26.00	27.63	29.00	29.25	30.75	31.25	32.00	33.75	34.38	35.63	37.13
	SD	0.00	1.65	1.58	1 32	1.55	1.19	0.91	1.55	1.65	2 17	1.65
	MIN	26.0	26.5	27.0	27.5	29.0	30.0	31.0	32.5	32.5	32.5	35.0
	MAX	26.0	30.0	30.5	30.5	32.5	32.5	33.0	36.0	36.0	37.5	39.0
	N	4	4	4	4	4	4	4	4	4	4	4
2	MEAN	26.25	26.63	29.88	31.38	31.25	31.88	32.50	32.88	35.25	36.13	38.50
	SD	0.87	2.78	3.40	1.70	1.19	1.44	0.71	1.11	1.89	2.02	3.34
	MIN	25.5	24.0	26.5	30.0	30.0	30.0	32.0	32.0	34.0	34.5	35.5
	MAX	27.5	30.5	33.5	33.5	32.5	33.5	33.5	34.5	38.0	39.0	42.5
	N	4	4	4	4	4	4	4	4	4	4	4
3	MEAN	26.00	25.63	30.63	31.63	31.75	32.50	32.38	34.38	35.38	35.63	36.38
	SD	1.41	0.95	4.33	1 18	1.50	0.71	0.75	1.11	1.49	1.60	2.14
	MIN	25.0	25.0	25.5	30.0	30.0	31.5	31.5	33.0	34.0	34.5	35.0
	MAX	28.0	27.0	35.5	32.5	33.0	33.0	33.0	35.5	37.5	38.0	39.5
	N	4	4	4	4	4	4	4	4	4	4	4
4	MEAN	25.25	25.50	28.88	30.25	30.88	31.38	32.13	32.75	33.63	34.75	34.50
	SD	1.71	1.29	3.52	1.85	0.85	1.38	0.85	1.32	1.31	1 55	2.27
	MIN	23.0	24.0	25.0	27.5	30.0	30.0	31.0	31.5	32.5	32.5	32.5
	MAX	27.0	27.0	33.5	31.5	32.0	33.0	33.0	34.5	35.0	36.0	37.5
	N	4	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	MEAN	37.13	37.25	37.38	40.13	38.25	38.88	39.25	39.63	40.63	41.00
	SD	0.48	0.50	0.63	2.78	1.04	1.03	1.50	1.80	1.31	1.47
	MIN	36.5	36.5	36.5	37.5	37.0	38.0	38.0	38.0	39.5	39.5
	MAX	37.5	37.5	38.0	43.0	39.5	40.0	41.0	42.0	42.0	42.5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	39.13	38.13	38.88	39.00	39.25	40.00	40.25	40.88	41.13	41.50
	SD	3.40	1.93	2.43	2.35	2.18	2 12	2.06	2.43	2.14	2.27
	MIN	35.5	37.0	37.5	37.5	38.0	38.0	38.5	38.5	39.5	39.5
	MAX	42.5	41.0	42.5	42.5	42.5	42.5	42.5	44.0	44.0	44.5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	37.50	37.50	37.75	38.00	40.38	39.00	39.25	39.88	40.00	40.75
	SD	2.92	2.04	1.76	1.78	2.17	1.41	1.32	1.97	1.78	2.02
	MIN	35.0	35.5	36.0	36.0	38.5	37.0	37.5	37.5	38.0	38.0
	MAX	40.5	39.5	39.5	39.5	43.5	40.0	40.5	41.5	41.5	42.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	35.63	36.00	37.25	38.38	38.75	39.63	40.13	40.25	40.50	40.75
	SD	2.32	2.16	1.66	2.29	0.87	1 25	1.84	1.85	1.63	1.85
	MIN	32.5	33.0	36.0	36.0	38.0	38.0	38.0	38.0	38.5	38.5
	MAX	38.0	38.0	39.5	41.0	39.5	41.0	42.5	42.5	42.5	43.0
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	MEAN	41.13	43.00	42.13	42.25	42.25	43.38
	SD	1.65	2.58	2 17	1.85	1.85	1.18
	MIN	39.5	40.0	40.0	40.5	40.5	42.5
	MAX	43.0	46.0	44.0	44.5	44.5	45.0
	N	4	4	4	4	4	4
2	MEAN	41.63	41.75	42.75	42.38	42.75	43.13
	SD	2.14	2.02	2 33	1.70	1.44	0.95
	MIN	40.0	40.0	40.5	41.0	41.0	42.5
	MAX	44.5	44.5	45.0	44.5	44.5	44.5
	N	4	4	4	4	4	4
3	MEAN	41.00	41.13	42.50	41.63	41.63	41.75
	SD	2.12	2.25	0.71	1 93	1 93	1.94
	MIN	38.0	38.0	41.5	39.0	39.0	39.0
	MAX	42.5	43.0	43.0	43.5	43.5	43.5
	N	4	4	4	4	4	4
4	MEAN	40.88	41.63	41.63	41.88	41.88	42.25
	SD	1.84	2.06	2.06	1.65	1.65	2.10
	MIN	38.5	39.0	39.0	40.0	40.0	40.0
	MAX	43.0	43.5	43.5	43.5	43.5	44.5
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	MEAN	25.00	27.25	28.75	28.50	29.88	30.13	30.88	31.63	33.00	33.88	35.00
	SD	1.22	2.25	2.96	2.74	1.60	1.60	1.49	2.02	1.08	1 31	1.96
	MIN	23.5	25.5	26.0	25.5	28.5	28.5	29.0	30.0	32.0	32.5	33.0
	MAX	26.5	30.5	32.0	31.5	31.5	31.5	32.5	34.5	34.5	35.0	37.5
	N	4	4	4	4	4	4	4	4	4	4	4
2	MEAN	25.38	26.75	29.13	29.88	30.13	31.38	31.75	32.63	34.00	34.88	36.88
	SD	1.38	1.55	1.70	1 11	0.75	1.49	1.94	1.97	2.68	2.06	2.29
	MIN	24.0	25.0	27.0	28.5	29.5	29.5	29.5	31.0	31.0	33.0	33.5
	MAX	27.0	28.5	30.5	31.0	31.0	33.0	34.0	35.0	37.5	37.5	38.5
	N	4	4	4	4	4	4	4	4	4	4	4
3	MEAN	26.50	26.13	29.75	30.25	30.88	31.25	31.50	32.38	34.38	34.63	34.75
	SD	2.52	1.03	2.40	2 18	1.49	1.19	1.00	1.38	1.03	0.75	0.65
	MIN	24.0	25.0	27.5	28.5	29.5	30.5	31.0	31.0	33.5	34.0	34.0
	MAX	30.0	27.0	32.5	33.0	33.0	33.0	33.0	34.0	35.5	35.5	35.5
	N	4	4	4	4	4	4	4	4	4	4	4
4	MEAN	24.75	25.25	28.38	29.63	30.38	30.75	31.38	32.13	33.50	34.63	33.88
	SD	0.96	0.87	2.59	2 25	1.03	1.04	1.31	1.75	1.08	0 95	0.95
	MIN	24.0	24.0	26.0	26.5	29.5	29.5	29.5	30.0	32.0	34.0	32.5
	MAX	26.0	26.0	31.5	31.5	31.5	32.0	32.5	34.0	34.5	36.0	34.5
	N	4	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	MEAN	34.88	35.75	35.88	38.63	36.50	38.63	39.13	39.50	39.75	39.25
	SD	1.18	0.87	1.44	3.90	1.47	2 32	2.39	2.86	2.47	1.71
	MIN	34.0	35.0	35.0	35.0	35.0	35.5	36.0	36.0	37.0	37.0
	MAX	36.5	37.0	38.0	42.0	38.0	41.0	41.0	42.5	42.5	41.0
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	37.88	37.38	37.38	37.50	37.75	38.63	39.00	39.38	39.63	40.13
	SD	2.95	2.06	2.06	2.12	2.22	3.07	2.94	2.56	2.29	2.43
	MIN	35.5	35.5	35.5	35.5	35.5	35.5	36.0	36.5	37.0	37.0
	MAX	42.0	40.0	40.0	40.0	40.5	41.5	42.0	42.0	42.0	42.5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	37.25	37.75	38.00	37.50	39.75	38.25	38.63	38.75	38.75	39.63
	SD	2.06	1.44	1.15	1.00	2.63	0 96	0.85	0.65	0.65	0.75
	MIN	35.0	36.5	37.0	37.0	37.5	37.5	37.5	38.0	38.0	39.0
	MAX	39.0	39.0	39.0	39.0	43.5	39.5	39.5	39.5	39.5	40.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	34.63	35.13	35.50	37.38	36.50	38.38	39.25	39.25	39.38	40.00
	SD	0.48	0.48	0.71	3.77	0.58	1 11	1.32	1.32	1.25	0.71
	MIN	34.0	34.5	34.5	35.0	36.0	37.5	38.0	38.0	38.0	39.5
	MAX	35.0	35.5	36.0	43.0	37.0	40.0	41.0	41.0	41.0	41.0
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	MEAN	39.50	40.25	40.88	40.50	40.50	41.38
	SD	1.29	2.06	2.02	1.47	1.47	1.49
	MIN	38.0	38.0	38.5	38.5	38.5	39.5
	MAX	41.0	43.0	43.0	42.0	42.0	43.0
	N	4	4	4	4	4	4
2	MEAN	40.13	40.25	40.50	40.88	41.13	41.13
	SD	2.43	2.60	2 20	1.75	1.65	1.65
	MIN	37.0	37.0	38.0	39.0	39.0	39.0
	MAX	42.5	43.0	43.0	43.0	43.0	43.0
	N	4	4	4	4	4	4
3	MEAN	40.00	40.25	41.00	40.88	40.88	40.88
	SD	0.71	0.29	1 35	0.75	0.75	0.75
	MIN	39.5	40.0	40.0	40.5	40.5	40.5
	MAX	41.0	40.5	43.0	42.0	42.0	42.0
	N	4	4	4	4	4	4
4	MEAN	40.25	41.13	41.13	41.00	41.13	41.50
	SD	0.87	1.80	0.85	1 22	1 31	1.22
	MIN	39.5	39.5	40.0	40.0	40.0	40.0
	MAX	41.5	43.5	42.0	42.5	42.5	42.5
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	MEAN	25.50	27.44	28.88	28.88	30.31	30.69	31.44	32.69	33.69	34.75	36.06
	SD	0.96	1.84	2.20	2.03	1.53	1.44	1.29	2.02	1.49	1 91	2.03
	MIN	23.5	25.5	26.0	25.5	28.5	28.5	29.0	30.0	32.0	32.5	33.0
	MAX	26.5	30.5	32.0	31.5	32.5	32.5	33.0	36.0	36.0	37.5	39.0
	N	8	8	8	8	8	8	8	8	8	8	8
2	MEAN	25.81	26.69	29.50	30.63	30.69	31.63	32.13	32.75	34.63	35.50	37.69
	SD	1.16	2.09	2.52	1 55	1.10	1.38	1.41	1.49	2.25	2.00	2.79
	MIN	24.0	24.0	26.5	28.5	29.5	29.5	29.5	31.0	31.0	33.0	33.5
	MAX	27.5	30.5	33.5	33.5	32.5	33.5	34.0	35.0	38.0	39.0	42.5
	N	8	8	8	8	8	8	8	8	8	8	8
3	MEAN	26.25	25.88	30.19	30.94	31.31	31.88	31.94	33.38	34.88	35.13	35.56
	SD	1.91	0.95	3.27	1.78	1.46	1.13	0.94	1.58	1.30	1 27	1.70
	MIN	24.0	25.0	25.5	28.5	29.5	30.5	31.0	31.0	33.5	34.0	34.0
	MAX	30.0	27.0	35.5	33.0	33.0	33.0	33.0	35.5	37.5	38.0	39.5
	N	8	8	8	8	8	8	8	8	8	8	8
4	MEAN	25.00	25.38	28.63	29.94	30.63	31.06	31.75	32.44	33.56	34.69	34.19
	SD	1.31	1.03	2.88	1 94	0.92	1.18	1.10	1.47	1.12	1 19	1.65
	MIN	23.0	24.0	25.0	26.5	29.5	29.5	29.5	30.0	32.0	32.5	32.5
	MAX	27.0	27.0	33.5	31.5	32.0	33.0	33.0	34.5	35.0	36.0	37.5
	N	8	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

[redacted] (b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	MEAN	36.00	36.50	36.63	39.38	37.38	38.75	39.19	39.56	40.19	40.13
	SD	1.46	1.04	1.30	3.24	1.51	1.67	1.85	2.21	1.89	1.75
	MIN	34.0	35.0	35.0	35.0	35.0	35.5	36.0	36.0	37.0	37.0
	MAX	37.5	37.5	38.0	43.0	39.5	41.0	41.0	42.5	42.5	42.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	38.50	37.75	38.13	38.25	38.50	39.31	39.63	40.13	40.38	40.81
	SD	3.02	1.89	2.23	2.22	2.19	2.55	2.45	2.45	2.20	2.30
	MIN	35.5	35.5	35.5	35.5	35.5	35.5	36.0	36.5	37.0	37.0
	MAX	42.5	41.0	42.5	42.5	42.5	42.5	42.5	44.0	44.0	44.5
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	37.38	37.63	37.88	37.75	40.06	38.63	38.94	39.31	39.38	40.19
	SD	2.34	1.64	1.38	1.36	2.26	1.19	1.08	1.49	1.41	1.53
	MIN	35.0	35.5	36.0	36.0	37.5	37.0	37.5	37.5	38.0	38.0
	MAX	40.5	39.5	39.5	39.5	43.5	40.0	40.5	41.5	41.5	42.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	35.13	35.56	36.38	37.88	37.63	39.00	39.69	39.75	39.94	40.38
	SD	1.64	1.52	1.51	2.94	1.38	1.28	1.56	1.58	1.47	1.36
	MIN	32.5	33.0	34.5	35.0	36.0	37.5	38.0	38.0	38.0	38.5
	MAX	38.0	38.0	39.5	43.0	39.5	41.0	42.5	42.5	42.5	43.0
	N	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 38

(b) (4)

HEIGHT MEASUREMENTS (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	MEAN	40.31	41.63	41.50	41.38	41.38	42.38
	SD	1.62	2.62	2.05	1.81	1.81	1.64
	MIN	38.0	38.0	38.5	38.5	38.5	39.5
	MAX	43.0	46.0	44.0	44.5	44.5	45.0
	N	8	8	8	8	8	8
2	MEAN	40.88	41.00	41.63	41.63	41.94	42.13
	SD	2.26	2.30	2.42	1.79	1.68	1.64
	MIN	37.0	37.0	38.0	39.0	39.0	39.0
	MAX	44.5	44.5	45.0	44.5	44.5	44.5
	N	8	8	8	8	8	8
3	MEAN	40.50	40.69	41.75	41.25	41.25	41.31
	SD	1.56	1.56	1 28	1.41	1.41	1.44
	MIN	38.0	38.0	40.0	39.0	39.0	39.0
	MAX	42.5	43.0	43.0	43.5	43.5	43.5
	N	8	8	8	8	8	8
4	MEAN	40.56	41.38	41.38	41.44	41.50	41.88
	SD	1.37	1.81	1.48	1.43	1.44	1.64
	MIN	38.5	39.0	39.0	40.0	40.0	40.0
	MAX	43.0	43.5	43.5	43.5	43.5	44.5
	N	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 39

(b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	1.63	1.38	0 25	1.50	0.50	0.75	1.75	0.63	1.25	1 50
	SD	1.65	2.32	0 29	2.38	0.41	0.50	1.19	0.95	1.89	1 22
	MIN	0.5	-1.5	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0
	MAX	4.0	3.5	0 5	5.0	1.0	1.0	3.0	2.0	4.0	2 5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	0.38	3.25	1 50	-0.13	0.63	0.63	0.38	2.38	0.88	2 38
	SD	3.52	4.63	1.78	0.63	0.75	0.95	0.48	1.03	0.85	2.78
	MIN	-3.5	-3.0	0.0	-1.0	0.0	0.0	0.0	1.5	0.0	0 5
	MAX	5.0	7.0	3 5	0.5	1.5	2.0	1.0	3.5	2.0	6 5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	-0.38	5.00	1.00	0.13	0.75	-0.13	2.00	1.00	0.25	0.75
	SD	1.80	3.54	4 55	1.25	1.19	0.25	1.35	0.82	0.29	0.65
	MIN	-3.0	0.5	-4.0	-1.5	0.0	-0.5	0.0	0.0	0.0	0.0
	MAX	1.0	8.5	7.0	1.5	2.5	0.0	3.0	2.0	0.5	1 5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	0.25	3.38	1 38	0.63	0.50	0.75	0.63	0.88	1.13	-0.25 A^3
	SD	2.22	3.09	2 59	1.89	1.00	0.65	0.95	0.85	1.31	1.66
	MIN	-3.0	1.0	-2.5	-1.5	0.0	0.0	0.0	0.0	0.0	-2.5
	MAX	2.0	7.5	3.0	3.0	2.0	1.5	2.0	2.0	3.0	1 5
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 39

(b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	0.00	0.13	0.13	2.75	-1.88	0.63	0.38	0 38	1.00	0.38
	SD	1.47	0.25	0.25	2.90	3.42	0.48	0.48	0.48	0.71	0.48
	MIN	-2.0	0.0	0.0	0.0	-5.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.5	0.5	0.5	5.5	2.0	1.0	1.0	1.0	1.5	1.0
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	0.63	-1.00 B^3	0.75	0.13 B^3	0.25 A^3	0.75	0.25	0.63	0.25 A^3	0.38
	SD	5.50	2.74	0.65	0.25	0.29	1.50	0.29	0.75	0.50	0.25
	MIN	-7.0	-4.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	6.0	2.0	1.5	0.5	0.5	3.0	0.5	1 5	1.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	1.13	0.00	0.25	0.25 C^3	2.38 C^3	-1.38 C^3	0.25	0.63	0.13 B^3	0.75
	SD	1.65	1.08	0.29	0.29	3.47	3.42	0.29	0.75	0.25	0.65
	MIN	0.0	-1.5	0.0	0.0	0.0	-6.5	0.0	0.0	0.0	0.0
	MAX	3.5	1.0	0.5	0.5	7.5	0.5	0.5	1 5	0.5	1.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	1.13	0.38	1.25	1.13	0.38	0.88	0.50	0 13	0.25 B^3	0.25
	SD	1.11	0.25	1.32	1.65	2.69	0.75	0.71	0 25	0.29	0.29
	MIN	0.0	0.0	0.0	0.0	-3.0	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	3.0	3.5	3.5	1.5	1.5	0 5	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238
1	MEAN	0.13	1.88	-0.88	0.13	0.00	1.13
	SD	0.25	1.93	2.39	0.85	0.00	0.75
	MIN	0.0	0.0	-3.5	-1.0	0.0	0.5
	MAX	0.5	4.0	2.0	1.0	0.0	2.0
	N	4	4	4	4	4	4
2	MEAN	0.13	0.13 B^3	1.00	-0.38	0.38	0.38 B^3
	SD	0.25	0.25	1.35	1.11	0.75	0.75
	MIN	0.0	0.0	0.0	-2.0	0.0	0.0
	MAX	0.5	0.5	3.0	0.5	1.5	1.5
	N	4	4	4	4	4	4
3	MEAN	0.25	0.13 B^3	1.38	-0.88	0.00	0.13 C^3
	SD	0.29	0.25	2.43	2.10	0.00	0.25
	MIN	0.0	0.0	0.0	-4.0	0.0	0.0
	MAX	0.5	0.5	5.0	0.5	0.0	0.5
	N	4	4	4	4	4	4
4	MEAN	0.13	0.75	0.00	0.25	0.00	0.38 A^3
	SD	0.25	0.87	0.00	0.50	0.00	0.75
	MIN	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	0.5	2.0	0.0	1.0	0.0	1.5
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 39

(b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	2.25	1.50	-0.25	1.38	0.25	0.75	0.75	1.38	0.88	1 13
	SD	3.18	4.53	1 32	1.25	0.29	0.96	0.96	1.25	1.44	2.69
	MIN	0.5	-4.0	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	-2.0
	MAX	7.0	6.5	1.0	3.0	0.5	2.0	2.0	3.0	3.0	4 5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	1.38	2.38	0.75	0.25	1.25	0.38	0.88	1.38	0.88	2.00
	SD	2.50	1.89	1 19	0.50	1.19	0.48	0.63	1.31	1.03	2.61
	MIN	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	4.0	4.5	2 5	1.0	2.5	1.0	1.5	2.5	2.0	5 5
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	-0.38	3.63	0 50	0.63	0.38	0.25	0.88	2.00	0.25	0 13
	SD	2.06	3.35	3.89	1.70	0.48	0.29	0.85	0.71	0.29	0.48
	MIN	-3.0	0.5	-4.0	-1.5	0.0	0.0	0.0	1.0	0.0	-0.5
	MAX	1.5	7.0	5 5	2.0	1.0	0.5	2.0	2.5	0.5	0 5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	0.50	3.13	1 25	0.75	0.38	0.63	0.75	1.38	1.13	-0.75 A^3
	SD	1.78	2.29	1 32	1.50	0.48	0.75	0.87	1.55	1.31	1.85
	MIN	-2.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-3.5
	MAX	2.0	6.0	3.0	3.0	1.0	1.5	2.0	3.5	2.5	0 5
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	-0.13	0.88	0.13	2.75	-2.13	2.13	0.50	0 38	0.25	-0.50
	SD	1.65	0.48	0.63	3.40	3.84	1.18	0.71	0.75	0.50	1.35
	MIN	-2.5	0.5	-0.5	0.0	-6.5	0.5	0.0	0.0	0.0	-2.5
	MAX	1.0	1.5	1.0	7.0	2.0	3.0	1.5	1 5	1.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
2	MEAN	1.00	-0.50 B^3	0.00	0.13 B^3	0.25 A^3	0.88	0.38	0 38	0.25 A^3	0.50
	SD	3.24	1.00	0.00	0.25	0.29	1.44	0.25	0.48	0.29	0.41
	MIN	-3.0	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	4.5	0.0	0.0	0.5	0.5	3.0	0.5	1.0	0.5	1.0
	N	4	4	4	4	4	4	4	4	4	4
3	MEAN	2.50	0.50	0.25	-0.50 C^3	2.25 C^3	-1.50 C^3	0.38	0 13	0.00 B^3	0.88
	SD	2.61	0.71	0.29	1.00	2.87	3.00	0.48	0 25	0.00	0.48
	MIN	0.0	0.0	0.0	-2.0	0.5	-6.0	0.0	0.0	0.0	0.5
	MAX	5.0	1.5	0.5	0.0	6.5	0.0	1.0	0 5	0.0	1.5
	N	4	4	4	4	4	4	4	4	4	4
4	MEAN	0.75	0.50	0.38	1.88	-0.88	1.88	0.88	0.00	0.13 B^3	0.63
	SD	0.65	0.00	0.48	3.42	4.13	1.55	0.48	0.00	0.25	0.75
	MIN	0.0	0.5	0.0	0.0	-7.0	0.5	0.5	0.0	0.0	0.0
	MAX	1.5	0.5	1.0	7.0	2.0	4.0	1.5	0.0	0.5	1.5
	N	4	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 39

(q) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238
1	MEAN	0.25	0.75	0.63	-0.38	0.00	0.88
	SD	0.50	0.96	1.70	1.11	0.00	1.18
	MIN	0.0	0.0	-1.0	-2.0	0.0	0.0
	MAX	1.0	2.0	3.0	0.5	0.0	2.5
	N	4	4	4	4	4	4
2	MEAN	0.00	0.13 B^3	0.25	0.38	0.25	0.00 B^3
	SD	0.00	0.25	0.50	0.48	0.50	0.00
	MIN	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	0.0	0.5	1.0	1.0	1.0	0.0
	N	4	4	4	4	4	4
3	MEAN	0.38	0.25 B^3	0.75	-0.13	0.00	0.00 C^3
	SD	0.25	0.65	1.50	0.63	0.00	0.00
	MIN	0.0	-0.5	0.0	-1.0	0.0	0.0
	MAX	0.5	1.0	3.0	0.5	0.0	0.0
	N	4	4	4	4	4	4
4	MEAN	0.25	0.88	0.00	-0.13	0.13	0.38 A^3
	SD	0.29	1.75	1.87	0.95	0.25	0.48
	MIN	0.0	0.0	-2.5	-1.5	0.0	0.0
	MAX	0.5	3.5	2.0	0.5	0.5	1.0
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	1.94	1.44	0.00	1.44	0.38	0.75	1.25	1.00	1.06	1 31
	SD	2.37	3.33	0 93	1.76	0.35	0.71	1.13	1.10	1.57	1 94
	MIN	0.5	-4.0	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	-2.0
	MAX	7.0	6.5	1.0	5.0	1.0	2.0	3.0	3.0	4.0	4 5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	0.88	2.81	1 13	0.06	0.94	0.50	0.63	1.88	0.88	2 19
	SD	2.88	3.31	1.46	0.56	0.98	0.71	0.58	1.22	0.88	2 51
	MIN	-3.5	-3.0	0.0	-1.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	5.0	7.0	3 5	1.0	2.5	2.0	1.5	3.5	2.0	6 5
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	-0.38	4.31	0.75	0.38	0.56	0.06	1.44	1.50	0.25	0.44
	SD	1.79	3.27	3 93	1.41	0.86	0.32	1.21	0.89	0.27	0.62
	MIN	-3.0	0.5	-4.0	-1.5	0.0	-0.5	0.0	0.0	0.0	-0.5
	MAX	1.5	8.5	7.0	2.0	2.5	0.5	3.0	2.5	0.5	1 5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.38	3.25	1 31	0.69	0.44	0.69	0.69	1.13	1.13	-0.50 A^3
	SD	1.87	2.52	1 91	1.58	0.73	0.65	0.84	1.19	1.22	1.65
	MIN	-3.0	0.5	-2.5	-1.5	0.0	0.0	0.0	0.0	0.0	-3.5
	MAX	2.0	7.5	3.0	3.0	2.0	1.5	2.0	3.5	3.0	1 5
	N	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 39

(b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	-0.06	0.50	0.13	2.75	-2.00	1.38	0.44	0 38	0.63	-0.06
	SD	1.45	0.53	0.44	2.93	3.37	1.16	0.56	0 58	0.69	1.05
	MIN	-2.5	0.0	-0.5	0.0	-6.5	0.0	0.0	0.0	0.0	-2.5
	MAX	1.5	1.5	1.0	7.0	2.0	3.0	1.5	1 5	1.5	1.0
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	0.81	-0.75 B^3	0.38	0.13 B^3	0.25 A^3	0.81	0.31	0 50	0.25 A^3	0.44
	SD	4.18	1.93	0.58	0.23	0.27	1.36	0.26	0.60	0.38	0.32
	MIN	-7.0	-4.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	6.0	2.0	1.5	0.5	0.5	3.0	0.5	1 5	1.0	1.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	1.81	0.25	0.25	-0.13 C^3	2.31 C^3	-1.44 C^3	0.31	0 38	0.06 B^3	0.81
	SD	2.15	0.89	0.27	0.79	2.95	2.98	0.37	0 58	0.18	0.53
	MIN	0.0	-1.5	0.0	-2.0	0.0	-6.5	0.0	0.0	0.0	0.0
	MAX	5.0	1.5	0.5	0.5	7.5	0.5	1.0	1 5	0.5	1.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.94	0.44	0.81	1.50	-0.25	1.38	0.69	0.06	0.19 B^3	0.44
	SD	0.86	0.18	1.03	2.52	3.30	1.25	0.59	0 18	0.26	0.56
	MIN	0.0	0.0	0.0	0.0	-7.0	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	3.0	7.0	3.5	4.0	1.5	0 5	0.5	1.5
	N	8	8	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 39

(b) (4)

HEIGHT MEASUREMENT CHANGES (cm) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238
1	MEAN	0.19	1.31	-0.13	-0.13	0.00	1.00
	SD	0.37	1.53	2.08	0.95	0.00	0.93
	MIN	0.0	0.0	-3.5	-2.0	0.0	0.0
	MAX	1.0	4.0	3.0	1.0	0.0	2.5
	N	8	8	8	8	8	8
2	MEAN	0.06	0.13 B^3	0.63	0.00	0.31	0.19 B^3
	SD	0.18	0.23	1.03	0.89	0.59	0.53
	MIN	0.0	0.0	0.0	-2.0	0.0	0.0
	MAX	0.5	0.5	3.0	1.0	1.5	1.5
	N	8	8	8	8	8	8
3	MEAN	0.31	0.19 B^3	1.06	-0.50	0.00	0.06 C^3
	SD	0.26	0.46	1.90	1.49	0.00	0.18
	MIN	0.0	-0.5	0.0	-4.0	0.0	0.0
	MAX	0.5	1.0	5.0	0.5	0.0	0.5
	N	8	8	8	8	8	8
4	MEAN	0.19	0.81	0.00	0.06	0.06	0.38 A^3
	SD	0.26	1.28	1.22	0.73	0.18	0.58
	MIN	0.0	0.0	-2.5	-1.5	0.0	0.0
	MAX	0.5	3.5	2.0	1.0	0.5	1.5
	N	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 40 (b) (4)

WEEKLY CAGE FOOD CONSUMPTION (g) SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
CAGE (MALES AND FEMALES)

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 1	Week 2
1	MEAN	212.5	286.0
	SD	22.5	23.3
	MIN	185	257
	MAX	238	313
	N	4	4
2	MEAN	205.5	287.5
	SD	22.9	16.3
	MIN	191	273
	MAX	239	311
	N	4	4
3	MEAN	176.9 **B**	269.5
	SD	4.2	10.8
	MIN	173	257
	MAX	183	283
	N	4	4
4	MEAN	220.3	282.6
	SD	28.6	30.9
	MIN	181	248
	MAX	245	320
	N	4	4

Significant differences against group 1: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across days: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

TABLE NO. 40 (b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
1	MEAN	153.9	175.7	198.0	218.8	232.0	230.9	246.4	257.2
	SD	16.2	31.8	29.1	42.8	37.1	28.0	40.6	29.3
	MIN	139	149	164	168	196	202	196	222
	MAX	176	214	228	263	269	258	281	283
	N	4	4	4	4	4	4	4	4
2	MEAN	146.1	162.6	186.7	206.6	224.0	243.1	240.0	257.3
	SD	23.5	26.6	35.9	32.7	46.8	45.5	42.2	48.7
	MIN	125	139	156	174	185	193	189	204
	MAX	171	192	227	239	282	304	284	316
	N	4	4	4	4	4	4	4	4
3	MEAN	140.2	151.1	165.4	185.2	192.8 B^3	216.0	201.9 B^3	216.4 B^3
	SD	19.6	8.9	13.0	28.9	21.1	26.5	23.8	25.7
	MIN	124	141	153	161	173	196	182	187
	MAX	163	162	180	221	221	253	236	243
	N	4	4	4	4	4	4	4	4
4	MEAN	147.1	164.8	179.0	201.3	223.5	221.0	226.3	236.9
	SD	15.8	16.5	10.8	23.5	31.0	21.8	31.7	40.3
	MIN	129	141	171	176	193	199	198	182
	MAX	166	178	194	228	255	242	255	269
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17	Week 18
1	MEAN	269.4	277.3	255.9	279.5	264.2	275.3	251.0	268.0
	SD	37.1	27.8	28.2	35.0	30.1	31.8	26.9	25.6
	MIN	236	258	229	238	224	241	214	242
	MAX	319	318	284	322	295	306	272	303
	N	4	4	4	4	4	4	4	4
2	MEAN	260.5	245.3	245.4	248.0	274.9	253.8	274.3 B^3	264 5
	SD	51.2	43.9	38.8	26.3	34.2	34.4	41.8	42.3
	MIN	208	191	198	209	235	210	227	217
	MAX	330	293	293	266	318	287	328	320
	N	4	4	4	4	4	4	4	4
3	MEAN	218.2 B^3	226.8 B^3	229.4	218.0 C^3	234.2	219 2 B^3	230.1	220.8 B^3
	SD	20.5	31.2	35.2	22.6	17.5	31.3	25.2	30.2
	MIN	200	204	181	198	209	183	207	188
	MAX	237	273	265	239	247	257	258	257
	N	4	4	4	4	4	4	4	4
4	MEAN	239.9	256.9	256.0	249.0	257.4	257.6	261.1	269 1
	SD	33.5	32.1	40.7	40.1	37.8	43.5	37.0	55.7
	MIN	206	226	215	202	212	213	211	220
	MAX	275	291	302	296	289	296	298	324
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 19	Week 20	Week 21	Week 22	Week 23	Week 24	Week 25	Week 26
1	MEAN	254.0	262.8	252.4	250.3	252.4	246.5	237.8	220.6
	SD	30.7	26.8	19.7	32.8	10.5	9.8	22.7	11.8
	MIN	227	236	239	223	238	233	210	205
	MAX	285	295	282	296	260	255	258	232
	N	4	4	4	4	4	4	4	4
2	MEAN	270.2 B^3	256.3	258.8	258.4	249.0	259.6 A^3	251.9 B^3	238.4 A^3
	SD	46.9	47.8	34.0	54.1	49.5	45.4	50.6	47.2
	MIN	240	207	233	218	211	232	220	202
	MAX	339	321	308	337	322	327	327	308
	N	4	4	4	4	4	4	4	4
3	MEAN	242.2	229.0 A^3	215.1	217.7	213.5	237.3	206 2	197.7
	SD	27.3	26.3	26.7	20.6	27.3	30.4	17.3	18.4
	MIN	206	199	179	200	176	203	191	170
	MAX	273	252	243	246	241	271	224	209
	N	4	4	4	4	4	4	4	4
4	MEAN	267.6 B^3	257.6	263.3	268.0	255.1	258.1 A^3	243 9	238.5
	SD	43.5	35.3	41.7	45.9	41.7	47.6	39.1	36.1
	MIN	211	213	208	203	197	206	188	200
	MAX	315	295	309	303	295	322	279	279
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
1	MEAN	127.3	146.0	161.8	181.8	196.1	184.9	205.3	206.2
	SD	11.2	18.0	22.2	34.2	27.3	17.8	25.4	20.9
	MIN	112	119	134	134	156	159	169	176
	MAX	137	159	187	208	216	198	229	223
	N	4	4	4	4	4	4	4	4
2	MEAN	128.1	148.8	168.8	188.1	201.4	216.2	216.0	230.7
	SD	13.4	9.0	13.6	21.2	24.2	37.9	35.3	47.3
	MIN	118	138	157	163	181	192	183	182
	MAX	148	160	184	214	230	273	263	295
	N	4	4	4	4	4	4	4	4
3	MEAN	108.1	125.6	136.8	155.0	168.1 B^3	181.5	182.4 B^3	189.4 B^3
	SD	18.9	11.2	12.1	10.6	14.3	16.5	35.8	20.9
	MIN	90	118	126	145	153	167	154	178
	MAX	135	142	149	166	186	204	234	221
	N	4	4	4	4	4	4	4	4
4	MEAN	127.3	153.5	164.8	183.6	197.4	210.3	216.2	220.9
	SD	16.5	21.3	19.0	29.1	25.8	22.9	12.8	13.3
	MIN	109	133	142	160	163	177	203	202
	MAX	145	183	186	224	223	229	231	233
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17	Week 18
1	MEAN	204.6	208.3	200.1	215.8	195.9	212.4	203.2	215.7
	SD	14.6	6.8	5.9	16.4	5.8	6.5	6.7	7.6
	MIN	191	200	192	196	190	204	197	209
	MAX	225	214	206	236	203	219	212	226
	N	4	4	4	4	4	4	4	4
2	MEAN	234.4	225.7	221.3	222.8	225.7	219.8	240.5 B^3	234 9
	SD	44.0	12.6	31.2	29.1	32.4	23.5	37.2	36.6
	MIN	186	213	199	193	197	197	204	194
	MAX	293	242	268	250	272	252	293	277
	N	4	4	4	4	4	4	4	4
3	MEAN	195.6 B^3	188.6 B^3	199.1	190.5 C^3	198.3	207 2 B^3	208.7	202.5 B^3
	SD	18.0	22.2	24.4	24.3	30.0	26.6	36.1	20.5
	MIN	175	162	172	171	164	184	183	179
	MAX	218	210	227	226	233	244	260	228
	N	4	4	4	4	4	4	4	4
4	MEAN	232.4	235.0	228.9	216.6	235.0	242.6	235.6	225.7
	SD	21.4	28.5	10.8	26.6	18.0	18.7	14.3	24.5
	MIN	203	199	219	196	220	225	218	208
	MAX	254	268	239	256	260	267	252	262
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 19	Week 20	Week 21	Week 22	Week 23	Week 24	Week 25	Week 26
1	MEAN	192.4	208.4	198.6	195.8	188.4	185.3	184 5	185.1
	SD	4.6	14.7	12.9	11.9	12.6	6.1	9.2	8.8
	MIN	189	189	183	180	177	177	172	172
	MAX	199	224	212	208	200	191	193	192
	N	4	4	4	4	4	4	4	4
2	MEAN	236.3 B^3	225.7	217.9	209.4	223.5	221.6 A^3	232.5 B^3	217.3 A^3
	SD	44.0	43.4	22.8	32.2	18.9	30.9	36.9	52.3
	MIN	193	190	194	168	208	199	198	176
	MAX	297	278	244	241	251	266	283	294
	N	4	4	4	4	4	4	4	4
3	MEAN	208.1	189.0 A^3	200.0	196.1	183.5	182.5	185 5	178.6
	SD	38.6	21.7	41.4	30.9	16.4	7.9	38.8	21.4
	MIN	176	172	169	167	172	173	151	165
	MAX	261	219	260	238	207	192	241	210
	N	4	4	4	4	4	4	4	4
4	MEAN	244.7 B^3	224.1	218.7	219.9	212.4	224.8 A^3	214 3	198.6
	SD	17.0	26.0	28.2	28.3	28.2	3.9	11.5	11.0
	MIN	225	200	194	186	183	222	202	187
	MAX	266	261	253	256	248	230	224	214
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
1	MEAN	140.6	160.8	179.9	200.3	214.0	207.9	225.9	231.7
	SD	19.2	28.7	30.8	40.9	35.7	32.8	38.3	36.0
	MIN	112	119	134	134	156	159	169	176
	MAX	176	214	228	263	269	258	281	283
	N	8	8	8	8	8	8	8	8
2	MEAN	137.1	155.7	177.7	197.4	212.7	229.7	228.0	244.0
	SD	20.2	19.8	26.9	27.4	36.5	41.3	38.2	46.6
	MIN	118	138	156	163	181	192	183	182
	MAX	171	192	227	239	282	304	284	316
	N	8	8	8	8	8	8	8	8
3	MEAN	124.2	138.4	151.1	170.1	180.5 B^3	198.8	192.2 B^3	202.9 B^3
	SD	24.7	16.5	19.2	25.8	21.3	27.5	30.0	26.0
	MIN	90	118	126	145	153	167	154	178
	MAX	163	162	180	221	221	253	236	243
	N	8	8	8	8	8	8	8	8
4	MEAN	137.2	159.1	171.9	192.5	210.4	215.6	221.2	228.9
	SD	18.3	18.6	16.2	26.3	29.8	21.5	23.0	29.1
	MIN	109	133	142	160	163	177	198	182
	MAX	166	183	194	228	255	242	255	269
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17	Week 18
1	MEAN	237.0	242.8	228.0	247.6	230.1	243.9	227.1	241.8
	SD	43.4	41.4	35.2	42.4	41.7	39.8	31.3	32.9
	MIN	191	200	192	196	190	204	197	209
	MAX	319	318	284	322	295	306	272	303
	N	8	8	8	8	8	8	8	8
2	MEAN	247.5	235.5	233.4	235.4	250.3	236.8	257.4 B^3	249.7
	SD	46.3	31.7	35.0	29.0	40.5	32.8	40.8	39.9
	MIN	186	191	198	193	197	197	204	194
	MAX	330	293	293	266	318	287	328	320
	N	8	8	8	8	8	8	8	8
3	MEAN	206.9 B^3	207.7 B^3	214.3	204.3 C^3	216.2	213 2 B^3	219.4	211.7 B^3
	SD	21.6	32.3	32.4	26.2	29.7	27.6	31.1	25.8
	MIN	175	162	172	171	164	183	183	179
	MAX	237	273	265	239	247	257	260	257
	N	8	8	8	8	8	8	8	8
4	MEAN	236.1	246.0	242.4	232.8	246.2	250.1	248.4	247.4
	SD	26.4	30.5	31.1	36.0	29.9	32.0	29.3	46.1
	MIN	203	199	215	196	212	213	211	208
	MAX	275	291	302	296	289	296	298	324
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 40 (b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 19	Week 20	Week 21	Week 22	Week 23	Week 24	Week 25	Week 26
1	MEAN	223.2	235.6	225.5	223.0	220.4	215.9	211 1	202.8
	SD	38.7	35.3	32.6	37.0	35.9	33.5	32.7	21.3
	MIN	189	189	183	180	177	177	172	172
	MAX	285	295	282	296	260	255	258	232
	N	8	8	8	8	8	8	8	8
2	MEAN	253.2 B^3	241.0	238.3	233.9	236.2	240.6 A^3	242.2 B^3	227.8 A^3
	SD	45.8	45.3	34.6	48.8	37.3	41.3	42.3	47.5
	MIN	193	190	194	168	208	199	198	176
	MAX	339	321	308	337	322	327	327	308
	N	8	8	8	8	8	8	8	8
3	MEAN	225.1	209.0 A^3	207.6	206.9	198.5	209.9	195.8	188.2
	SD	35.9	30.9	33.2	26.9	26.3	35.8	29.9	21.1
	MIN	176	172	169	167	172	173	151	165
	MAX	273	252	260	246	241	271	241	210
	N	8	8	8	8	8	8	8	8
4	MEAN	256.2 B^3	240.9	241.0	243.9	233.8	241.4 A^3	229 1	218.6
	SD	32.9	33.8	40.7	43.7	40.1	36.0	31.0	32.6
	MIN	211	200	194	186	183	206	188	187
	MAX	315	295	309	303	295	322	279	279
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 41

[redacted] (b) (4)

BODY TEMPERATURE (RECTAL) (Degree Celsius) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	MEAN	38.18	38.30	38.45	38.30	38.43	38.15	38.18	38.63
	SD	0.05	0.14	0.24	0 27	0.48	0.34	0.10	0.17
	MIN	38.1	38.2	38.2	38.1	38.0	37.7	38.1	38.4
	MAX	38.2	38.5	38.7	38.7	39.1	38.5	38.3	38.8
	N	4	4	4	4	4	4	4	4
2	MEAN	38.18	38.40	38.30	38.40	38.45	38.10	38.10	38.90
	SD	0.15	0.22	0.12	0 36	0.47	0.24	0.41	0.28
	MIN	38.1	38.1	38.2	38.1	38.1	37.8	37.5	38.7
	MAX	38.4	38.6	38.4	38.9	39.1	38.4	38.4	39.3
	N	4	4	4	4	4	4	4	4
3	MEAN	38.20	38.33	38.53	38.53	38.35	38.15	38.15	38.65
	SD	0.22	0.21	0.13	0 17	0.24	0.24	0.31	0.30
	MIN	37.9	38.1	38.4	38.3	38.1	37.9	37.8	38.4
	MAX	38.4	38.5	38.7	38.7	38.6	38.4	38.5	39.0
	N	4	4	4	4	4	4	4	4
4	MEAN	38.33	38.45	38.38	38.38	38.55	38.50	38.25	38.68
	SD	0.58	0.25	0.25	0 10	0.29	0.18	0.25	0.15
	MIN	37.7	38.1	38.1	38.3	38.2	38.3	38.0	38.5
	MAX	39.1	38.7	38.7	38.5	38.9	38.7	38.6	38.8
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 41 [redacted] (b) (4)

BODY TEMPERATURE (RECTAL) (Degree Celsius) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS
1	MEAN	38.33
	SD	0.15
	MIN	38.1
	MAX	38.5
	N	4
2	MEAN	38.35
	SD	0.17
	MIN	38.2
	MAX	38.6
	N	4
3	MEAN	38.36
	SD	0.06
	MIN	38.3
	MAX	38.4
	N	4
4	MEAN	38.44
	SD	0.15
	MIN	38.3
	MAX	38.6
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 41

(b) (4)2

BODY TEMPERATURE (RECTAL) (Degree Celsius) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	MEAN	38.15	38.43	38.30	38.28	38.53	38.40	38.35	39.00
	SD	0.25	0.21	0.12	0 26	0.22	0.12	0.42	0.39
	MIN	37.8	38.2	38.2	37.9	38.3	38.3	37.8	38.6
	MAX	38.4	38.6	38.4	38.5	38.8	38.5	38.8	39.5
	N	4	4	4	4	4	4	4	4
2	MEAN	38.33	38.45	38.40	38.50	38.65	38.40	38.33	38.75
	SD	0.71	0.13	0.14	0 37	0.13	0.08	0.36	0.13
	MIN	37.7	38.3	38.3	38.1	38.5	38.3	38.0	38.6
	MAX	39.2	38.6	38.6	38.9	38.8	38.5	38.8	38.9
	N	4	4	4	4	4	4	4	4
3	MEAN	38.28	38.25	38.33	38.43	38.35	38.28	38.25	38.75
	SD	0.32	0.38	0.17	0 19	0.17	0.13	0.33	0.44
	MIN	38.0	38.0	38.1	38.3	38.2	38.1	37.9	38.4
	MAX	38.6	38.8	38.5	38.7	38.6	38.4	38.7	39.3
	N	4	4	4	4	4	4	4	4
4	MEAN	38.40	38.30	38.35	38.30	38.45	38.38	38.18	38.50
	SD	0.62	0.14	0.13	0.41	0.37	0.21	0.15	0.14
	MIN	37.9	38.2	38.2	38.0	38.0	38.1	38.0	38.3
	MAX	39.3	38.5	38.5	38.9	38.8	38.6	38.3	38.6
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 41 [redacted] (b) (4)

BODY TEMPERATURE (RECTAL) (Degree Celsius) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS
1	MEAN	38.43
	SD	0.18
	MIN	38.3
	MAX	38.7
	N	4
2	MEAN	38.48
	SD	0.16
	MIN	38.3
	MAX	38.7
	N	4
3	MEAN	38.36
	SD	0.12
	MIN	38.3
	MAX	38.5
	N	4
4	MEAN	38.36
	SD	0.21
	MIN	38.1
	MAX	38.6
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 41

(b) (4)

BODY TEMPERATURE (RECTAL) (Degree Celsius) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	MEAN	38.16	38.36	38.38	38.29	38.48	38.28	38.26	38.81
	SD	0.17	0.18	0.19	0 25	0.35	0.27	0.30	0.34
	MIN	37.8	38.2	38.2	37.9	38.0	37.7	37.8	38.4
	MAX	38.4	38.6	38.7	38.7	39.1	38.5	38.8	39.5
	N	8	8	8	8	8	8	8	8
2	MEAN	38.25	38.43	38.35	38.45	38.55	38.25	38.21	38.83
	SD	0.48	0.17	0.13	0 34	0.34	0.23	0.38	0.22
	MIN	37.7	38.1	38.2	38.1	38.1	37.8	37.5	38.6
	MAX	39.2	38.6	38.6	38.9	39.1	38.5	38.8	39.3
	N	8	8	8	8	8	8	8	8
3	MEAN	38.24	38.29	38.43	38.48	38.35	38.21	38.20	38.70
	SD	0.26	0.29	0.18	0 18	0.19	0.19	0.30	0.35
	MIN	37.9	38.0	38.1	38.3	38.1	37.9	37.8	38.4
	MAX	38.6	38.8	38.7	38.7	38.6	38.4	38.7	39.3
	N	8	8	8	8	8	8	8	8
4	MEAN	38.36	38.38	38.36	38.34	38.50	38.44	38.21	38.59
	SD	0.56	0.21	0.18	0 28	0.31	0.19	0.20	0.16
	MIN	37.7	38.1	38.1	38.0	38.0	38.1	38.0	38.3
	MAX	39.3	38.7	38.7	38.9	38.9	38.7	38.6	38.8
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 41 (b) (4)

BODY TEMPERATURE (RECTAL) (Degree Celsius) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS
1	MEAN	38.38
	SD	0.16
	MIN	38.1
	MAX	38.7
	N	8
2	MEAN	38.41
	SD	0.17
	MIN	38.2
	MAX	38.7
	N	8
3	MEAN	38.36
	SD	0.09
	MIN	38.3
	MAX	38.5
	N	8
4	MEAN	38.40
	SD	0.18
	MIN	38.1
	MAX	38.6
	N	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 42

(b) (4)

HEART RATE (Beats/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	MEAN	181.0	173.0	160.0	154.0	145.0	131.0	148.0	128.0
	SD	2.0	14.0	10.3	5.2	19.4	16.5	32.2	9.8
	MIN	180	152	148	148	116	116	120	116
	MAX	184	180	172	160	156	152	188	140
	N	4	4	4	4	4	4	4	4
2	MEAN	201.0	186.0	177.0	152.0	158.0	146.0	144.0	141.0
	SD	24.5	16.5	13.2	15.0	31.7	27.4	37.2	27.8
	MIN	184	164	164	132	116	124	92	112
	MAX	236	204	192	168	192	184	180	172
	N	4	4	4	4	4	4	4	4
3	MEAN	169.0	188.0	148.0	135.0	135.0	128.0	117.0	127.0
	SD	8 2	6.5	15.3	11.5	15.4	8.6	17.1	19.4
	MIN	160	180	136	128	120	120	96	116
	MAX	180	196	168	152	156	140	136	156
	N	4	4	4	4	4	4	4	4
4	MEAN	165.0 A^2	149.0 A^2	162.0 A^2	132.0 A^2	129.0 A^2	131.0 A^2	119.0 A^2	124.0 A^2
	SD	31.2	20.0	6.9	24.0	12.4	3.8	15.1	11.8
	MIN	120	120	152	96	112	128	104	112
	MAX	188	164	168	144	140	136	140	140
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 42

(b) (4)

HEART RATE (Beats/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS
1	MEAN	152.5
	SD	5.4
	MIN	146
	MAX	157
	N	4
2	MEAN	163.1
	SD	20.0
	MIN	139
	MAX	182
	N	4
3	MEAN	143.4
	SD	6.4
	MIN	138
	MAX	152
	N	4
4	MEAN	138.9 A^2
	SD	7.8
	MIN	129
	MAX	148
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 42

(b) (4)

HEART RATE (Beats/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	MEAN	174.0	178.0	158.0	163.0	154.0	136.0	139.0	128.0
	SD	6.9	20.3	6.9	6.0	13.7	10.8	25.2	18.8
	MIN	168	164	152	160	140	128	120	108
	MAX	184	208	168	172	172	152	176	144
	N	4	4	4	4	4	4	4	4
2	MEAN	178.0	176.0	155.0	143.0	141.0	137.0	122.0	125.0
	SD	11.5	5.7	18.6	10.0	13.2	15.4	20.0	13.2
	MIN	164	168	132	132	132	128	100	112
	MAX	192	180	172	156	160	160	148	140
	N	4	4	4	4	4	4	4	4
3	MEAN	183.0 C^2	163.0 C^2	133.0 C^2	128.0 C^2	120.0 C^2	114.0 C^2	113.0 C^2	119.0 C^2
	SD	22.9	6.8	13.2	9.2	25.5	4.0	6.0	28.9
	MIN	156	156	120	120	96	112	108	92
	MAX	204	172	148	136	144	120	120	160
	N	4	4	4	4	4	4	4	4
4	MEAN	195.0	171.0	152.0	132.0	139.0	143.0	133.0	118.0
	SD	33.4	20.0	17.3	26.5	8.2	20.5	22.9	12.4
	MIN	172	144	128	96	128	116	112	100
	MAX	244	192	168	160	148	164	160	128
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 42

(b) (4)

HEART RATE (Beats/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS
1	MEAN	153.8
	SD	10.2
	MIN	146
	MAX	169
	N	4
2	MEAN	147.1
	SD	5.0
	MIN	143
	MAX	153
	N	4
3	MEAN	134.1 C^2
	SD	9.8
	MIN	126
	MAX	148
	N	4
4	MEAN	147.9
	SD	5.2
	MIN	141
	MAX	154
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 43 (b) (4)

RESPIRATORY RATE (Resp/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	MEAN	62.0	68.0	60.0	41.0	48.0	41.0	45.0	40.0
	SD	19.2	9.8	15.7	8.9	19.0	8.9	10.5	3.3
	MIN	44	56	44	28	36	32	36	36
	MAX	88	80	80	48	76	52	56	44
	N	4	4	4	4	4	4	4	4
2	MEAN	68.0	60.0	50.0	37.0	44.0	38.0	34.0	49.0
	SD	11.8	3.3	5.2	12.8	6.5	6.9	2.3	21.3
	MIN	56	56	44	28	36	32	32	32
	MAX	80	64	56	56	52	48	36	80
	N	4	4	4	4	4	4	4	4
3	MEAN	69.0	61.0	52.0	39.0	37.0	36.0	36.0	38.0
	SD	14.4	8.2	8.0	3.8	6.8	3.3	6.5	10.1
	MIN	48	52	48	36	28	32	28	28
	MAX	80	72	64	44	44	40	44	52
	N	4	4	4	4	4	4	4	4
4	MEAN	62.0	64.0	55.0	38.0	41.0	35.0	39.0	41.0
	SD	16.8	6.5	3.8	12.4	12.8	6.0	6.0	6.8
	MIN	44	56	52	28	28	28	32	32
	MAX	80	72	60	56	52	40	44	48
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 43

(b) (4)

RESPIRATORY RATE (Resp/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS
1	MEAN	50.6
	SD	9.3
	MIN	45
	MAX	65
	N	4
2	MEAN	47.5
	SD	3.6
	MIN	43
	MAX	51
	N	4
3	MEAN	46.0
	SD	4.4
	MIN	42
	MAX	52
	N	4
4	MEAN	46.9
	SD	2.6
	MIN	44
	MAX	50
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 43

(b) (4)

RESPIRATORY RATE (Resp/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	MEAN	55.0	54.0	46.0	40.0	44.0	39.0	38.0	34.0
	SD	9.5	12.4	6.9	9.2	6.5	3.8	10.1	8.3
	MIN	48	36	36	32	36	36	28	24
	MAX	68	64	52	48	52	44	52	44
	N	4	4	4	4	4	4	4	4
2	MEAN	63.0	60.0	44.0	38.0	49.0	34.0	35.0	39.0
	SD	8.9	9.8	7.3	10.6	12.4	5.2	8.9	6.8
	MIN	52	52	36	28	32	28	28	32
	MAX	72	72	52	52	60	40	48	48
	N	4	4	4	4	4	4	4	4
3	MEAN	59.0	54.0	50.0	35.0	39.0	31.0	36.0	36.0
	SD	15.4	5.2	5.2	3.8	11.5	3.8	4.6	9.8
	MIN	44	48	44	32	32	28	32	28
	MAX	76	60	56	40	56	36	40	48
	N	4	4	4	4	4	4	4	4
4	MEAN	75.0 B^2	57.0 B^2	54.0 B^2	40.0 B^2	42.0 B^2	49.0 B^2	50.0 B^2	38.0 B^2
	SD	14.0	5.0	13.3	10.8	10.6	7.6	10.1	7.7
	MIN	60	52	44	32	32	44	36	32
	MAX	92	64	72	56	56	60	60	48
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 43

(b) (4)

RESPIRATORY RATE (Resp/min) - SUMMARY
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS
1	MEAN	43.8
	SD	2.4
	MIN	41
	MAX	46
	N	4
2	MEAN	45.3
	SD	4.5
	MIN	40
	MAX	51
	N	4
3	MEAN	42.5
	SD	4.0
	MIN	38
	MAX	47
	N	4
4	MEAN	50.6 B^2
	SD	2.8
	MIN	48
	MAX	53
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	5.343	118.0	0.378	70.85	22.08	311.8	13.80	354.0
	SD	0.199	5.5	0.022	1.39	0.36	4.0	0.45	83.5
	MIN	5.22	114	0.36	68.9	21.6	306	13.2	290
	MAX	5.64	126	0.41	71.9	22.4	315	14.3	475
	N	4	4	4	4	4	4	4	4
2	MEAN	5.638	117.8	0.380	67.15 C^3	20.90 B^1	310 5	15.20 A^1	323.8
	SD	0.291	8.7	0.024	0.96	0.69	5.7	1.37	48.5
	MIN	5.30	106	0.35	65.9	19.9	302	14.1	269
	MAX	5.99	127	0.41	68.0	21.4	314	17.1	386
	N	4	4	4	4	4	4	4	4
3	MEAN	5.203	114.0 A^1	0.363 B^1	70.18	21.95	312.8	13.68	331.3
	SD	0.392	6.2	0.025	1.53	0.64	6.0	0.49	58.8
	MIN	4.65	106	0.33	67.9	21.3	307	13.2	252
	MAX	5.56	121	0.39	71.1	22.8	321	14.3	391
	N	4	4	4	4	4	4	4	4
4	MEAN	5 107 A^1	110.3 B^1	0.357 B^1	69.67	21.53 A^1	308.7	13.63	392.0 C^3
	SD	0.366	9.3	0.021	0.74	0.99	11.9	1.01	33.7
	MIN	4.76	104	0.34	69.1	20.4	295	12.7	363
	MAX	5.49	121	0.38	70.5	22.2	317	14.7	429
	N	3	3	3	3	3	3	3	3

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	11.100	5.730	4.448	0.608	0.190	0.055	0.073
	SD	1.049	0.992	0.249	0.146	0.068	0.013	0.029
	MIN	10.04	4.78	4.14	0.42	0.14	0.04	0.05
	MAX	12.06	6.77	4.65	0.77	0.29	0.07	0.11
	N	4	4	4	4	4	4	4
2	MEAN	11.270	5.675	4.745	0.518	0.220	0.048	0.063
	SD	1.377	1.423	0.464	0.097	0.055	0.010	0.013
	MIN	9.63	3.75	4.05	0.38	0.16	0.04	0.05
	MAX	12.99	7 11	5.00	0.61	0.29	0.06	0.08
	N	4	4	4	4	4	4	4
3	MEAN	11.795	6.265	4.613	0.578	0.238	0.043	0.060
	SD	3.250	2.666	0.423	0.236	0.064	0.010	0.018
	MIN	8.70	3 93	4.02	0.39	0.18	0.03	0.04
	MAX	16.33	10.07	4.99	0.92	0.33	0.05	0.08
	N	4	4	4	4	4	4	4
4	MEAN	11.223	5.573	4.533	0.753	0.273	0.043	0.057
	SD	1.733	0.813	0.813	0.205	0.071	0.012	0.021
	MIN	9.79	4 91	3.64	0.55	0.21	0.03	0.04
	MAX	13.15	6.48	5.23	0.96	0.35	0.05	0.08
	N	3	3	3	3	3	3	3

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	51.35	40.25	5.48	1.75	0.48	0.70	167.30	3.15
	SD	4.28	3.67	1.17	0.78	0.17	0.32	23.92	0.56
	MIN	47.6	36.4	4.1	1.2	0.3	0.4	148.2	2.6
	MAX	56.7	44.9	6.5	2.9	0.7	1.1	201.0	3.9
	N	4	4	4	4	4	4	4	4
2	MEAN	49.78	42.55	4.63	2.00	0.43	0.58 B^3	155.50	2.75
	SD	7.80	6.71	0.91	0.71	0.10	0.13	35.10	0.66
	MIN	38.9	36.5	3.4	1.5	0.3	0.4	105.8	1.9
	MAX	56.1	51.4	5.6	3.0	0.5	0.7	183.5	3.5
	N	4	4	4	4	4	4	4	4
3	MEAN	51.63	40.53	4.83	2.10	0.40	0.53 B^3	130.20 C^1	2.48 C^1
	SD	7.15	6.88	0.84	0.85	0.08	0.05	26.97	0.41
	MIN	45.1	30.6	3.7	1.3	0.3	0.5	98.9	2.1
	MAX	61.7	46.2	5.6	3.1	0.5	0.6	158.7	3.0
	N	4	4	4	4	4	4	4	4
4	MEAN	49.80	40.30	6.63	2.43	0.37	0.50 A^3	118.30 C^1	2.33 C^1
	SD	4.37	3.44	0.91	0.31	0.06	0.10	21.16	0.29
	MIN	45.7	37.2	5.6	2.1	0.3	0.4	94.6	2.0
	MAX	54.4	44.0	7.3	2.7	0.4	0.6	135.3	2.5
	N	3	3	3	3	3	3	3	3

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	5.520	123.3	0.393	71.33	22.30	312 5	13.20	237.5
	SD	0.141	3.3	0.013	1.11	0.37	2.6	0.58	32.0
	MIN	5.35	119	0.38	69.7	21.8	310	12.7	211
	MAX	5.65	127	0.41	72.2	22.7	316	13.8	282
	N	4	4	4	4	4	4	4	4
2	MEAN	5.863	123.8	0.403	68.88 C^3	21.13 B^1	306.8	14.85 A^1	360.5
	SD	0.359	8.8	0.021	2.84	1.28	7.0	1.59	69.0
	MIN	5.36	115	0.38	65.5	19.7	301	13.2	264
	MAX	6.21	134	0.42	71.6	22.7	317	17.0	427
	N	4	4	4	4	4	4	4	4
3	MEAN	5.440	119.0 A^1	0.380 B^1	69.88	21.90	313 5	12.88	334.8
	SD	0.245	6.5	0.022	1.66	0.57	2.5	0.28	56.3
	MIN	5.11	113	0.36	68.3	21.2	310	12.6	281
	MAX	5.70	128	0.41	71.8	22.5	316	13.2	413
	N	4	4	4	4	4	4	4	4
4	MEAN	5 268 A^1	112.5 B^1	0.370 B^1	70.50	21.43 A^1	303 5	14.18	398.5 C^3
	SD	0.190	3.1	0.008	2.18	1.23	8.2	1.83	57.1
	MIN	5.06	108	0.36	67.3	19.7	293	13.1	322
	MAX	5.50	115	0.38	72.1	22.4	310	16.9	456
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	9.490	5.235	3.370	0.618	0.155	0.043	0.070
	SD	1.327	1.481	0.516	0.207	0.079	0.013	0.027
	MIN	8.30	3 97	2.67	0.40	0.10	0.03	0.05
	MAX	11.23	6 96	3.90	0.86	0.27	0.06	0.11
	N	4	4	4	4	4	4	4
2	MEAN	10.320	5.190	4.235	0.583	0.220	0.045	0.045
	SD	0.326	0.356	0.367	0.124	0.167	0.013	0.013
	MIN	10.07	4.81	3.69	0.46	0.12	0.03	0.03
	MAX	10.80	5.61	4.49	0.75	0.47	0.06	0.06
	N	4	4	4	4	4	4	4
3	MEAN	10.433	5.460	4.090	0.550	0.250	0.030	0.053
	SD	2.274	2.045	0.507	0.126	0.063	0.008	0.005
	MIN	8.49	3.66	3.49	0.45	0.17	0.02	0.05
	MAX	12.83	7 31	4.73	0.72	0.31	0.04	0.06
	N	4	4	4	4	4	4	4
4	MEAN	11.390	5.715	4.770	0.643	0.148	0.048	0.063
	SD	3.127	1.898	1.454	0.219	0.033	0.022	0.010
	MIN	8.74	3.74	3.87	0.41	0.11	0.03	0.05
	MAX	15.44	7 39	6.94	0.88	0.19	0.08	0.07
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	54.35	36.28	6.45	1.70	0.45	0.75	169.45	3.08
	SD	8.27	8.94	1.71	0.96	0.17	0.31	47.21	0.91
	MIN	46.0	27.3	4.7	0.9	0.3	0.5	107.6	1.9
	MAX	61.9	45.2	8.8	3.1	0.7	1.2	219.3	4.1
	N	4	4	4	4	4	4	4	4
2	MEAN	50.28	41.05	5.68	2.15	0.45	0.43 B^3	173.68	2.95
	SD	2.66	3.25	1.21	1.64	0.13	0.15	50.53	0.72
	MIN	47.2	36.7	4.6	1.2	0.3	0.3	137.1	2.4
	MAX	53.0	44.0	7.4	4.6	0.6	0.6	246.8	4.0
	N	4	4	4	4	4	4	4	4
3	MEAN	51.00	40.53	5.30	2.40	0.35	0.48 B^3	106.25 C^1	1.95 C^1
	SD	9.01	9.16	0.62	0.32	0.10	0.05	27.16	0.50
	MIN	43.1	29.3	4.5	2.0	0.3	0.4	78.1	1.4
	MAX	61.3	48.0	6.0	2.7	0.5	0.5	143.4	2.6
	N	4	4	4	4	4	4	4	4
4	MEAN	49.73	42.30	5.60	1.35	0.40	0.58 A^3	146.10 C^1	2.75 C^1
	SD	7.02	7.36	1.13	0.39	0.08	0.10	66.18	1.15
	MIN	42.8	31.6	4.5	0.9	0.3	0.5	92.8	1.8
	MAX	59.5	48.4	7.1	1.8	0.5	0.7	241.8	4.4
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	5.431	120.6	0.385	71.09	22.19	312 1	13.50	295.8
	SD	0.186	5.0	0.019	1.19	0.36	3.2	0.58	85.5
	MIN	5.22	114	0.36	68.9	21.6	306	12.7	211
	MAX	5.65	127	0.41	72.2	22.7	316	14.3	475
	N	8	8	8	8	8	8	8	8
2	MEAN	5.750	120.8	0.391	68.01 C^3	21.01 B^1	308.6	15.03 A^1	342.1
	SD	0.326	8.7	0.024	2.17	0.96	6.3	1.39	58.6
	MIN	5.30	106	0.35	65.5	19.7	301	13.2	264
	MAX	6.21	134	0.42	71.6	22.7	317	17.1	427
	N	8	8	8	8	8	8	8	8
3	MEAN	5.321	116.5 A^1	0.371 B^1	70.03	21.93	313 1	13.28	333.0
	SD	0.328	6.4	0.024	1.48	0.56	4.3	0.56	53.3
	MIN	4.65	106	0.33	67.9	21.2	307	12.6	252
	MAX	5.70	128	0.41	71.8	22.8	321	14.3	413
	N	8	8	8	8	8	8	8	8
4	MEAN	5 199 A^1	111.6 B^1	0.364 B^1	70.14	21.47 A^1	305.7	13.94	395.7 C^3
	SD	0.265	5.9	0.015	1.66	1.04	9.4	1.45	45.0
	MIN	4.76	104	0.34	67.3	19.7	293	12.7	322
	MAX	5.50	121	0.38	72.1	22.4	317	16.9	456
	N	7	7	7	7	7	7	7	7

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	10.295	5.483	3.909	0.613	0.173	0.049	0.071
	SD	1.402	1.197	0.687	0.166	0.070	0.014	0.026
	MIN	8.30	3 97	2.67	0.40	0.10	0.03	0.05
	MAX	12.06	6 96	4.65	0.86	0.29	0.07	0.11
	N	8	8	8	8	8	8	8
2	MEAN	10.795	5.433	4.490	0.550	0.220	0.046	0.054
	SD	1.057	0.995	0.474	0.109	0.115	0.011	0.015
	MIN	9.63	3.75	3.69	0.38	0.12	0.03	0.03
	MAX	12.99	7 11	5.00	0.75	0.47	0.06	0.08
	N	8	8	8	8	8	8	8
3	MEAN	11.114	5.863	4.351	0.564	0.244	0.036	0.056
	SD	2.697	2.241	0.515	0.176	0.060	0.011	0.013
	MIN	8.49	3.66	3.49	0.39	0.17	0.02	0.04
	MAX	16.33	10.07	4.99	0.92	0.33	0.05	0.08
	N	8	8	8	8	8	8	8
4	MEAN	11.319	5.654	4.669	0.690	0.201	0.046	0.060
	SD	2.429	1.424	1.137	0.204	0.082	0.017	0.014
	MIN	8.74	3.74	3.64	0.41	0.11	0.03	0.04
	MAX	15.44	7 39	6.94	0.96	0.35	0.08	0.08
	N	7	7	7	7	7	7	7

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	52.85	38.26	1.73	0.46	0.73	168.38	3.11
	SD	6 30	6.67	0.81	0.16	0.29	34.67	0.70
	MIN	46.0	27.3	0.9	0.3	0.4	107.6	1.9
	MAX	61.9	45.2	3.1	0.7	1.2	219.3	4.1
	N	8	8	8	8	8	8	8
2	MEAN	50.03	41.80	2.08	0.44	0.50 B^3	164.59	2.85
	SD	5.40	4.95	1.17	0.11	0.15	41.43	0.65
	MIN	38.9	36.5	1.2	0.3	0.3	105.8	1.9
	MAX	56.1	51.4	4.6	0.6	0.7	246.8	4.0
	N	8	8	8	8	8	8	8
3	MEAN	51.31	40.53	2.25	0.38	0.50 B^3	118.23 C^1	2.21 C^1
	SD	7 54	7.50	0.61	0.09	0.05	28.14	0.51
	MIN	43.1	29.3	1.3	0.3	0.4	78.1	1.4
	MAX	61.7	48.0	3.1	0.5	0.6	158.7	3.0
	N	8	8	8	8	8	8	8
4	MEAN	49.76	41.44	1.81	0.39	0.54 A^3	134.19 C^1	2.57 C^1
	SD	5 57	5.67	0.66	0.07	0.10	50.60	0.86
	MIN	42.8	31.6	0.9	0.3	0.4	92.8	1.8
	MAX	59.5	48.4	2.7	0.5	0.7	241.8	4.4
	N	7	7	7	7	7	7	7

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	6.065	135.8	0.418	68.83	22.33	324.5	13.43	348.3
	SD	0 255	4.6	0.015	0.78	0.40	3.3	0.46	74.3
	MIN	5.82	130	0.40	67.9	22.0	321	12.9	277
	MAX	6 30	140	0.43	69.8	22.9	329	13.9	451
	N	4	4	4	4	4	4	4	4
2	MEAN	6.020	128.5	0.400	66.15	21.35 B^1	323.3	13.65 A^1	295.8
	SD	0.405	11.4	0.029	2.12	0.77	5.2	0.80	49.5
	MIN	5 58	113	0.36	64.1	20.3	317	13.1	254
	MAX	6.46	140	0.43	69.0	22.1	328	14.8	367
	N	4	4	4	4	4	4	4	4
3	MEAN	5 918	131.3 A^1	0.405 B^1	68.25	22.20	325.3	12.85	319.3
	SD	0 195	4.1	0.013	2.14	0.58	3.0	0.26	59.6
	MIN	5.71	126	0.39	66.8	21.6	322	12.5	258
	MAX	6 18	135	0.42	71.4	23.0	329	13.1	397
	N	4	4	4	4	4	4	4	4
4	MEAN	5.983 A^1	130.0 B^1	0.400 B^1	66.98	21.73 A^1	324.8	13.05	378.3
	SD	0 349	8.2	0.024	1.44	0.50	3.0	0.48	26.4
	MIN	5 54	122	0.38	65.4	21.2	321	12.4	340
	MAX	6 33	141	0.43	68.6	22.2	328	13.5	398
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	10.663	5.408	4.310	0.535	0.333	0.038	0.043
	SD	1.764	0.934	0.661	0.145	0.123	0.013	0.015
	MIN	8.27	4 15	3.41	0.37	0.19	0.02	0.02
	MAX	12.44	6 34	4.84	0.70	0.48	0.05	0.05
	N	4	4	4	4	4	4	4
2	MEAN	11.660	6.418	4.255	0.590	0.273	0.060	0.068
	SD	1.817	1.086	0.896	0.079	0.054	0.022	0.019
	MIN	9.91	5 12	3.64	0.52	0.22	0.04	0.04
	MAX	14.20	7.60	5.55	0.70	0.34	0.09	0.08
	N	4	4	4	4	4	4	4
3	MEAN	10.855	5.860	4.018	0.588	0.293	0.053	0.048
	SD	2.379	1.160	0.935	0.229	0.084	0.034	0.031
	MIN	8.91	4.77	3.08	0.36	0.21	0.02	0.02
	MAX	14.05	7 28	5.31	0.90	0.37	0 10	0.09
	N	4	4	4	4	4	4	4
4	MEAN	12.020	6.123	4.878	0.625	0.280	0.060	0.053
	SD	1.999	1.534	0.643	0.200	0.102	0.008	0.017
	MIN	9.76	4 26	4.29	0.46	0.15	0.05	0.03
	MAX	14.18	7.71	5.79	0.88	0.39	0.07	0.07
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	50.68	40.50	4.95	3.13	0.35	0.40	114.00	1.90
	SD	0.56	1.43	0.77	0.96	0.06	0.08	21.98	0.37
	MIN	50.2	38.9	4.1	1.7	0.3	0.3	85.1	1.5
	MAX	51.3	42.1	5.6	3.8	0.4	0.5	137.7	2.4
	N	4	4	4	4	4	4	4	4
2	MEAN	54.98	36.35	5.18	2.43	0.53	0.58	89.98	1.50
	SD	3.91	3.06	1.26	0.72	0.15	0.22	7.83	0.16
	MIN	51.6	32.0	4.2	2.0	0.4	0.3	80.7	1.3
	MAX	60.6	39.1	7.0	3.5	0.7	0.8	97.5	1.7
	N	4	4	4	4	4	4	4	4
3	MEAN	54.18	37.05	5.30	2.65	0.45	0.40	86.25 C^1	1.45 C^1
	SD	2.65	3.08	1.04	0.39	0.17	0.18	26.60	0.44
	MIN	51.8	34.6	3.9	2.3	0.3	0.2	63.8	1.1
	MAX	56.9	41.1	6.4	3.2	0.7	0.6	124.6	2.1
	N	4	4	4	4	4	4	4	4
4	MEAN	50.53	41.15	5.10	2.28	0.50	0.43	71.18 C^1	1.18 C^1
	SD	6.23	6.68	0.84	0.47	0.08	0.10	25.53	0.42
	MIN	43.7	32.7	4.2	1.6	0.4	0.3	38.9	0.6
	MAX	58.8	49.0	6.2	2.7	0.6	0.5	101.3	1.6
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	6.488	145.8	0.448	68.85	22.53	327.0	13.25	298.5
	SD	0.457	8.9	0.028	0.53	0.59	6.1	0.37	45.3
	MIN	6.09	135	0.42	68.4	21.9	320	12.8	245
	MAX	7.06	154	0.48	69.6	23.2	333	13.6	355
	N	4	4	4	4	4	4	4	4
2	MEAN	6 525	144.5	0.445	68.33	22.13 B^1	323.8	13.68 A^1	289.3
	SD	0 121	4.5	0.010	1.58	0.53	5.7	0.89	61.8
	MIN	6.40	139	0.43	67.1	21.7	317	13.1	218
	MAX	6.66	150	0.45	70.4	22.8	331	15.0	328
	N	4	4	4	4	4	4	4	3
3	MEAN	5 930	132.3 A^1	0.403 B^1	68.18	22.30	327.0	12.65	319.8
	SD	0 195	5.3	0.017	1.37	0.72	5.0	0.24	52.8
	MIN	5.66	126	0.38	67.2	21.6	321	12.4	252
	MAX	6 12	138	0.42	70.2	23.3	333	12.9	381
	N	4	4	4	4	4	4	4	4
4	MEAN	5.770 A^1	126.0 B^1	0.390 B^1	67.23	21.88 A^1	324.8	13.23	338.8
	SD	0 192	7.3	0.022	2.85	0.96	0.5	0.50	39.5
	MIN	5.60	116	0.36	63.7	20.7	324	12.7	300
	MAX	6.01	133	0.41	70.0	22.8	325	13.9	389
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	11.365	5.580	4.763	0.605	0.325	0.055	0.045
	SD	1.806	1.634	0.444	0.104	0.131	0.010	0.006
	MIN	9.35	4.01	4.33	0.48	0.20	0.05	0.04
	MAX	13.30	7.05	5.17	0.73	0.47	0.07	0.05
	N	4	4	4	4	4	4	4
2	MEAN	11.420	6.125	4.298	0.640	0.235	0.068	0.055
	SD	1.689	0.852	0.882	0.175	0.109	0.029	0.021
	MIN	9.23	5.42	3.01	0.53	0.15	0.03	0.03
	MAX	13.35	7 28	4.88	0.90	0.39	0 10	0.08
	N	4	4	4	4	4	4	4
3	MEAN	10.553	5.975	3.695	0.600	0.203	0.040	0.038
	SD	1.863	1.832	0.729	0.213	0.067	0.014	0.017
	MIN	8.79	4.81	2.97	0.39	0.15	0.03	0.02
	MAX	13.13	8.71	4.40	0.85	0.30	0.06	0.06
	N	4	4	4	4	4	4	4
4	MEAN	10.785	5.670	4.298	0.503	0.220	0.050	0.048
	SD	1.623	0.808	0.862	0.102	0.051	0.008	0.015
	MIN	8.77	4.68	3.38	0.38	0.15	0.04	0.03
	MAX	12.33	6 55	5.45	0.63	0.27	0.06	0.06
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	48.35	42.60	5.38	2.88	0.48	0.38	120.73	1.85
	SD	7.16	6.82	0.97	1.09	0.05	0.05	38.18	0.48
	MIN	41.6	34.9	4.6	1.7	0.4	0.3	84.9	1.4
	MAX	55.9	49.2	6.7	3.8	0.5	0.4	170.0	2.4
	N	4	4	4	4	4	4	4	4
2	MEAN	53.85	37.48	5.58	2.08	0.58	0.45	101.98	1.55
	SD	4.32	3.95	1.08	0.93	0.25	0.17	18.89	0.30
	MIN	48.2	32.7	4.6	1.3	0.3	0.3	90.8	1.4
	MAX	58.7	42.2	6.7	3.4	0.9	0.7	130.1	2.0
	N	4	4	4	4	4	4	4	4
3	MEAN	55.98	35.83	5.58	1.90	0.38	0.33	71.00 C^1	1.18 C^1
	SD	8.39	8.84	1.14	0.29	0.10	0.10	16.93	0.28
	MIN	48.9	24.2	4.4	1.6	0.3	0.2	52.9	0.9
	MAX	66.3	43.6	6.6	2.3	0.5	0.4	89.8	1.5
	N	4	4	4	4	4	4	4	4
4	MEAN	52.68	39.75	4.63	2.08	0.45	0.43	67.85 C^1	1.18 C^1
	SD	2.67	3.25	0.59	0.64	0.06	0.10	29.62	0.53
	MIN	49.0	36.5	4.0	1.5	0.4	0.3	39.4	0.7
	MAX	55.4	44.2	5.3	3.0	0.5	0.5	108.3	1.9
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	6 276	140.8	0.433	68.84	22.43	325.8	13.34	323.4
	SD	0.410	8.5	0.026	0.61	0.48	4.7	0.40	62.9
	MIN	5.82	130	0.40	67.9	21.9	320	12.8	245
	MAX	7.06	154	0.48	69.8	23.2	333	13.9	451
	N	8	8	8	8	8	8	8	8
2	MEAN	6 273	136.5	0.423	67.24	21.74 B^1	323.5	13.66 A^1	293.0
	SD	0 387	11.7	0.032	2.08	0.74	5.1	0.79	50.1
	MIN	5 58	113	0.36	64.1	20.3	317	13.1	218
	MAX	6.66	150	0.45	70.4	22.8	331	15.0	367
	N	8	8	8	8	8	8	8	7
3	MEAN	5 924	131.8 A^1	0.404 B^1	68.21	22.25	326.1	12.75	319.5
	SD	0 180	4.4	0.014	1.67	0.61	3.9	0.26	52.1
	MIN	5.66	126	0.38	66.8	21.6	321	12.4	252
	MAX	6 18	138	0.42	71.4	23.3	333	13.1	397
	N	8	8	8	8	8	8	8	8
4	MEAN	5.876 A^1	128.0 B^1	0.395 B^1	67.10	21.80 A^1	324.8	13.14	358.5
	SD	0 285	7.5	0.022	2.09	0.71	2.0	0.46	37.6
	MIN	5 54	116	0.36	63.7	20.7	321	12.4	300
	MAX	6 33	141	0.43	70.0	22.8	328	13.9	398
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	11.014	5.494	4.536	0.570	0.329	0.046	0.044
	SD	1.695	1.236	0.575	0.123	0.118	0.014	0.011
	MIN	8.27	4.01	3.41	0.37	0.19	0.02	0.02
	MAX	13.30	7.05	5.17	0.73	0.48	0.07	0.05
	N	8	8	8	8	8	8	8
2	MEAN	11.540	6.271	4.276	0.615	0.254	0.064	0.061
	SD	1.629	0.917	0.823	0.128	0.082	0.024	0.020
	MIN	9.23	5 12	3.01	0.52	0.15	0.03	0.03
	MAX	14.20	7.60	5.55	0.90	0.39	0 10	0.08
	N	8	8	8	8	8	8	8
3	MEAN	10.704	5.918	3.856	0.594	0.248	0.046	0.043
	SD	1.985	1.421	0.795	0.205	0.085	0.025	0.024
	MIN	8.79	4.77	2.97	0.36	0.15	0.02	0.02
	MAX	14.05	8.71	5.31	0.90	0.37	0 10	0.09
	N	8	8	8	8	8	8	8
4	MEAN	11.403	5.896	4.588	0.564	0.250	0.055	0.050
	SD	1.810	1.161	0.770	0.161	0.081	0.009	0.015
	MIN	8.77	4 26	3.38	0.38	0.15	0.04	0.03
	MAX	14.18	7.71	5.79	0.88	0.39	0.07	0.07
	N	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	49.51	41.55	3.00	0.41	0.39	117.36	1.88
	SD	4.86	4.70	0.96	0.08	0.06	29.06	0.40
	MIN	41.6	34.9	1.7	0.3	0.3	84.9	1.4
	MAX	55.9	49.2	3.8	0.5	0.5	170.0	2.4
	N	8	8	8	8	8	8	8
2	MEAN	54.41	36.91	2.25	0 55	0.51	95.98	1.53
	SD	3.86	3.32	0.79	0 19	0.20	14.84	0.23
	MIN	48.2	32.0	1.3	0.3	0.3	80.7	1.3
	MAX	60.6	42.2	3.5	0.9	0.8	130.1	2.0
	N	8	8	8	8	8	8	8
3	MEAN	55.08	36.44	2.28	0.41	0.36	78.63 C^1	1.31 C^1
	SD	5.84	6.16	0.51	0 14	0.14	22.19	0.37
	MIN	48.9	24.2	1.6	0.3	0.2	52.9	0.9
	MAX	66.3	43.6	3.2	0.7	0.6	124.6	2.1
	N	8	8	8	8	8	8	8
4	MEAN	51.60	40.45	2.18	0.48	0.43	69.51 C^1	1.18 C^1
	SD	4.59	4.92	0.53	0.07	0.09	25.66	0.44
	MIN	43.7	32.7	1.5	0.4	0.3	38.9	0.6
	MAX	58.8	49.0	3.0	0.6	0.5	108.3	1.9
	N	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	6.400	147.3	0.450	70.00	23.08	329 5	12.68	265.0
	SD	0.562	9.3	0.034	1.01	0.59	5.1	0.45	53.1
	MIN	5.68	135	0.41	69.3	22.4	323	12.3	224
	MAX	7.02	157	0.49	71.5	23.8	334	13.3	339
	N	4	4	4	4	4	4	4	4
2	MEAN	6.678	148.8	0.448	67.15 C^3	22.23 B^1	331 3	12.90 A^1	274.0
	SD	0.488	12.5	0.038	1.62	0.78	4.6	0.73	41.8
	MIN	6.19	132	0.40	64.9	21.3	328	12.3	238
	MAX	7.28	162	0.49	68.7	23.2	338	13.9	322
	N	4	4	4	4	4	4	4	4
3	MEAN	6.518	149.0 A^1	0.448 B^1	68.58 B^3	22.83	332 5	12.55	269.3
	SD	0.316	8.2	0.028	1.76	0.67	4.4	0.39	53.8
	MIN	6.29	141	0.42	66.4	22.3	327	12.2	228
	MAX	6.97	157	0.48	70.7	23.8	336	13.1	342
	N	4	4	4	4	4	4	4	4
4	MEAN	6 283 A^1	142.8 B^1	0.433 B^1	68.65 B^3	22.73 A^1	331 3	12.60	301.8
	SD	0.765	16.4	0.054	0.90	0.33	7.3	0.69	26.1
	MIN	5.57	126	0.39	67.4	22.5	324	12.1	267
	MAX	7.30	164	0.51	69.4	23.2	338	13.6	329
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	9.098	4.710	3.378	0.538	0.383	0.048	0.040
	SD	0.784	0.490	0.301	0.050	0.175	0.024	0.028
	MIN	8.01	4.09	2.98	0.47	0.21	0.03	0.02
	MAX	9.69	5 21	3.63	0.59	0.57	0.08	0.08
	N	4	4	4	4	4	4	4
2	MEAN	10.810	6.223	3.593	0.618	0.265 B^3	0.060	0.053
	SD	1.690	1.611	0.276	0.196	0.024	0.028	0.039
	MIN	9.58	4 91	3.37	0.43	0.24	0.04	0.03
	MAX	13.23	8 55	3.94	0.87	0.29	0 10	0.11
	N	4	4	4	4	4	4	4
3	MEAN	9.795	5.183	3.635	0.528	0.318 B^3	0.065	0.063
	SD	1.888	1.277	0.647	0.067	0.068	0.024	0.022
	MIN	7.54	3.68	2.95	0.46	0.25	0.05	0.04
	MAX	12.12	6 54	4.44	0.61	0.41	0 10	0.09
	N	4	4	4	4	4	4	4
4	MEAN	8.345	4.118	3.438	0.448	0.260 B^3	0.045	0.038
	SD	1.457	1.042	0.237	0.122	0.148	0.017	0.010
	MIN	6.68	2.87	3.24	0.28	0.12	0.03	0.03
	MAX	9.73	5 11	3.78	0.56	0.45	0.07	0.05
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	51.70	37.15	6.00	4.20	0.53	0.43	83.08	1.28
	SD	1.46	0.33	1.04	1.85	0.26	0.29	36.84	0.49
	MIN	50.5	36.7	4.9	2.2	0.3	0.2	57.5	1.0
	MAX	53.8	37.5	7.4	6.3	0.8	0.8	137.1	2.0
	N	4	4	4	4	4	4	4	4
2	MEAN	56.93	33.93	5.65	2.50 B^3	0.53	0.45	72.68	1.10
	SD	5.82	6.22	0.97	0.48	0.15	0.24	9.48	0.22
	MIN	50.5	25.5	4.5	1.8	0.4	0.3	64.0	0.9
	MAX	64.6	40.5	6.6	2.9	0.7	0.8	83.9	1.4
	N	4	4	4	4	4	4	4	4
3	MEAN	52.53	37.33	5.50	3.30 B^3	0.65	0.65	62.58 C^1	1.00 C^1
	SD	4.54	3.28	1.21	0.71	0.17	0.19	14.27	0.24
	MIN	48.8	33.0	4.8	2.7	0.5	0.4	47.5	0.8
	MAX	58.3	40.5	7.3	4.3	0.8	0.8	78.7	1.3
	N	4	4	4	4	4	4	4	4
4	MEAN	48.83	41.95	5.33	2.93 B^3	0.53	0.45	57.80 C^1	0.93 C^1
	SD	4.69	6.09	0.69	1.28	0.21	0.06	18.12	0.22
	MIN	43.0	36.1	4.3	1.7	0.3	0.4	34.4	0.6
	MAX	54.4	50.1	5.8	4.6	0.8	0.5	78.3	1.1
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	6.925	159.0	0.485	70.05	23.00	328 5	12.60	224.8
	SD	0.678	11.7	0.044	0.93	0.61	6.6	0.70	15.0
	MIN	6.03	145	0.43	69.2	22.6	321	11.7	212
	MAX	7.53	171	0.52	71.2	23.9	337	13.2	246
	N	4	4	4	4	4	4	4	4
2	MEAN	7.180	161.8	0.495	68.98 C^3	22.60 B^1	327 5	12.78 A^1	236.0
	SD	0.313	4.2	0.017	0.84	0.48	6.5	0.30	35.6
	MIN	6.94	159	0.48	68.3	22.1	323	12.4	200
	MAX	7.63	168	0.52	70.2	23.1	337	13.1	274
	N	4	4	4	4	4	4	4	4
3	MEAN	6.598	149.5 A^1	0.450 B^1	68.45 B^3	22.70	331.8	12.43	231.0
	SD	0.222	7.1	0.022	1.42	0.42	2.6	0.43	28.7
	MIN	6.28	140	0.42	67.1	22.3	328	11.9	198
	MAX	6.75	157	0.47	70.3	23.3	334	12.9	268
	N	4	4	4	4	4	4	4	4
4	MEAN	6.615 A^1	148.5 B^1	0.450 B^1	68.15 B^3	22.50 A^1	330.0	12.45	266.5
	SD	0.379	9.3	0.029	2.49	0.89	1.4	0.35	18.3
	MIN	6.34	136	0.41	65.3	21.5	329	12.1	249
	MAX	7.17	158	0.48	70.7	23.3	332	12.8	286
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	9.185	4.573	3.698	0.500	0.325	0.048	0.045
	SD	0.967	1.071	0.092	0.132	0.141	0.013	0.006
	MIN	8.17	3.47	3.60	0.35	0.15	0.03	0.04
	MAX	10.15	5.70	3.81	0.67	0.47	0.06	0.05
	N	4	4	4	4	4	4	4
2	MEAN	10.113	5.178	4.068	0.518	0.238 B^3	0.058	0.055
	SD	1.486	1.184	0.564	0.175	0.052	0.021	0.010
	MIN	8.32	3.80	3.52	0.31	0.19	0.04	0.04
	MAX	11.83	6.67	4.83	0.73	0.30	0.08	0.06
	N	4	4	4	4	4	4	4
3	MEAN	9.835	5.550	3.378	0.625	0.188 B^3	0.053	0.040
	SD	3.116	2.088	0.723	0.324	0.033	0.022	0.022
	MIN	7.68	4 25	2.66	0.44	0.15	0.03	0.02
	MAX	14.39	8.64	4.32	1.11	0.23	0.08	0.07
	N	4	4	4	4	4	4	4
4	MEAN	8.565	4.105	3.693	0.483	0.198 B^3	0.048	0.043
	SD	0.879	0.509	0.360	0.046	0.051	0.017	0.015
	MIN	7.41	3.49	3.25	0.42	0.15	0.03	0.03
	MAX	9.26	4.64	4.11	0.53	0.27	0.07	0.06
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	49.23	40.63	5.48	3.65	0.50	0.50	85.43	1.20
	SD	6.48	4.91	1.59	1.78	0.12	0.00	59.37	0.76
	MIN	42.4	36.5	4.3	1.5	0.4	0.5	40.6	0.6
	MAX	56.1	46.6	7.8	5.8	0.6	0.5	170.5	2.3
	N	4	4	4	4	4	4	4	4
2	MEAN	50.85	40.58	4.98	2.40 B^3	0.55	0.55	71.43	0.98
	SD	5.58	5.78	1.12	0.86	0.13	0.13	28.66	0.33
	MIN	45.7	34.8	3.7	1.6	0.4	0.4	42.1	0.6
	MAX	56.4	45.7	6.1	3.6	0.7	0.7	110.4	1.4
	N	4	4	4	4	4	4	4	4
3	MEAN	55.83	35.05	6.13	2.08 B^3	0.50	0.43	61.98 C^1	0.93 C^1
	SD	3.03	3.67	1.07	0.77	0.08	0.10	17.78	0.22
	MIN	53.3	30.0	5.4	1.2	0.4	0.3	46.6	0.7
	MAX	60.0	38.0	7.7	2.9	0.6	0.5	83.2	1.2
	N	4	4	4	4	4	4	4	4
4	MEAN	47.85	43.15	5.63	2.35 B^3	0.55	0.50	46.50 C^1	0.68 C^1
	SD	1.58	1.45	0.15	0.73	0.13	0.12	15.40	0.22
	MIN	46.8	41.1	5.4	1.6	0.4	0.4	33.0	0.5
	MAX	50.2	44.4	5.7	3.3	0.7	0.6	68.3	1.0
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	6.663	153.1	0.468	70.03	23.04	329.0	12.64	244.9
	SD	0.641	11.7	0.041	0.90	0.55	5.5	0.54	42.0
	MIN	5.68	135	0.41	69.2	22.4	321	11.7	212
	MAX	7.53	171	0.52	71.5	23.9	337	13.3	339
	N	8	8	8	8	8	8	8	8
2	MEAN	6.929	155.3	0.471	68.06 C^3	22.41 B^1	329.4	12.84 A^1	255.0
	SD	0.465	11.1	0.037	1.54	0.63	5.6	0.52	41.3
	MIN	6.19	132	0.40	64.9	21.3	323	12.3	200
	MAX	7.63	168	0.52	70.2	23.2	338	13.9	322
	N	8	8	8	8	8	8	8	8
3	MEAN	6.558	149.3 A^1	0.449 B^1	68.51 B^3	22.76	332 1	12.49	250.1
	SD	0.256	7.1	0.023	1.48	0.52	3.4	0.38	44.9
	MIN	6.28	140	0.42	66.4	22.3	327	11.9	198
	MAX	6.97	157	0.48	70.7	23.8	336	13.1	342
	N	8	8	8	8	8	8	8	8
4	MEAN	6.449 A^1	145.6 B^1	0.441 B^1	68.40 B^3	22.61 A^1	330.6	12.53	284.1
	SD	0.587	12.7	0.042	1.75	0.63	4.9	0.51	28.1
	MIN	5.57	126	0.39	65.3	21.5	324	12.1	249
	MAX	7.30	164	0.51	70.7	23.3	338	13.6	329
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	9.141	4.641	3.538	0.519	0.354	0.048	0.043
	SD	0.816	0.774	0.268	0.095	0.150	0.018	0.019
	MIN	8.01	3.47	2.98	0.35	0.15	0.03	0.02
	MAX	10.15	5.70	3.81	0.67	0.57	0.08	0.08
	N	8	8	8	8	8	8	8
2	MEAN	10.461	5.700	3.830	0.568	0.251 B^3	0.059	0.054
	SD	1.520	1.423	0.483	0.180	0.040	0.023	0.026
	MIN	8.32	3.80	3.37	0.31	0.19	0.04	0.03
	MAX	13.23	8 55	4.83	0.87	0.30	0 10	0.11
	N	8	8	8	8	8	8	8
3	MEAN	9.815	5.366	3.506	0.576	0.253 B^3	0.059	0.051
	SD	2.385	1.614	0.650	0.223	0.085	0.022	0.024
	MIN	7.54	3.68	2.66	0.44	0.15	0.03	0.02
	MAX	14.39	8.64	4.44	1.11	0.41	0 10	0.09
	N	8	8	8	8	8	8	8
4	MEAN	8.455	4.111	3.565	0.465	0.229 B^3	0.046	0.040
	SD	1.120	0.759	0.313	0.088	0.108	0.016	0.012
	MIN	6.68	2.87	3.24	0.28	0.12	0.03	0.03
	MAX	9.73	5 11	4.11	0.56	0.45	0.07	0.06
	N	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	50.46	38.89	3.93	0.51	0.46	84.25	1.24
	SD	4.54	3.72	1.70	0.19	0.19	45.76	0.59
	MIN	42.4	36.5	1.5	0.3	0 2	40.6	0.6
	MAX	56.1	46.6	6.3	0.8	0.8	170.5	2.3
	N	8	8	8	8	8	8	8
2	MEAN	53.89	37.25	2.45 B^3	0.54	0.50	72.05	1.04
	SD	6.20	6.60	0.65	0.13	0.19	19.77	0.27
	MIN	45.7	25.5	1.6	0.4	0 3	42.1	0.6
	MAX	64.6	45.7	3.6	0.7	0.8	110.4	1.4
	N	8	8	8	8	8	8	8
3	MEAN	54.18	36.19	2.69 B^3	0.58	0.54	62.28 C^1	0.96 C^1
	SD	3.99	3.44	0.95	0.15	0.18	14.93	0.22
	MIN	48.8	30.0	1.2	0.4	0 3	46.6	0.7
	MAX	60.0	40.5	4.3	0.8	0.8	83.2	1.3
	N	8	8	8	8	8	8	8
4	MEAN	48.34	42.55	2.64 B^3	0.54	0.48	52.15 C^1	0.80 C^1
	SD	3.28	4.15	1.01	0.16	0.09	16.70	0.24
	MIN	43.0	36.1	1.6	0.3	0.4	33.0	0.5
	MAX	54.4	50.1	4.6	0.8	0.6	78.3	1.1
	N	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	7.063	162.5	0.488	69.63	23.03	330.8	13.73	250.8
	SD	0.533	11.8	0.034	1.11	0.66	4.8	0.67	52.2
	MIN	6.37	145	0.44	68.6	22.6	327	13.1	202
	MAX	7.58	171	0.52	71.2	24.0	337	14.4	324
	N	4	4	4	4	4	4	4	4
2	MEAN	7.335	163.3	0.495	67.40 B^3	22.23 B^1	329.8	13.58 A^1	224.5
	SD	0.560	12.0	0.039	1.94	0.61	4.6	0.51	33.7
	MIN	6.84	149	0.45	65.3	21.6	324	12.9	184
	MAX	7.97	175	0.54	69.9	23.0	335	14.1	266
	N	4	4	4	4	4	4	4	4
3	MEAN	6.835	156.0 A^1	0.470 B^1	68.70	22.85	332 3	12.93	234.8
	SD	0.214	7.0	0.028	2.12	0.56	5.9	0.76	45.7
	MIN	6.55	146	0.43	66.1	22.3	324	12.0	189
	MAX	7.07	162	0.49	71.1	23.6	337	13.6	294
	N	4	4	4	4	4	4	4	4
4	MEAN	7.063 A^1	163.0 B^1	0.490 B^1	69.28	23.05 A^1	333 5	13.00	255.8
	SD	0.540	12.0	0.039	0.53	0.26	2.4	0.94	10.5
	MIN	6.31	147	0.44	68.5	22.7	331	12.2	243
	MAX	7.56	174	0.53	69.6	23.3	336	14.2	268
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	8.853	5.040	2.980	0.378	0.353	0.068	0.035
	SD	1.515	1.301	0.278	0.083	0.173	0.024	0.024
	MIN	6.78	3 37	2.63	0.26	0.16	0.05	0.02
	MAX	10.28	6 25	3.28	0.44	0.54	0 10	0.07
	N	4	4	4	4	4	4	4
2	MEAN	9.913	5.773	3.285	0.423	0.328	0.060	0.043
	SD	1.032	0.802	0.473	0.010	0.049	0.008	0.022
	MIN	8.68	4 58	2.61	0.41	0.29	0.05	0.02
	MAX	10.78	6 27	3.65	0.43	0.40	0.07	0.07
	N	4	4	4	4	4	4	4
3	MEAN	10.123	5.940	3.233	0.490	0.350	0.073	0.035
	SD	2.990	2.069	0.771	0.103	0.093	0.052	0.013
	MIN	6.66	3.74	2.20	0.36	0.26	0.04	0.02
	MAX	13.88	8.67	3.99	0.61	0.44	0 15	0.05
	N	4	4	4	4	4	4	4
4	MEAN	9.320	5.255	3.208	0.498	0.283	0.053	0.028
	SD	0.895	0.827	0.108	0.062	0.087	0.028	0.005
	MIN	8.06	4 14	3.11	0.41	0.20	0.02	0.02
	MAX	10.06	6.08	3.34	0.55	0.40	0.08	0.03
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	56.28	34.10	4.23	4.25	0.80	0.33	47.18	0.68
	SD	5.71	3.82	0.33	2.54	0.16	0.19	24.78	0.30
	MIN	49.7	30.3	3.8	1 5	0.6	0.2	29.0	0.4
	MAX	61.3	38.9	4.6	6.6	1.0	0.6	83.8	1.1
	N	4	4	4	4	4	4	4	4
2	MEAN	58.13	33.20	4.33	3.30	0.65	0.40	51.48	0.73
	SD	4.45	4.32	0.50	0.33	0.06	0.14	7.26	0.13
	MIN	52.8	27.6	3.9	2 9	0.6	0.3	42.0	0.6
	MAX	63.7	38.1	5.0	3.7	0.7	0.6	59.7	0.9
	N	4	4	4	4	4	4	4	4
3	MEAN	58.08	32.38	4 95 A^4	3.60	0.70	0.35	41.03 C^1	0.60 C^1
	SD	3.15	2.43	0.58	1.02	0.32	0.10	10.91	0.14
	MIN	55.5	28.8	4.4	2 5	0.4	0.3	25.4	0.4
	MAX	62.5	34.2	5.5	4.7	1.1	0.5	49.7	0.7
	N	4	4	4	4	4	4	4	4
4	MEAN	56.10	34.68	5.33 B^4	3.03	0.58	0.28	42.70 C^1	0.60 C^1
	SD	3.76	3.99	0.25	0.88	0.29	0.05	17.68	0.24
	MIN	51.3	30.9	5.0	2.4	0.2	0.2	22.6	0.3
	MAX	60.4	40.3	5.6	4 3	0.8	0.3	65.0	0.9
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	7.643	179.0	0.538	70.28	23.45	333.8	13.55	187.0
	SD	0.483	12.5	0.037	0.70	0.59	5.7	0.54	20.8
	MIN	7.07	161	0.49	69.6	22.8	328	12.9	172
	MAX	8.25	190	0.58	71.2	24.0	340	14.0	217
	N	4	4	4	4	4	4	4	4
2	MEAN	7.525	171.3	0.520	68.90 B^3	22.75 B^1	330.0	13.58 A^1	219.8
	SD	0.318	7.1	0.020	1.16	0.49	2.6	0.67	44.6
	MIN	7.09	161	0.49	67.9	22.2	327	12.7	165
	MAX	7.79	177	0.53	70.5	23.4	333	14.1	273
	N	4	4	4	4	4	4	4	4
3	MEAN	7.070	163.3 A^1	0.490 B^1	69.23	23.05	333.0	12.85	214.5
	SD	0.312	11.8	0.032	1.18	0.75	6.3	0.72	19.4
	MIN	6.66	148	0.45	68.2	22.2	326	12.0	201
	MAX	7.39	173	0.52	70.3	24.0	341	13.5	243
	N	4	4	4	4	4	4	4	4
4	MEAN	7 130 A^1	162.0 B^1	0.490 B^1	68.88	22.75 A^1	330 5	13.15	236.8
	SD	0.410	8.8	0.022	2.47	0.95	4.7	0.66	23.8
	MIN	6.73	154	0.47	65.8	21.5	326	12.3	222
	MAX	7.62	174	0.52	71.2	23.8	335	13.9	272
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	9.110	4.788	3.295	0.585	0.303	0.093	0.048
	SD	1.706	0.954	0.792	0.170	0.061	0.022	0.022
	MIN	7.24	4.03	2.47	0.38	0.23	0.06	0.02
	MAX	10.64	6.05	4.37	0.73	0.37	0 11	0.07
	N	4	4	4	4	4	4	4
2	MEAN	9.568	5.210	3.525	0.428	0.275	0.088	0.038
	SD	0.335	0.529	0.293	0.098	0.087	0.033	0.005
	MIN	9.15	4.46	3.17	0.35	0.20	0.04	0.03
	MAX	9.89	5.70	3.84	0.57	0.35	0 11	0.04
	N	4	4	4	4	4	4	4
3	MEAN	7.440	3.993	2.788	0.328	0.243	0.060	0.030
	SD	1.017	0.664	0.480	0.039	0.166	0.040	0.012
	MIN	6.15	3.09	2.23	0.28	0.14	0.04	0.02
	MAX	8.39	4.68	3.32	0.36	0.49	0 12	0.04
	N	4	4	4	4	4	4	4
4	MEAN	8.135	4.190	3.290	0.415	0.158	0.058	0.028
	SD	1.060	1.023	0.150	0.033	0.029	0.026	0.010
	MIN	6.80	2 99	3.15	0.39	0.14	0.03	0.02
	MAX	9.29	5.46	3.50	0.46	0.20	0.08	0.04
	N	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	52.70	36.13	6.33	3.35	1.05	0.48	74.98	0.98
	SD	5.14	4.38	0.73	0.54	0.17	0.15	28.92	0.34
	MIN	47.0	31.1	5.3	2.7	0.9	0.3	36.2	0.5
	MAX	57.8	41.1	6.9	4.0	1.3	0.6	106.1	1.3
	N	4	4	4	4	4	4	4	4
2	MEAN	54.43	36.93	4.45 C^4	2.88	0.93	0.40	63.88	0.85
	SD	4.07	3.95	0.97	0.90	0.29	0.08	26.43	0.34
	MIN	48.8	32.4	3.5	2.1	0.5	0.3	38.9	0.5
	MAX	58.3	42.0	5.8	3.8	1.1	0.5	98.9	1.3
	N	4	4	4	4	4	4	4	4
3	MEAN	53.53	37.55	4.40 C^4	3.38	0.80	0.40	44.55 C^1	0.65 C^1
	SD	3.03	4.91	0.08	2.36	0.41	0.12	18.27	0.31
	MIN	50.3	31.3	4.3	1.9	0.5	0.3	27.5	0.4
	MAX	56.4	41.9	4.5	6.9	1.4	0.5	70.3	1.1
	N	4	4	4	4	4	4	4	4
4	MEAN	50.90	40.98	5 13 C^4	1.95	0.70	0.35	44.60 C^1	0.63 C^1
	SD	6.07	5.53	0.51	0.44	0.23	0.06	17.51	0.21
	MIN	43.9	34.0	4.5	1.5	0.5	0.3	25.6	0.4
	MAX	58.7	47.5	5.7	2.5	0.9	0.4	68.0	0.9
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	MEAN	7.353	170.8	0.513	69.95	23.24	332 3	13.64	218.9
	SD	0.564	14.3	0.042	0.93	0.62	5.1	0.57	50.2
	MIN	6.37	145	0.44	68.6	22.6	327	12.9	172
	MAX	8.25	190	0.58	71.2	24.0	340	14.4	324
	N	8	8	8	8	8	8	8	8
2	MEAN	7.430	167.3	0.508	68.15 B^3	22.49 B^1	329 9	13.58 A^1	222.1
	SD	0.433	10.1	0.032	1.68	0.59	3.4	0.55	36.7
	MIN	6.84	149	0.45	65.3	21.6	324	12.7	165
	MAX	7.97	177	0.54	70.5	23.4	335	14.1	273
	N	8	8	8	8	8	8	8	8
3	MEAN	6.953	159.6 A^1	0.480 B^1	68.96	22.95	332.6	12.89	224.6
	SD	0.278	9.8	0.030	1.62	0.62	5.7	0.69	34.3
	MIN	6.55	146	0.43	66.1	22.2	324	12.0	189
	MAX	7.39	173	0.52	71.1	24.0	341	13.6	294
	N	8	8	8	8	8	8	8	8
4	MEAN	7.096 A^1	162.5 B^1	0.490 B^1	69.08	22.90 A^1	332.0	13.08	246.3
	SD	0.446	9.8	0.029	1.67	0.66	3.8	0.76	19.8
	MIN	6.31	147	0.44	65.8	21.5	326	12.2	222
	MAX	7.62	174	0.53	71.2	23.8	336	14.2	272
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44

[redacted] (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	MEAN	8.981	4.914	3.138	0.481	0.328	0.080	0.041
	SD	1.500	1.065	0.575	0.166	0.123	0.025	0.022
	MIN	6.78	3 37	2.47	0.26	0.16	0.05	0.02
	MAX	10.64	6 25	4.37	0.73	0.54	0 11	0.07
	N	8	8	8	8	8	8	8
2	MEAN	9.740	5.491	3.405	0.425	0.301	0.074	0.040
	SD	0.734	0.697	0.386	0.065	0.071	0.027	0.015
	MIN	8.68	4.46	2.61	0.35	0.20	0.04	0.02
	MAX	10.78	6 27	3.84	0.57	0.40	0 11	0.07
	N	8	8	8	8	8	8	8
3	MEAN	8.781	4.966	3.010	0.409	0.296	0.066	0.033
	SD	2.516	1.763	0.640	0.113	0.137	0.043	0.012
	MIN	6.15	3.09	2.20	0.28	0.14	0.04	0.02
	MAX	13.88	8.67	3.99	0.61	0.49	0 15	0.05
	N	8	8	8	8	8	8	8
4	MEAN	8.728	4.723	3.249	0.456	0.220	0.055	0.028
	SD	1.107	1.032	0.129	0.064	0.090	0.025	0.007
	MIN	6.80	2 99	3.11	0.39	0.14	0.02	0.02
	MAX	10.06	6.08	3.50	0.55	0.40	0.08	0.04
	N	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	54.49	35.11	3.80	0 93	0.40	61.08	0.83
	SD	5.38	3.96	1.76	0 21	0.18	29.02	0.34
	MIN	47.0	30.3	1.5	0.6	0.2	29.0	0.4
	MAX	61.3	41.1	6.6	1.3	0.6	106.1	1.3
	N	8	8	8	8	8	8	8
2	MEAN	56.28	35.06	3.09	0.79	0.40	57.68	0.79
	SD	4.42	4.32	0.67	0 24	0.11	19.13	0.25
	MIN	48.8	27.6	2.1	0.5	0.3	38.9	0.5
	MAX	63.7	42.0	3.8	1.1	0.6	98.9	1.3
	N	8	8	8	8	8	8	8
3	MEAN	55.80	34.96	3.49	0.75	0.38	42.79 **C[1]**	0.63 **C[1]**
	SD	3.75	4.53	1.69	0 34	0.10	14.06	0.23
	MIN	50.3	28.8	1.9	0.4	0.3	25.4	0.4
	MAX	62.5	41.9	6.9	1.4	0.5	70.3	1.1
	N	8	8	8	8	8	8	8
4	MEAN	53.50	37.83	2.49	0.64	0.31	43.65 **C[1]**	0.61 **C[1]**
	SD	5.44	5.59	0.86	0 25	0.06	16.32	0.21
	MIN	43.9	30.9	1.5	0.2	0.2	22.6	0.3
	MAX	60.4	47.5	4.3	0.9	0.4	68.0	0.9
	N	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 [redacted]

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCH (pg)	MCHC (g/L)	RDW (%)
1	MEAN	6.218	140.9	0.433	22.63	324.1	13.41
	SD	0.313	5.2	0.020	0.43	3.1	0 26
	MIN	5.92	137	0.42	22.4	322	13.3
	MAX	6.64	148	0.46	23.3	329	13.8
	N	4	4	4	4	4	4
2	MEAN	6.418	139.6	0.431	21.68 B^1	323.7	13.83 A^1
	SD	0.418	10.7	0.031	0.68	3.0	0.77
	MIN	5.99	125	0.39	20.8	320	13.3
	MAX	6.86	149	0.46	22.4	327	15.0
	N	4	4	4	4	4	4
3	MEAN	6.118	137.6 A^1	0.421 B^1	22.46	325.7	13.00
	SD	0.114	2.7	0.012	0.60	2.8	0 36
	MIN	5.97	134	0.41	21.9	322	12.5
	MAX	6.25	140	0.43	23.3	328	13.3
	N	4	4	4	4	4	4
4	MEAN	6 193 A^1	138.6 B^1	0.424 B^1	22.30 A^1	326.0	13.08
	SD	0.492	10.9	0.031	0.23	4.4	0 57
	MIN	5.55	125	0.39	22.0	322	12.4
	MAX	6.67	150	0.46	22.5	332	13.8
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	BASO (x10^9/L)
1	MEAN	9.928	5.222	3.779	0.514	0.052
	SD	1.046	0.754	0.287	0.091	0.015
	MIN	8.61	4.27	3.50	0.40	0.04
	MAX	10.81	6.01	4.05	0.60	0.07
	N	4	4	4	4	4
2	MEAN	10.913	6.022	3.969	0.537	0.057
	SD	1.026	0.799	0.447	0.047	0.013
	MIN	9.73	4.86	3.43	0.48	0.04
	MAX	11.92	6.61	4.51	0.59	0.07
	N	4	4	4	4	4
3	MEAN	10.642	5.812	3.874	0.546	0.058
	SD	2.112	1.369	0.645	0.089	0.028
	MIN	7.95	4.11	3.06	0.47	0.04
	MAX	12.91	7.10	4.64	0.67	0.10
	N	4	4	4	4	4
4	MEAN	10.099	5.211	3.966	0.561	0.051
	SD	1.219	0.890	0.380	0.124	0.014
	MIN	9.03	4.24	3.61	0.43	0.04
	MAX	11.60	6.06	4.48	0.73	0.07
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	52.50	38.00	102.89	1.75
	SD	2.46	1.63	15.18	0.19
	MIN	49.7	37.0	85.6	1.5
	MAX	55.7	40.4	122.5	1.9
	N	4	4	4	4
2	MEAN	54.95	36.51	92.41	1.52
	SD	4.06	3.19	12.86	0.26
	MIN	49.8	32.8	75.0	1.3
	MAX	59.3	40.2	105.6	1.9
	N	4	4	4	4
3	MEAN	54.10	36.82	80.01 C^1	1.38 C^1
	SD	2.65	1.67	6.63	0.13
	MIN	51.8	34.7	71.4	1.2
	MAX	57.5	38.3	85.3	1.5
	N	4	4	4	4
4	MEAN	51.33	39.63	68.34 C^1	1.16 C^1
	SD	4.10	4.33	18.66	0.29
	MIN	47.3	34.2	51.8	0.8
	MAX	57.0	44.0	95.0	1.5
	N	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCH (pg)	MCHC (g/L)	RDW (%)
1	MEAN	6.644	151.8	0.466	22.82	325.4	13.15
	SD	0.385	8.0	0.027	0.44	3.4	0 23
	MIN	6.28	143	0.44	22.4	322	13.0
	MAX	7.12	161	0.50	23.4	330	13.5
	N	4	4	4	4	4	4
2	MEAN	6.773	150.3	0.466	22.15 B^1	322.0	13.72 A^1
	SD	0.145	4.4	0.012	0.54	3.5	0.74
	MIN	6.60	145	0.45	21.8	318	13.0
	MAX	6.95	155	0.47	23.0	326	14.7
	N	4	4	4	4	4	4
3	MEAN	6.259	141.0 A^1	0.431 B^1	22.49	326.3	12.70
	SD	0.138	6.4	0.017	0.61	3.2	0 19
	MIN	6.10	134	0.41	21.8	323	12.4
	MAX	6.40	149	0.45	23.3	330	12.8
	N	4	4	4	4	4	4
4	MEAN	6 196 A^1	137.3 B^1	0.425 B^1	22.14 A^1	322.2	13.25
	SD	0.241	6.3	0.017	0.98	2.7	0.75
	MIN	5.98	129	0.41	20.9	318	12.7
	MAX	6.53	144	0.45	23.1	325	14.4
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	BASO (x10^9/L)
1	MEAN	9.788	5.044	3.781	0.577	0.059
	SD	0.961	1.107	0.361	0.073	0.005
	MIN	8.58	3.99	3.46	0.49	0.06
	MAX	10.63	6.05	4.30	0.67	0.07
	N	4	4	4	4	4
2	MEAN	10.355	5.426	4.031	0.542	0.064
	SD	0.729	0.543	0.328	0.136	0.012
	MIN	9.77	4.79	3.58	0.43	0.05
	MAX	11.29	6.12	4.36	0.74	0.08
	N	4	4	4	4	4
3	MEAN	9.565	5.244	3.488	0.526	0.046
	SD	0.937	0.808	0.365	0.099	0.020
	MIN	8.42	4.14	3.20	0.43	0.03
	MAX	10.46	6.05	3.95	0.66	0.08
	N	4	4	4	4	4
4	MEAN	9.719	4.920	4.013	0.511	0.051
	SD	1.591	1.032	0.668	0.089	0.012
	MIN	7.93	3.73	3.52	0.43	0.04
	MAX	11.40	5.99	5.00	0.61	0.06
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	51.16	38.91	112.64	1.78
	SD	6.69	6.21	37.67	0.52
	MIN	44.3	32.5	67.3	1.1
	MAX	57.0	45.5	158.6	2.3
	N	4	4	4	4
2	MEAN	52.35	39.01	102.74	1.58
	SD	2.96	2.81	18.55	0.27
	MIN	48.9	36.5	85.0	1.3
	MAX	55.4	41.7	119.1	1.8
	N	4	4	4	4
3	MEAN	54.08	37.24	70.94 **C[1]**	1.18 **C[1]**
	SD	4.24	4.77	13.56	0.24
	MIN	49.2	31.8	59.2	1.0
	MAX	58.7	42.9	87.9	1.5
	N	4	4	4	4
4	MEAN	50.29	41.54	76.26 **C[1]**	1.31 **C[1]**
	SD	3.96	3.95	18.59	0.31
	MIN	46.8	35.8	53.0	1.0
	MAX	56.0	44.6	98.5	1.7
	N	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44 (b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCH (pg)	MCHC (g/L)	RDW (%)
1	MEAN	6.431	146.3	0.449	22.72	324.8	13.28
	SD	0.397	8.5	0.028	0.41	3.1	0 27
	MIN	5.92	137	0.42	22.4	322	13.0
	MAX	7.12	161	0.50	23.4	330	13.8
	N	8	8	8	8	8	8
2	MEAN	6.595	144.9	0.448	21.91 B^1	322.8	13.78 A^1
	SD	0.346	9.5	0.029	0.62	3.2	0.70
	MIN	5.99	125	0.39	20.8	318	13.0
	MAX	6.95	155	0.47	23.0	327	15.0
	N	8	8	8	8	8	8
3	MEAN	6.189	139.3 A^1	0.426 B^1	22.47	326.0	12.85
	SD	0.139	4.9	0.015	0.56	2.8	0 31
	MIN	5.97	134	0.41	21.8	322	12.4
	MAX	6.40	149	0.45	23.3	330	13.3
	N	8	8	8	8	8	8
4	MEAN	6 194 A^1	137.9 B^1	0.425 B^1	22.22 A^1	324.1	13.16
	SD	0.359	8.2	0.023	0.67	4.0	0.62
	MIN	5.55	125	0.39	20.9	318	12.4
	MAX	6.67	150	0.46	23.1	332	14.4
	N	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	BASO (x10^9/L)
1	MEAN	9.858	5.133	3.780	0.546	0.056
	SD	0.933	0.882	0.302	0.083	0.011
	MIN	8.58	3.99	3.46	0.40	0.04
	MAX	10.81	6.05	4.30	0.67	0.07
	N	8	8	8	8	8
2	MEAN	10.634	5.724	4.000	0.539	0.061
	SD	0.876	0.708	0.364	0.094	0.012
	MIN	9.73	4.79	3.43	0.43	0.04
	MAX	11.92	6.61	4.51	0.74	0.08
	N	8	8	8	8	8
3	MEAN	10.103	5.528	3.681	0.536	0.052
	SD	1.619	1.084	0.527	0.088	0.023
	MIN	7.95	4.11	3.06	0.43	0.03
	MAX	12.91	7.10	4.64	0.67	0.10
	N	8	8	8	8	8
4	MEAN	9.909	5.065	3.989	0.536	0.051
	SD	1.328	0.905	0.504	0.104	0.012
	MIN	7.93	3.73	3.52	0.43	0.04
	MAX	11.60	6.06	5.00	0.73	0.07
	N	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 44

(b) (4)

HEMATOLOGY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	RETIC (x10^9/L)	RETIC (%)
1	MEAN	51.83	38.45	107.77	1.76
	SD	4.72	4.23	27.10	0.36
	MIN	44.3	32.5	67.3	1.1
	MAX	57.0	45.5	158.6	2.3
	N	8	8	8	8
2	MEAN	53.65	37.76	97.57	1.55
	SD	3.57	3.09	15.77	0.25
	MIN	48.9	32.8	75.0	1.3
	MAX	59.3	41.7	119.1	1.9
	N	8	8	8	8
3	MEAN	54.09	37.03	75.48 **C[1]**	1.28 **C[1]**
	SD	3.28	3.31	11.01	0.21
	MIN	49.2	31.8	59.2	1.0
	MAX	58.7	42.9	87.9	1.5
	N	8	8	8	8
4	MEAN	50.81	40.59	72.30 **C[1]**	1.24 **C[1]**
	SD	3.77	3.97	17.76	0.29
	MIN	46.8	34.2	51.8	0.8
	MAX	57.0	44.6	98.5	1.7
	N	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	27.5	27.3	240.0	4.755	0.460	7.15	3.28	23.5
	SD	1.7	3.0	129.8	0.451	0.144	0.19	0.57	2.4
	MIN	25	24	114	4.39	0.30	6.9	2.8	21
	MAX	29	31	422	5.40	0.65	7.3	4.1	26
	N	4	4	4	4	4	4	4	4
2	MEAN	31.8 C^3	33.5	209.8	4 915	0.583 A^3	6.30 C^3	4.58 C^3	30.3
	SD	2.2	10.4	47.5	0 283	0.104	0.58	0.40	5.4
	MIN	29	26	161	4.52	0.47	5.8	4.0	24
	MAX	34	48	275	5.16	0.72	6.8	4.9	37
	N	4	4	4	4	4	4	4	4
3	MEAN	29.8	29.8	223.0	4 598	0.515 B^3	6.78	4.43 B^3	26.5
	SD	5.1	3.6	114.7	0.417	0.127	0.39	1.07	5.4
	MIN	24	27	115	4.02	0.37	6.2	3.4	20
	MAX	34	35	382	4.98	0.64	7.0	5.9	33
	N	4	4	4	4	4	4	4	4
4	MEAN	38.3 C^3	45.7 C^1	253.7	3.317 C^3	0.390	6.33 B^3	6.43 C^3	25.0
	SD	5.5	26.5	109.3	0.486	0.046	0.32	0.84	3.6
	MIN	33	27	163	2.85	0.34	6.1	5.9	21
	MAX	44	76	375	3.82	0.43	6.7	7.4	28
	N	3	3	3	3	3	3	3	3

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	48.15	32.58	15.58	2.113	2 980	2.793	144.8	5.445	105.1
	SD	2.37	1.19	1.80	0.242	0.082	0.041	1.0	0 237	0.9
	MIN	45.2	31.4	13.5	1.88	2.86	2.74	144	5.23	104
	MAX	51.0	33.6	17.4	2.35	3.04	2.84	146	5.78	106
	N	4	4	4	4	4	4	4	4	4
2	MEAN	47.70	32.60	15.10	2.178	2 923	2.770	145.0	5 393	104.6
	SD	1.36	0.49	1.63	0.247	0.059	0.045	2.2	0 299	1.6
	MIN	46.5	32.0	13.5	1.86	2.86	2.71	143	5.03	103
	MAX	49.2	33.0	17.2	2.44	3.00	2.81	148	5.75	106
	N	4	4	4	4	4	4	4	4	4
3	MEAN	46.83	32.78	14.05	2.340	2 943	2.845	146.3 B^1	5 330	105.3
	SD	2.28	2.23	0.87	0.218	0.095	0.161	1.5	0 330	1.4
	MIN	43.9	30.7	13.2	2.04	2.86	2.62	145	4.84	104
	MAX	49.0	34.8	15.2	2.54	3.08	2.97	148	5.56	107
	N	4	4	4	4	4	4	4	4	4
4	MEAN	49.07	33.70	15.37	2.220	2.877	2.650 A^1	146.0	5.440	106.3
	SD	2.24	0.10	2.21	0.304	0 107	0.137	1.0	0 501	1.0
	MIN	47.1	33.6	13.5	1.89	2.81	2.53	145	4.96	105
	MAX	51.5	33.8	17.8	2.49	3.00	2.80	147	5.96	107
	N	3	3	3	3	3	3	3	3	3

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	83.3	409.8	4.80	350 5	0.755
	SD	18.0	49.6	4.68	39.9	0.039
	MIN	60	339	1.3	297	0.70
	MAX	98	448	11.7	393	0.79
	N	4	4	4	4	4
2	MEAN	194.8 B^3	530.0	4.43	390 3	0.740
	SD	79.4	117.8	3.22	35.7	0.035
	MIN	93	417	2.4	352	0.69
	MAX	286	667	9.2	438	0.77
	N	4	4	4	4	4
3	MEAN	89.0	409.8	5.95	383 5	0.760
	SD	45.5	100.2	2.83	28.7	0.008
	MIN	53	311	3.3	351	0.75
	MAX	155	545	9.5	418	0.77
	N	4	4	4	4	4
4	MEAN	205.0 C^3	539.3	2.97	370 3	0.793 C^1
	SD	142.3	125.4	1.00	21.5	0.012
	MIN	87	461	2.0	349	0.78
	MAX	363	684	4.0	392	0.80
	N	3	3	3	3	3

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	28.5	29.8	193.0	5.008	0.405	6.95	3.40	24.8
	SD	3.3	2.2	39.8	0 135	0.052	0.10	0.22	2.4
	MIN	24	28	142	4.85	0.33	6.8	3.1	23
	MAX	32	33	238	5.18	0.44	7.0	3.6	28
	N	4	4	4	4	4	4	4	4
2	MEAN	36.8 C^3	39.3	197.0	4.440	0.500 A^3	6.23 C^3	4.28 C^3	28.5
	SD	4.5	5.9	88.0	0.676	0.091	0.54	0.92	8.3
	MIN	31	33	125	3.76	0.43	5.5	3.5	18
	MAX	42	47	325	5.19	0.62	6.8	5.6	38
	N	4	4	4	4	4	4	4	4
3	MEAN	30.8	27.5	243.8	4 995	0.663 B^3	6.75	4.03 B^3	27.0
	SD	2.9	4.2	114.4	0 582	0.148	0.37	0.74	7.4
	MIN	29	23	144	4.15	0.48	6.5	3.2	16
	MAX	35	32	389	5.40	0.84	7.3	5.0	32
	N	4	4	4	4	4	4	4	4
4	MEAN	40.0 C^3	45.8 C^1	246.8	3.513 C^3	0.408	6.78 B^3	6.05 C^3	26.8
	SD	4.7	15.6	53.6	0.436	0.010	0.61	0.93	3.0
	MIN	37	30	192	2.93	0.40	6.2	4.9	24
	MAX	47	64	313	3.89	0.42	7.4	7.1	31
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

[redacted] (b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	48.43	32.98	15.45	2.160	2 963	2.643	144.0	5 253	103.9
	SD	0.86	1.61	1.53	0.341	0 102	0.093	0.8	0 291	1.9
	MIN	47.4	31.6	13.2	1.95	2.84	2.51	143	4.88	102
	MAX	49.5	35.2	16.4	2.67	3.08	2.72	145	5.56	106
	N	4	4	4	4	4	4	4	4	4
2	MEAN	47.65	33.03	14.63	2.295	2 935	2.790	145 5	5.463	105.5
	SD	1.01	1.81	1.79	0.402	0.030	0.094	1.9	0 273	0.8
	MIN	46.6	30.6	12.5	1.91	2.91	2.65	143	5.14	105
	MAX	48.9	34.6	16.2	2.77	2.97	2.85	147	5.80	107
	N	4	4	4	4	4	4	4	4	4
3	MEAN	47.58	33.08	14.50	2.293	2 925	2.710	145.5 B^1	5.055	104.3
	SD	2.02	2.04	0.91	0.221	0 137	0.147	1.9	0 116	0.9
	MIN	45.0	30.7	13.7	2.06	2.73	2.49	144	4.97	103
	MAX	49.8	35.6	15.8	2.51	3.05	2.79	148	5.22	106
	N	4	4	4	4	4	4	4	4	4
4	MEAN	48.30	33.70	14.60	2.315	2 943	2.763 A^1	145.0	5.600	104.7
	SD	0.96	0.50	0.86	0.143	0.093	0.050	0.8	0 351	1.1
	MIN	47.3	33.1	13.8	2.14	2.84	2.69	144	5.36	103
	MAX	49.6	34.3	15.8	2.49	3.06	2.80	146	6.11	106
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	67.8	411.5	5.00	378.0	0.750
	SD	9.2	58.4	3.90	5.8	0.046
	MIN	59	335	1.4	372	0.71
	MAX	78	477	10.1	386	0.79
	N	4	4	4	4	4
2	MEAN	95.3 B^3	640.0	9.05	403.8	0.765
	SD	27.0	367.7	9.89	40.7	0.017
	MIN	64	379	2.1	365	0.74
	MAX	122	1183	23.5	446	0.78
	N	4	4	4	4	4
3	MEAN	71.0	392.5	11.40	330.0	0.750
	SD	34.4	75.1	8.31	33.7	0.055
	MIN	47	327	4.6	284	0.71
	MAX	122	497	23.3	364	0.83
	N	4	4	4	4	4
4	MEAN	140.5 C^3	441.0	8.35	395.8	0.803 C^1
	SD	74.5	36.6	7.31	45.4	0.028
	MIN	74	402	2.1	353	0.77
	MAX	206	487	16.0	435	0.83
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	28.0	28.5	216.5	4.881	0.433	7.05	3.34	24.1
	SD	2.5	2.8	92.4	0 337	0.104	0.18	0.40	2.3
	MIN	24	24	114	4.39	0.30	6.8	2.8	21
	MAX	32	33	422	5.40	0.65	7.3	4.1	28
	N	8	8	8	8	8	8	8	8
2	MEAN	34.3 C^3	36.4	203.4	4.678	0.541 A^3	6.26 C^3	4.43 C^3	29.4
	SD	4.2	8.4	65.8	0 543	0.101	0.52	0.68	6.6
	MIN	29	26	125	3.76	0.43	5.5	3.5	18
	MAX	42	48	325	5.19	0.72	6.8	5.6	38
	N	8	8	8	8	8	8	8	8
3	MEAN	30.3	28.6	233.4	4.796	0.589 B^3	6.76	4.23 B^3	26.8
	SD	3.8	3.8	106.6	0 515	0.150	0.35	0.88	6.0
	MIN	24	23	115	4.02	0.37	6.2	3.2	16
	MAX	35	35	389	5.40	0.84	7.3	5.9	33
	N	8	8	8	8	8	8	8	8
4	MEAN	39.3 C^3	45.7 C^1	249.7	3.429 C^3	0.400	6.59 B^3	6.21 C^3	26.0
	SD	4.7	18.9	73.7	0.430	0.029	0.53	0.84	3.1
	MIN	33	27	163	2.85	0.34	6.1	4.9	21
	MAX	47	76	375	3.89	0.43	7.4	7.4	31
	N	7	7	7	7	7	7	7	7

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)
1	MEAN	48.29	32.78	15.51	2 136	2.971	2.718	144.4	5.349
	SD	1.66	1.33	1.54	0 275	0.086	0 104	0 9	0.266
	MIN	45.2	31.4	13.2	1.88	2.84	2.51	143	4.88
	MAX	51.0	35.2	17.4	2.67	3.08	2.84	146	5.78
	N	8	8	8	8	8	8	8	8
2	MEAN	47.68	32.81	14.86	2 236	2.929	2.780	145.3	5.428
	SD	1 11	1.25	1.60	0 315	0.044	0.069	1 9	0.268
	MIN	46.5	30.6	12.5	1.86	2.86	2.65	143	5.03
	MAX	49.2	34.6	17.2	2.77	3.00	2.85	148	5.80
	N	8	8	8	8	8	8	8	8
3	MEAN	47.20	32.93	14.28	2 316	2.934	2.778	145.9 B^1	5.193
	SD	2.03	1.99	0.86	0 205	0.110	0 160	1.6	0.272
	MIN	43.9	30.7	13.2	2.04	2.73	2.49	144	4.84
	MAX	49.8	35.6	15.8	2.54	3.08	2.97	148	5.56
	N	8	8	8	8	8	8	8	8
4	MEAN	48.63	33.70	14.93	2 274	2.914	2.714 A^1	145.4	5.531
	SD	1 51	0.36	1.47	0 209	0.097	0 106	1.0	0.390
	MIN	47.1	33.1	13.5	1.89	2.81	2.53	144	4.96
	MAX	51.5	34.3	17.8	2.49	3.06	2.80	147	6.11
	N	7	7	7	7	7	7	7	7

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	75.5	410.6	4.90	364 3	0.753
	SD	15.6	50.2	3.99	30.2	0.040
	MIN	59	335	1.3	297	0.70
	MAX	98	477	11.7	393	0.79
	N	8	8	8	8	8
2	MEAN	145.0 B^3	585.0	6.74	397.0	0.753
	SD	76.5	259.5	7.24	36.2	0.029
	MIN	64	379	2.1	352	0.69
	MAX	286	1183	23.5	446	0.78
	N	8	8	8	8	8
3	MEAN	80.0	401.1	8.68	356.8	0.755
	SD	38.5	82.5	6.44	40.7	0.037
	MIN	47	311	3.3	284	0.71
	MAX	155	545	23.3	418	0.83
	N	8	8	8	8	8
4	MEAN	168.1 C^3	483.1	6.04	384 9	0.799 C^1
	SD	103.5	93.2	5.94	37.0	0.021
	MIN	74	402	2.0	349	0.77
	MAX	363	684	16.0	435	0.83
	N	7	7	7	7	7

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	29.0	28.0	199.3	6.180	0.398	6.23	3.95	30.3
	SD	1.2	2.4	120.0	0.533	0.017	0.26	0.52	1.3
	MIN	28	25	121	5.49	0.38	6.0	3.3	29
	MAX	30	30	378	6.63	0.42	6.5	4.5	32
	N	4	4	4	4	4	4	4	4
2	MEAN	28.3	27.8	180.3	6.510	0.385	6.10	4.75	32.8
	SD	2.6	3.4	36.3	0.799	0.033	0.36	0.17	3.3
	MIN	26	25	139	5.63	0.35	5.7	4.6	29
	MAX	32	32	227	7.57	0.43	6.4	5.0	37
	N	4	4	4	4	4	4	4	4
3	MEAN	30.5	28.3	199.3	5.808	0.393	6.65	4.50	32.3
	SD	5.0	6.1	106.8	0.551	0.070	0.40	0.52	1.0
	MIN	25	24	106	5.14	0.30	6.1	4.0	31
	MAX	37	37	352	6.40	0.46	7.0	5.0	33
	N	4	4	4	4	4	4	4	4
4	MEAN	34.3	46.3 C^1	201.3	5.403 C^3	0.290 C^3	6.05	4.53	29.5 B^3
	SD	5.9	27.3	26.7	0.365	0.024	0.25	0.68	4.0
	MIN	26	30	173	4.89	0.26	5.7	3.6	26
	MAX	39	87	226	5.71	0.32	6.3	5.2	35
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	49.98	31.48	18.50	1.713	2.855	2.575	146.0	5.075	106.8
	SD	2.54	1.41	1.93	0.179	0.076	0.115	1.4	0 133	0.9
	MIN	46.4	29.9	16.5	1.52	2.78	2.44	145	4.97	105
	MAX	52.4	33.3	20.8	1.91	2.95	2.72	148	5.27	108
	N	4	4	4	4	4	4	4	4	4
2	MEAN	49.65	31.45	18.20	1.738	2.843	2.493	146.8	5.058	108.1
	SD	1.28	0.60	1.28	0.136	0.029	0.148	0.5	0.079	2.0
	MIN	48.1	30.8	16.9	1.61	2.82	2.32	146	4.98	106
	MAX	50.8	32.2	19.4	1.91	2.88	2.68	147	5.14	110
	N	4	4	4	4	4	4	4	4	4
3	MEAN	51.53	33.75	17.78	1.905	2 905	2.518	147.0 B^1	4.865	108.3
	SD	0.56	0.81	0.84	0.124	0.078	0.099	0.0	0 105	0.9
	MIN	50.9	33.0	17.1	1.74	2.82	2.42	147	4.72	107
	MAX	52.0	34.9	19.0	2.04	3.00	2.63	147	4.97	109
	N	4	4	4	4	4	4	4	4	4
4	MEAN	51.73	32.65	19.08	1.720	2.890	2.420 A^1	146.0	5 235	107.8
	SD	0.95	1.08	1.22	0.163	0.042	0.151	1.4	0.466	1.7
	MIN	50.7	31.4	17.3	1.61	2.85	2.20	145	4.78	107
	MAX	52.8	33.9	20.0	1.96	2.95	2.54	148	5.79	110
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	74.3	294.3	4.53	501.8	0.733
	SD	50.3	33.4	4.81	53.7	0.031
	MIN	42	265	1.7	431	0.69
	MAX	149	342	11.7	560	0.76
	N	4	4	4	4	4
2	MEAN	59.0	286.3	1.63	582.5	0.698
	SD	10.7	60.2	0.66	60.7	0.022
	MIN	48	225	1.2	520	0.67
	MAX	73	358	2.6	656	0.72
	N	4	4	4	4	4
3	MEAN	80.8	488.5	1.43	562.5	0.725
	SD	41.3	229.8	0.26	42.0	0.006
	MIN	52	305	1.2	515	0.72
	MAX	141	806	1.8	609	0.73
	N	4	4	4	4	4
4	MEAN	97.0	301.5	20.07	496.8	0.775 C^1
	SD	74.9	54.1	14.89	80.3	0.037
	MIN	48	252	3.6	428	0.74
	MAX	207	369	32.6	589	0.82
	N	4	4	3	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	32.0	28.0	178.5	6.445	0.393	6.38	4.35	35.3
	SD	5.5	3.4	32.7	0.136	0.045	0.59	0.59	3.0
	MIN	26	26	146	6.31	0.37	5.5	3.8	31
	MAX	39	33	222	6.63	0.46	6.7	5.0	38
	N	4	4	4	4	4	4	4	4
2	MEAN	31.5	31.3	151.8	6.240	0.385	6.15	4.38	33.5
	SD	3.1	3.0	67.3	0.614	0.050	0.41	0.76	4.4
	MIN	28	28	97	5.61	0.32	5.8	3.7	27
	MAX	35	35	249	7.07	0.44	6.6	5.3	36
	N	4	4	4	4	4	4	4	4
3	MEAN	27.3	27.8	210.5	6.130	0.400	6.38	4.38	32.5
	SD	2.1	9.6	85.5	0.677	0.162	0.33	0.74	3.7
	MIN	25	22	130	5.13	0.26	6.0	3.3	28
	MAX	30	42	330	6.56	0.63	6.8	5.0	37
	N	4	4	4	4	4	4	4	4
4	MEAN	31.3	43.8 C^1	193.8	5.353 C^3	0.275 C^3	6.33	4.95	28.3 B^3
	SD	6.6	23.2	35.4	0.682	0.041	0.61	0.59	3.6
	MIN	23	25	143	4.70	0.23	5.9	4.3	25
	MAX	37	76	220	6.05	0.31	7.2	5.5	33
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	52.15	34.00	18.15	1.873	2.893	2.558	146 5	5 168	105.4
	SD	1.54	1.01	0.57	0.030	0.093	0.112	1.3	0 380	1.4
	MIN	51.0	33.3	17.7	1.83	2.83	2.41	145	4.77	103
	MAX	54.4	35.5	18.9	1.90	3.03	2.65	148	5.67	106
	N	4	4	4	4	4	4	4	4	4
2	MEAN	51.83	33.73	18.10	1.870	2 938	2.570	145.8	5.018	105.8
	SD	0.79	0.56	1.12	0.145	0.096	0.133	1.0	0 373	1.0
	MIN	50.7	32.9	16.7	1.70	2.87	2.44	145	4.70	105
	MAX	52.5	34.1	19.3	2.04	3.08	2.75	147	5.42	107
	N	4	4	4	4	4	4	4	4	4
3	MEAN	51.70	33.78	17.93	1.893	2 928	2.580	146.8 **B[1]**	4.803	108.1 **C[4]**
	SD	2.33	1.35	1.49	0.153	0.075	0.171	1.7	0 212	1.2
	MIN	49.4	31.8	16.3	1.74	2.82	2.39	145	4.59	107
	MAX	54.6	34.7	19.9	2.09	2.98	2.80	149	4.99	109
	N	4	4	4	4	4	4	4	4	4
4	MEAN	51.28	33.65	17.63	1.913	2.888	2.463 **A[1]**	146.8	4 920	108.0 **C[4]**
	SD	2.77	2.60	0.78	0.168	0.057	0.137	1.0	0 218	0.6
	MIN	48.8	31.6	17.2	1.79	2.83	2.32	146	4.69	108
	MAX	54.6	37.3	18.8	2.16	2.95	2.65	148	5.18	109
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	101.8	312.8	10.63	533.3	0.760
	SD	58.0	30.0	13.05	42.3	0.061
	MIN	46	275	1.1	470	0.67
	MAX	170	346	29.9	558	0.80
	N	4	4	4	4	4
2	MEAN	63.3	298.0	17.37	584.8	0.735
	SD	9.8	14.7	26.37	65.9	0.044
	MIN	58	278	1.4	529	0.71
	MAX	78	312	47.8	667	0.80
	N	4	4	3	4	4
3	MEAN	50.8	264.8	11.37	517.8	0.748
	SD	9.1	28.0	12.41	31.4	0.062
	MIN	44	235	1.5	494	0.68
	MAX	64	295	25.3	564	0.80
	N	4	4	3	4	4
4	MEAN	54.5	273.8	12.93	544.3	0.785 C^1
	SD	7.6	53.0	12.48	56.3	0.039
	MIN	48	215	2.0	477	0.73
	MAX	65	322	28.2	614	0.82
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	30.5	28.0	188.9	6.313	0.395	6.30	4.15	32.8
	SD	4.0	2.7	82.2	0.387	0.032	0.43	0.56	3.4
	MIN	26	25	121	5.49	0.37	5.5	3.3	29
	MAX	39	33	378	6.63	0.46	6.7	5.0	38
	N	8	8	8	8	8	8	8	8
2	MEAN	29.9	29.5	166.0	6.375	0.385	6.13	4.56	33.1
	SD	3.2	3.5	52.3	0.675	0.039	0.36	0.55	3.6
	MIN	26	25	97	5.61	0.32	5.7	3.7	27
	MAX	35	35	249	7.57	0.44	6.6	5.3	37
	N	8	8	8	8	8	8	8	8
3	MEAN	28.9	28.0	204.9	5.969	0.396	6.51	4.44	32.4
	SD	3.9	7.5	89.7	0.597	0.116	0.37	0.60	2.5
	MIN	25	22	106	5.13	0.26	6.0	3.3	28
	MAX	37	42	352	6.56	0.63	7.0	5.0	37
	N	8	8	8	8	8	8	8	8
4	MEAN	32.8	45.0 **C**[1]	197.5	5.378 **C**[3]	0.283 **C**[3]	6.19	4.74	28.9 **B**[3]
	SD	6.0	23.5	29.3	0.507	0.032	0.46	0.63	3.6
	MIN	23	25	143	4.70	0.23	5.7	3.6	25
	MAX	39	87	226	6.05	0.32	7.2	5.5	35
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)
1	MEAN	51.06	32.74	18.33	1.793	2.874	2 566	146.3	5.121
	SD	2 26	1.76	1.33	0 146	0.081	0 106	1 3	0.268
	MIN	46.4	29.9	16.5	1.52	2.78	2.41	145	4.77
	MAX	54.4	35.5	20.8	1.91	3.03	2.72	148	5.67
	N	8	8	8	8	8	8	8	8
2	MEAN	50.74	32.59	18.15	1.804	2.890	2 531	146.3	5.038
	SD	1 52	1.33	1.11	0 148	0.083	0 137	0 9	0.251
	MIN	48.1	30.8	16.7	1.61	2.82	2.32	145	4.70
	MAX	52.5	34.1	19.4	2.04	3.08	2.75	147	5.42
	N	8	8	8	8	8	8	8	8
3	MEAN	51.61	33.76	17.85	1.899	2.916	2 549	146.9 B^1	4.834
	SD	1 57	1.03	1.12	0 129	0.072	0 133	1 1	0.158
	MIN	49.4	31.8	16.3	1.74	2.82	2.39	145	4.59
	MAX	54.6	34.9	19.9	2.09	3.00	2.80	149	4.99
	N	8	8	8	8	8	8	8	8
4	MEAN	51.50	33.15	18.35	1.816	2.889	2.441 A^1	146.4	5.078
	SD	1 93	1.92	1.22	0 184	0.046	0 136	1 2	0.376
	MIN	48.8	31.4	17.2	1.61	2.83	2.20	145	4.69
	MAX	54.6	37.3	20.0	2.16	2.95	2.65	148	5.79
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	88.0	303.5	7.58	517.5	0.746
	SD	52.3	31.0	9.67	47.8	0.047
	MIN	42	265	1.1	431	0.67
	MAX	170	346	29.9	560	0.80
	N	8	8	8	8	8
2	MEAN	61.1	292.1	8.37	583.6	0.716
	SD	9.8	41.1	17.40	58.7	0.038
	MIN	48	225	1.2	520	0.67
	MAX	78	358	47.8	667	0.80
	N	8	8	7	8	8
3	MEAN	65.8	376.6	5.69	540.1	0.736
	SD	32.0	193.1	8.92	41.9	0.042
	MIN	44	235	1.2	494	0.68
	MAX	141	806	25.3	609	0.80
	N	8	8	7	8	8
4	MEAN	75.8	287.6	15.99	520.5	0.780 C^1
	SD	54.3	51.8	12.90	69.1	0.035
	MIN	48	215	2.0	428	0.73
	MAX	207	369	32.6	614	0.82
	N	8	8	7	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	25.5	34.0	152.5	6.325	0.355	6.28	4.78	43.5
	SD	2.5	4.2	89.8	0.473	0.047	0.21	0.82	2.4
	MIN	23	29	89	6.00	0.32	6.1	3.9	41
	MAX	29	38	285	7.02	0.42	6.5	5.8	46
	N	4	4	4	4	4	4	4	4
2	MEAN	28.8	35.5	140.5	6.783	0.498 C^3	5.60 C^3	4.65	44.8
	SD	3.0	13.5	23.5	0.481	0.046	0.29	0.21	4.6
	MIN	26	23	108	6.27	0.44	5.3	4.4	40
	MAX	33	52	162	7.36	0.54	6.0	4.9	51
	N	4	4	4	4	4	4	4	4
3	MEAN	30.3	38.0	149.3	5.930	0.425 A^3	5.90 A^3	5.23	50.5
	SD	3.5	13.3	80.7	0.091	0.095	0.36	0.51	4.4
	MIN	26	24	83	5.83	0.29	5.4	4.7	45
	MAX	34	53	266	6.03	0.50	6.2	5.9	55
	N	4	4	4	4	4	4	4	4
4	MEAN	34.8	69.0 C^1	164.0	5.375	0.315	5.90	5.70 B^3	43.5 A^3
	SD	2.2	52.3	23.3	0.797	0.072	0.24	0.75	7.5
	MIN	33	37	140	4.27	0.23	5.6	5.1	36
	MAX	38	147	191	6.17	0.40	6.2	6.8	54
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	51.13	33.65	17.48	1.995	2.770	2.275	146.8	4.665	107.1
	SD	1.28	2.89	3.11	0.551	0.068	0.190	1.0	0.141	1.7
	MIN	49.9	31.4	13.7	1.47	2.68	2.02	146	4.49	105
	MAX	52.7	37.9	21.3	2.77	2.84	2.48	148	4.81	109
	N	4	4	4	4	4	4	4	4	4
2	MEAN	52.35	33.45	18.90	1.823	2.755	2.223	146.5	4.798	108.0
	SD	0.30	3.08	2.83	0.466	0.053	0.102	1.3	0.098	1.8
	MIN	52.1	30.0	15.2	1.36	2.71	2.08	145	4.67	106
	MAX	52.7	37.5	22.1	2.47	2.83	2.32	148	4.90	110
	N	4	4	4	4	4	4	4	4	4
3	MEAN	53.33	33.65	19.68 C^3	1.715	2.755	2.160	147.3 B^1	4.510	108.6
	SD	2.02	0.90	1.51	0.126	0.064	0.085	0.5	0.170	0.6
	MIN	51.9	32.7	18.1	1.59	2.70	2.06	147	4.34	108
	MAX	56.3	34.6	21.7	1.89	2.81	2.26	148	4.73	109
	N	4	4	4	4	4	4	4	4	4
4	MEAN	52.40	34.70	17.70	1.968	2.760	2.188 A^1	146.8	4.610	107.7
	SD	1.40	1.84	0.63	0.164	0.091	0.171	1.3	0.148	1.1
	MIN	51.2	32.9	17.0	1.78	2.66	2.03	145	4.48	106
	MAX	54.2	36.7	18.5	2.11	2.88	2.35	148	4.81	108
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45 [redacted] (b) (4)]

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	43.0	227.8	1.30	613.0	0.733
	SD	13.1	17.6	0.28	86.3	0.013
	MIN	33	203	1.1	509	0.72
	MAX	62	244	1.5	694	0.75
	N	4	4	2	4	4
2	MEAN	64.0	245.0	9.90	775.5	0.708
	SD	10.4	46.2	NA	85.0	0.017
	MIN	55	189	9.9	694	0.69
	MAX	79	302	9.9	885	0.73
	N	4	4	1	4	4
3	MEAN	107.8	236.0	2.05	738.8	0.728
	SD	54.8	50.5	1.06	55.0	0.017
	MIN	41	178	1.3	668	0.71
	MAX	175	300	2.8	799	0.75
	N	4	4	2	4	4
4	MEAN	112.8	268.3	2.90	739.0	0.765 C^1
	SD	60.5	85.9	1.70	208.2	0.041
	MIN	42	172	1.7	543	0.72
	MAX	175	380	4.1	1031	0.82
	N	4	4	2	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	31.0	35.0	130.5	6.370	0.373	6.20	4.70	48.0
	SD	8.9	6.2	26.5	0.413	0.059	0.59	0.16	4.8
	MIN	24	30	101	5.76	0.31	5.7	4.5	44
	MAX	44	44	165	6.67	0.45	7.0	4.9	55
	N	4	4	4	4	4	4	4	4
2	MEAN	32.0	42.3	111.0	5.593	0.473 C^3	5.73 C^3	4.58	47.5
	SD	3.2	6.6	39.8	1.033	0.057	0.15	0.70	5.0
	MIN	28	35	75	4.55	0.42	5.6	3.9	42
	MAX	35	51	167	7.02	0.54	5.9	5.4	54
	N	4	4	4	4	4	4	4	4
3	MEAN	29.3	35.0	156.8	5.970	0.418 A^3	5.85 A^3	4.95	48.0
	SD	1.0	12.5	73.0	0.338	0.093	0.26	1.21	2.2
	MIN	28	26	92	5.49	0.32	5.6	4.0	45
	MAX	30	53	259	6.23	0.54	6.2	6.7	50
	N	4	4	4	4	4	4	4	4
4	MEAN	32.3	61.3 C^1	145.8	5.830	0.360	5.93	5.63 B^3	39.8 A^3
	SD	5.0	32.7	19.7	1.010	0.052	0.21	1.18	2.6
	MIN	28	40	118	4.43	0.30	5.7	4.3	36
	MAX	39	109	164	6.83	0.42	6.2	7.0	42
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	52.95	36.10	16.85	2.153	2.745	2.165	146.8	4.603	107.8
	SD	1.80	0.55	1.48	0.179	0.058	0.056	0.5	0.248	0.9
	MIN	50.9	35.5	15.1	1.97	2.67	2.11	146	4.36	107
	MAX	55.3	36.7	18.6	2.37	2.81	2.24	147	4.91	109
	N	4	4	4	4	4	4	4	4	4
2	MEAN	52.83	35.53	17.30	2.078	2.803	2.218	146.8	4.573	107.6
	SD	1.33	1.84	1.87	0.310	0.090	0.102	0.5	0.340	0.3
	MIN	51.1	33.3	15.6	1.73	2.67	2.10	146	4.32	107
	MAX	54.1	37.8	19.2	2.39	2.87	2.34	147	5.04	108
	N	4	4	4	4	4	4	4	4	4
3	MEAN	53.45	34.65	18.80 C^3	1.855	2.793	2.113	147.5 B^1	4.503	108.4
	SD	1.52	1.58	1.40	0.193	0.084	0.066	0.6	0.086	1.1
	MIN	51.3	33.6	17.4	1.68	2.70	2.02	147	4.38	108
	MAX	54.8	37.0	20.0	2.08	2.89	2.16	148	4.58	110
	N	4	4	4	4	4	4	4	4	4
4	MEAN	52.63	35.25	17.38	2.040	2.795	2.030 A^1	146.8	4.495	107.6
	SD	2.11	1.05	1.51	0.154	0.098	0.134	0.5	0.170	0.4
	MIN	50.1	33.8	16.3	1.82	2.67	1.88	146	4.37	107
	MAX	54.9	36.3	19.5	2.18	2.91	2.19	147	4.74	108
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45 (b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	53.3	460.0	4.85	631.3	0.733
	SD	36.6	537.4	2.90	80.4	0.022
	MIN	29	183	2.8	529	0.70
	MAX	107	1266	6.9	725	0.75
	N	4	4	2	4	4
2	MEAN	84.5	248.3	5.88	678.5	0.730
	SD	19.2	16.8	3.66	126.1	0.018
	MIN	71	231	2.6	532	0.71
	MAX	113	265	10.5	838	0.75
	N	4	4	4	4	4
3	MEAN	47.5	192.0	2.40	621.0	0.725
	SD	5.3	19.4	2.25	68.9	0.041
	MIN	42	173	1.0	551	0.68
	MAX	52	212	5.0	708	0.76
	N	4	4	3	4	4
4	MEAN	61.0	211.3	3.70	601.3	0.780 C^1
	SD	28.0	25.3	3.24	116.5	0.020
	MIN	42	180	1.0	476	0.77
	MAX	102	242	8.2	741	0.81
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	28.3	34.5	141.5	6.348	0.364	6.24	4.74	45.8
	SD	6.7	5.0	62.4	0.412	0.050	0.41	0.55	4.3
	MIN	23	29	89	5.76	0.31	5.7	3.9	41
	MAX	44	44	285	7.02	0.45	7.0	5.8	55
	N	8	8	8	8	8	8	8	8
2	MEAN	30.4	38.9	125.8	6.188	0.485 C^3	5.66 C^3	4.61	46.1
	SD	3.3	10.5	34.1	0.980	0.050	0.23	0.48	4.7
	MIN	26	23	75	4.55	0.42	5.3	3.9	40
	MAX	35	52	167	7.36	0.54	6.0	5.4	54
	N	8	8	8	8	8	8	8	8
3	MEAN	29.8	36.5	153.0	5.950	0.421 A^3	5.88 A^3	5.09	49.3
	SD	2.4	12.1	71.4	0.230	0.087	0.29	0.87	3.5
	MIN	26	24	83	5.49	0.29	5.4	4.0	45
	MAX	34	53	266	6.23	0.54	6.2	6.7	55
	N	8	8	8	8	8	8	8	8
4	MEAN	33.5	65.1 C^1	154.9	5.603	0.338	5.91	5.66 B^3	41.6 A^3
	SD	3.8	40.6	22.2	0.877	0.063	0.21	0.91	5.6
	MIN	28	37	118	4.27	0.23	5.6	4.3	36
	MAX	39	147	191	6.83	0.42	6.2	7.0	54
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)
1	MEAN	52.04	34.88	17.16	2.074	2.758	2.220	146.8	4.634
	SD	1.75	2.33	2.28	0.388	0.060	0.142	0.7	0.190
	MIN	49.9	31.4	13.7	1.47	2.67	2.02	146	4 36
	MAX	55.3	37.9	21.3	2.77	2.84	2.48	148	4 91
	N	8	8	8	8	8	8	8	8
2	MEAN	52.59	34.49	18.10	1.950	2.779	2.220	146.6	4.685
	SD	0.93	2.60	2.38	0.391	0.073	0.095	0.9	0.261
	MIN	51.1	30.0	15.2	1.36	2.67	2.08	145	4 32
	MAX	54.1	37.8	22.1	2.47	2.87	2.34	148	5.04
	N	8	8	8	8	8	8	8	8
3	MEAN	53.39	34.15	19.24 C^3	1.785	2.774	2.136	147.4 B^1	4.506
	SD	1.65	1.30	1.42	0.168	0.072	0.075	0.5	0.125
	MIN	51.3	32.7	17.4	1.59	2.70	2.02	147	4 34
	MAX	56.3	37.0	21.7	2.08	2.89	2.26	148	4.73
	N	8	8	8	8	8	8	8	8
4	MEAN	52.51	34.98	17.54	2.004	2.778	2.109 A^1	146.8	4.553
	SD	1.66	1.42	1.08	0.152	0.090	0.165	0.9	0.160
	MIN	50.1	32.9	16.3	1.78	2.66	1.88	145	4 37
	MAX	54.9	36.7	19.5	2.18	2.91	2.35	148	4.81
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	48.1	343.9	3.08	622.1	0.733
	SD	26.0	373.2	2.65	77.8	0.017
	MIN	29	183	1.1	509	0.70
	MAX	107	1266	6.9	725	0.75
	N	8	8	4	8	8
2	MEAN	74.3	246.6	6.68	727.0	0.719
	SD	18.0	32.2	3.65	112.3	0.020
	MIN	55	189	2.6	532	0.69
	MAX	113	302	10.5	885	0.75
	N	8	8	5	8	8
3	MEAN	77.6	214.0	2.26	679.9	0.726
	SD	48.3	42.5	1.69	85.4	0.029
	MIN	41	173	1.0	551	0.68
	MAX	175	300	5.0	799	0.76
	N	8	8	5	8	8
4	MEAN	86.9	239.8	3.43	670.1	0.773 C^1
	SD	51.7	66.1	2.66	172.7	0.031
	MIN	42	172	1.0	476	0.72
	MAX	175	380	8.2	1031	0.82
	N	8	8	6	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	28.0	37.3	113.8	6.215	0 368	5.68	5.10	51.3
	SD	0.8	3.9	61.1	0.357	0.079	0.38	0.70	4.6
	MIN	27	32	65	5.79	0.30	5.3	4.4	48
	MAX	29	41	201	6.65	0.47	6.2	5.7	58
	N	4	4	4	4	4	4	4	4
2	MEAN	29.8 A^3	30.3	98.3	6.243	0.460	5.45	5.43	52.8
	SD	2.4	5.6	17.7	0.749	0.083	0.35	0.64	4.5
	MIN	28	25	78	5.37	0.39	5.1	4.5	49
	MAX	33	36	115	7.20	0.58	5.8	5.9	59
	N	4	4	4	4	4	4	4	4
3	MEAN	29.5	37.3	113.3	5.558	0.430	5.63	5.40	58.3 A^3
	SD	2.6	14.9	56.6	0.260	0 103	0.51	0.39	5.4
	MIN	27	24	67	5.33	0.31	5.0	5.0	53
	MAX	33	55	195	5.93	0.56	6.2	5.9	65
	N	4	4	4	4	4	4	4	4
4	MEAN	36.3 C^3	62.3 C^1	137.5	5.675	0 388	5.70	6.28 C^3	52.0
	SD	1.7	21.8	19.2	0.644	0.056	0.24	0.81	7.9
	MIN	34	40	120	4.94	0.31	5.4	5.1	43
	MAX	38	89	163	6.41	0.44	5.9	6.9	60
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45 (b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	54.33	34.43	19.90	1.743	2.710	1.955	147.8	4.673	108.3
	SD	1.76	2.58	1.42	0.241	0.037	0.180	1.3	0.135	1.1
	MIN	52.3	32.4	18.4	1.51	2.67	1.74	146	4.47	107
	MAX	56.5	38.1	21.8	2.07	2.75	2.14	149	4.75	109
	N	4	4	4	4	4	4	4	4	4
2	MEAN	53.23 A^3	34.88	18.35 B^3	1.915	2.725	1.950	146.8	4.555	108.5
	SD	0.80	1.67	1.48	0.257	0.037	0.041	0.5	0.192	0.7
	MIN	52.2	33.1	16.2	1.73	2.68	1.89	146	4.33	108
	MAX	54.1	36.9	19.5	2.28	2.76	1.98	147	4.72	109
	N	4	4	4	4	4	4	4	4	4
3	MEAN	54.28	36.55	17.73 C^3	2.085	2.703	1.938	148.0 B^1	4.670	109.9
	SD	2.22	1.69	2.00	0.304	0.063	0.167	1.2	0.254	2.4
	MIN	52.3	34.2	15.0	1.89	2.63	1.74	147	4.34	108
	MAX	57.3	38.0	19.8	2.53	2.78	2.14	149	4.94	113
	N	4	4	4	4	4	4	4	4	4
4	MEAN	57.28	37.65	19.63	1.923	2.810	1.910 A^1	149.3	4.715	109.8
	SD	2.34	1.08	1.44	0.107	0.036	0.055	2.6	0.291	2.6
	MIN	54.2	36.4	17.8	1.78	2.76	1.87	147	4.54	108
	MAX	59.2	39.0	21.2	2.04	2.84	1.99	153	5.15	114
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	57.5	194.8	1.75	700.0	0.730
	SD	23.7	22.2	0.78	98.2	0.027
	MIN	44	165	1.2	589	0.71
	MAX	93	218	2.3	827	0.77
	N	4	4	2	4	4
2	MEAN	73.8 A^3	199.0	1.65	847.0	0.713
	SD	23.7	26.1	0.92	143.3	0.034
	MIN	53	170	1.0	744	0.68
	MAX	103	223	2.3	1049	0.76
	N	4	4	2	4	4
3	MEAN	64.3	211.3	4.77	786.0	0.730
	SD	14.4	116.1	2.40	88.7	0.018
	MIN	54	145	2.0	693	0.71
	MAX	85	385	6.2	888	0.75
	N	4	4	3	4	4
4	MEAN	85.8 B^3	262.0	2.10	682.8	0.775 C^1
	SD	30.3	94.4	0.56	110.8	0.049
	MIN	46	196	1.3	558	0.72
	MAX	116	402	2.6	807	0.83
	N	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	28.8	39.5	98.5	6.128	0.430	5.80	4.88	55.8
	SD	2.2	6.6	21.2	0.540	0.088	0.55	0.77	4.6
	MIN	26	32	73	5.73	0.34	5.1	4.0	50
	MAX	31	48	123	6.91	0.55	6.4	5.7	60
	N	4	4	4	4	4	4	4	4
2	MEAN	31.0 A^3	42.0	79.8	5.673	0.450	5.23	5.58	56.0
	SD	2.8	3.6	27.1	1.377	0.073	0.26	0.75	6.0
	MIN	29	39	57	4.32	0.36	5.0	4.6	49
	MAX	35	47	116	7.59	0.53	5.6	6.4	61
	N	4	4	4	4	4	4	4	4
3	MEAN	26.5	37.0	114.5	5.795	0.420	5.48	5.28	58.8 A^3
	SD	1.7	13.0	50.3	0.837	0 100	0.28	0.57	5.1
	MIN	24	27	72	5.19	0.29	5.2	4.7	53
	MAX	28	55	187	6.98	0.52	5.8	5.9	64
	N	4	4	4	4	4	4	4	4
4	MEAN	34.8 C^3	63.0 C^1	112.3	5.303	0.405	5.55	5.65 C^3	46.8
	SD	2.6	29.6	4.3	0.625	0.054	0.39	0.66	4.6
	MIN	31	39	107	4.47	0.36	5.2	5.0	42
	MAX	37	102	117	5.91	0.47	6.1	6.5	52
	N	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	MEAN	55.93	36.25	19.68	1.858	2.725	1.753	147.0	4.653	108.0
	SD	0.85	1 30	1.73	0.216	0.070	0.133	1.2	0.164	0.9
	MIN	54.9	34.7	18.0	1.57	2.64	1.60	146	4.46	107
	MAX	56.8	37.6	22.1	2.09	2.80	1.92	148	4.86	109
	N	4	4	4	4	4	4	4	4	4
2	MEAN	53.73 A^3	36.40	17.33 B^3	2.118	2.748	1.963	147.0	4.423	108.6
	SD	1.54	2 15	1.23	0.253	0.054	0.131	1.2	0.260	1.7
	MIN	51.7	33.6	16.0	1.86	2.68	1.85	146	4.17	107
	MAX	55.2	38.6	18.6	2.34	2.80	2.14	148	4.78	111
	N	4	4	4	4	4	4	4	4	4
3	MEAN	54.70	37.50	17.20 C^3	2.183	2.728	1.808	148.0 B^1	4.415	109.0
	SD	2.87	2 54	0.87	0.154	0.091	0.147	1.2	0.070	2.1
	MIN	52.8	35.0	16.4	1.96	2.62	1.68	147	4.35	107
	MAX	58.9	40.9	18.0	2.30	2.84	2.01	149	4.48	112
	N	4	4	4	4	4	4	4	4	4
4	MEAN	54.85	36.75	18.10	2.035	2.725	1.748 A^1	147.3	4.453	108.7
	SD	1.37	0.70	0.98	0.101	0.051	0.064	1.0	0.190	0.5
	MIN	53.3	36.1	16.9	1.91	2.65	1.66	146	4.21	108
	MAX	56.1	37.7	19.3	2.15	2.76	1.80	148	4.64	109
	N	4	4	4	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45

(b) (4)2

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	45.5	162.5	2.53	706.0	0.743
	SD	6.2	21.0	2.06	118.7	0.030
	MIN	39	139	1.1	547	0.71
	MAX	54	186	4.9	830	0.78
	N	4	4	3	4	4
2	MEAN	86.5 A^3	200.8	4.53	708.5	0.755
	SD	32.0	39.7	3.10	92.6	0.026
	MIN	50	162	1.5	626	0.72
	MAX	127	236	7.2	820	0.78
	N	4	4	4	4	4
3	MEAN	51.8	143.0	3.57	591.0	0.743
	SD	8.5	12.0	2.53	94.6	0.041
	MIN	43	128	1.3	523	0.69
	MAX	63	157	6.3	729	0.79
	N	4	4	3	4	4
4	MEAN	92.3 B^3	195.5	3.93	634.0	0.778 C^1
	SD	55.0	39.9	1.33	141.3	0.024
	MIN	49	171	2.4	519	0.76
	MAX	170	255	4.8	829	0.81
	N	4	4	3	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	MEAN	28.4	38.4	106.1	6.171	0 399	5.74	4.99	53.5
	SD	1.6	5.1	43.1	0.427	0.085	0.44	0.69	4.9
	MIN	26	32	65	5.73	0.30	5.1	4.0	48
	MAX	31	48	201	6.91	0.55	6.4	5.7	60
	N	8	8	8	8	8	8	8	8
2	MEAN	30.4 A^3	36.1	89.0	5.958	0.455	5.34	5.50	54.4
	SD	2.5	7.6	23.4	1.071	0.072	0.31	0.65	5.2
	MIN	28	25	57	4.32	0.36	5.0	4.5	49
	MAX	35	47	116	7.59	0.58	5.8	6.4	61
	N	8	8	8	8	8	8	8	8
3	MEAN	28.0	37.1	113.9	5.676	0.425	5.55	5.34	58.5 A^3
	SD	2.6	12.9	49.6	0.588	0.094	0.39	0.46	4.9
	MIN	24	24	67	5.19	0.29	5.0	4.7	53
	MAX	33	55	195	6.98	0.56	6.2	5.9	65
	N	8	8	8	8	8	8	8	8
4	MEAN	35.5 C^3	62.6 C^1	124.9	5.489	0 396	5.63	5.96 C^3	49.4
	SD	2.2	24.1	18.6	0.620	0.052	0.31	0.76	6.6
	MIN	31	39	107	4.47	0.31	5.2	5.0	42
	MAX	38	102	163	6.41	0.47	6.1	6.9	60
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)
1	MEAN	55.13	35.34	19.79	1.800	2.718	1.854	147.4	4.663
	SD	1.54	2.13	1.47	0.220	0.052	0.182	1.2	0.140
	MIN	52.3	32.4	18.0	1.51	2.64	1.60	146	4.46
	MAX	56.8	38.1	22.1	2.09	2.80	2.14	149	4.86
	N	8	8	8	8	8	8	8	8
2	MEAN	53.48 A^3	35.64	17.84 B^3	2.016	2.736	1.956	146.9	4.489
	SD	1.17	1.96	1.37	0.260	0.044	0.090	0.8	0.223
	MIN	51.7	33.1	16.0	1.73	2.68	1.85	146	4.17
	MAX	55.2	38.6	19.5	2.34	2.80	2.14	148	4.78
	N	8	8	8	8	8	8	8	8
3	MEAN	54.49	37.03	17.46 C^3	2.134	2.715	1.873	148.0 B^1	4.543
	SD	2.39	2.06	1.45	0.229	0.074	0.162	1.1	0.220
	MIN	52.3	34.2	15.0	1.89	2.62	1.68	147	4.34
	MAX	58.9	40.9	19.8	2.53	2.84	2.14	149	4.94
	N	8	8	8	8	8	8	8	8
4	MEAN	56.06	37.20	18.86	1.979	2.768	1.829 A^1	148.3	4.584
	SD	2.20	0.97	1.40	0.114	0.061	0.103	2.1	0.267
	MIN	53.3	36.1	16.9	1.78	2.65	1.66	146	4.21
	MAX	59.2	39.0	21.2	2.15	2.84	1.99	153	5.15
	N	8	8	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	51.5	178.6	2.22	703.0	0.736
	SD	17.3	26.4	1.57	100.9	0.027
	MIN	39	139	1.1	547	0.71
	MAX	93	218	4.9	830	0.78
	N	8	8	5	8	8
2	MEAN	80.1 A^3	199.9	3.57	777.8	0.734
	SD	26.9	31.1	2.85	134.0	0.036
	MIN	50	162	1.0	626	0.68
	MAX	127	236	7.2	1049	0.78
	N	8	8	6	8	8
3	MEAN	58.0	177.1	4.17	688.5	0.736
	SD	12.8	84.7	2.30	134.4	0.030
	MIN	43	128	1.3	523	0.69
	MAX	85	385	6.3	888	0.79
	N	8	8	6	8	8
4	MEAN	89.0 B^3	228.8	2.89	658.4	0.776 C^1
	SD	41.3	75.9	1.31	120.4	0.036
	MIN	46	171	1.3	519	0.72
	MAX	170	402	4.8	829	0.83
	N	8	8	7	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	ALT (U/L)	ALP (U/L)
1	MEAN	31.6	176.4
	SD	2.4	99.4
	MIN	28	97
	MAX	33	322
	N	4	4
2	MEAN	31.8	157.2
	SD	7.6	30.3
	MIN	25	122
	MAX	42	195
	N	4	4
3	MEAN	33.3	171.2
	SD	9.2	89.6
	MIN	25	93
	MAX	45	299
	N	4	4
4	MEAN	55.9 C^1	182.8
	SD	29.6	41.6
	MIN	35	149
	MAX	100	239
	N	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	ALB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)
1	MEAN	33.03	1.891	2.829	2.399	146.3	4.964
	SD	1.44	0.208	0.023	0.112	0.6	0.097
	MIN	32.2	1.72	2.80	2.30	146	4.85
	MAX	35.2	2.16	2.85	2.55	147	5.07
	N	4	4	4	4	4	4
2	MEAN	33.09	1.913	2.811	2.359	146.3	4.951
	SD	1.08	0.101	0.034	0.052	0.9	0.119
	MIN	31.8	1.79	2.79	2.30	146	4.85
	MAX	34.2	2.02	2.86	2.42	148	5.09
	N	4	4	4	4	4	4
3	MEAN	34.18	2.011	2.826	2.365	147.1 B^1	4.844
	SD	0.99	0.145	0.065	0.065	0.3	0.153
	MIN	32.9	1.89	2.77	2.31	147	4.71
	MAX	35.1	2.15	2.90	2.46	148	5.03
	N	4	4	4	4	4	4
4	MEAN	34.73	1.939	2.829	2.266 A^1	147.0	4.949
	SD	0.42	0.109	0.043	0.070	1.2	0.287
	MIN	34.5	1.80	2.79	2.21	146	4.62
	MAX	35.4	2.07	2.89	2.37	149	5.27
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45 (b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	4.08	541 3	0.738
	SD	2.61	63.7	0.011
	MIN	1.9	457	0.72
	MAX	7.5	608	0.75
	N	4	4	4
2	MEAN	3.28	648.8	0.714
	SD	2.36	61.9	0.020
	MIN	1.9	578	0.70
	MAX	6.8	707	0.74
	N	4	4	4
3	MEAN	3.55	617.7	0.736
	SD	0.93	38.4	0.007
	MIN	2.3	574	0.73
	MAX	4.4	662	0.75
	N	4	4	4
4	MEAN	7.74	591 1	0.774 **C[1]**
	SD	5.96	79.0	0.030
	MIN	1.7	488	0.74
	MAX	13.1	672	0.81
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	ALT (U/L)	ALP (U/L)
1	MEAN	33.1	150.1
	SD	4.5	25.1
	MIN	29	131
	MAX	40	187
	N	4	4
2	MEAN	38.7	134.9
	SD	1.7	55.2
	MIN	38	90
	MAX	41	214
	N	4	4
3	MEAN	31.8	181.4
	SD	9.7	79.9
	MIN	25	110
	MAX	46	291
	N	4	4
4	MEAN	53.4 C^1	174.6
	SD	22.3	24.8
	MIN	34	140
	MAX	80	198
	N	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	ALB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)
1	MEAN	34.83	2.011	2.831	2.279	146.1	4.919
	SD	1.04	0.124	0.038	0.032	0.3	0.110
	MIN	33.9	1.85	2.79	2.24	146	4.77
	MAX	36.3	2.15	2.88	2.31	147	5.01
	N	4	4	4	4	4	4
2	MEAN	34.67	2.090	2.856	2.385	146.3	4.869
	SD	0.87	0.177	0.051	0.090	0.6	0.190
	MIN	33.4	1.86	2.79	2.28	146	4.65
	MAX	35.3	2.29	2.91	2.48	147	5.07
	N	4	4	4	4	4	4
3	MEAN	34.75	2.056	2.843	2.303	146.9 B^1	4.694
	SD	1.64	0.123	0.083	0.055	0.9	0.091
	MIN	33.2	1.88	2.74	2.23	146	4.61
	MAX	37.1	2.15	2.93	2.36	148	4.82
	N	4	4	4	4	4	4
4	MEAN	34.84	2.076	2.838	2.251 A^1	146.4	4.867
	SD	1.01	0.022	0.061	0.072	0.6	0.201
	MIN	34.0	2.05	2.75	2.18	146	4.71
	MAX	36.1	2.10	2.88	2.35	147	5.15
	N	4	4	4	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	5.83	562 1	0.746
	SD	3.68	46.7	0.030
	MIN	2.7	519	0.70
	MAX	11.1	604	0.77
	N	4	4	4
2	MEAN	8.91	593 9	0.746
	SD	5.88	77.8	0.021
	MIN	3.9	518	0.73
	MAX	15.2	689	0.78
	N	4	4	4
3	MEAN	8.03	514 9	0.741
	SD	3.95	35.3	0.045
	MIN	3.4	485	0.70
	MAX	12.3	566	0.80
	N	4	4	4
4	MEAN	7.86	543.8	0.786 C^1
	SD	5.66	87.6	0.012
	MIN	2.6	456	0.77
	MAX	14.1	655	0.80
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 45 (b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	ALT (U/L)	ALP (U/L)
1	MEAN	32.3	163.3
	SD	3.4	68.6
	MIN	28	97
	MAX	40	322
	N	8	8
2	MEAN	35.2	146.0
	SD	6.3	42.9
	MIN	25	90
	MAX	42	214
	N	8	8
3	MEAN	32.6	176.3
	SD	8.8	78.8
	MIN	25	93
	MAX	46	299
	N	8	8
4	MEAN	54.7 C^1	178.7
	SD	24.3	32.0
	MIN	34	140
	MAX	100	239
	N	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	ALB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)
1	MEAN	33.93	1.951	2.830	2.339	146.2	4.942
	SD	1.51	0.171	0.029	0.100	0.4	0.099
	MIN	32.2	1.72	2.79	2.24	146	4.77
	MAX	36.3	2.16	2.88	2.55	147	5.07
	N	8	8	8	8	8	8
2	MEAN	33.88	2.002	2.833	2.372	146.3	4.910
	SD	1.24	0.164	0.047	0.070	0.7	0.153
	MIN	31.8	1.79	2.79	2.28	146	4.65
	MAX	35.3	2.29	2.91	2.48	148	5.09
	N	8	8	8	8	8	8
3	MEAN	34.47	2.033	2.835	2.334	147.0 B^1	4.769
	SD	1.29	0.127	0.070	0.065	0.6	0.142
	MIN	32.9	1.88	2.74	2.23	146	4.61
	MAX	37.1	2.15	2.93	2.46	148	5.03
	N	8	8	8	8	8	8
4	MEAN	34.78	2.007	2.833	2.258 A^1	146.7	4.908
	SD	0.72	0.103	0.049	0.066	0.9	0.234
	MIN	34.0	1.80	2.75	2.18	146	4.62
	MAX	36.1	2.10	2.89	2.37	149	5.27
	N	8	8	8	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 45

(b) (4)

CLINICAL CHEMISTRY - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	MEAN	4.96	551.7	0.742
	SD	3.10	52.9	0.022
	MIN	1.9	457	0.70
	MAX	11.1	608	0.77
	N	8	8	8
2	MEAN	6.09	621 3	0.730
	SD	5.12	71.4	0.026
	MIN	1.9	518	0.70
	MAX	15.2	707	0.78
	N	8	8	8
3	MEAN	5.79	566 3	0.738
	SD	3.58	64.7	0.030
	MIN	2.3	485	0.70
	MAX	12.3	662	0.80
	N	8	8	8
4	MEAN	7.80	567.4	0.780 C^1
	SD	5.38	81.3	0.022
	MIN	1.7	456	0.74
	MAX	14.1	672	0.81
	N	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 13
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	PT (Sec)	APTT (Sec)	FIB (g/L)
1	MEAN	7.78	27.30	2.38
	SD	0.26	1.99	0.28
	MIN	7.5	24.5	2 1
	MAX	8.0	29.2	2.7
	N	4	4	4
2	MEAN	7.73	25.35 A^3	2.22
	SD	0.19	2.26	0.10
	MIN	7.6	22.9	2 1
	MAX	8.0	27.6	2 3
	N	4	4	4
3	MEAN	7.73	24.35 B^3	2.15
	SD	0.26	1.47	0.23
	MIN	7.5	22.6	2.0
	MAX	8.0	25.8	2.4
	N	4	4	4
4	MEAN	7.78	25.88 A^3	2.13
	SD	0.28	2.02	0.22
	MIN	7.5	23.6	1 9
	MAX	8.1	27.9	2.4
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 13
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	PT (Sec)	APTT (Sec)	FIB (g/L)
1	MEAN	7.88	26.60	2.03
	SD	0.17	2.31	0.10
	MIN	7.7	23.6	1 9
	MAX	8.1	28.7	2 2
	N	4	4	4
2	MEAN	7.78	24.35 A^3	2.20
	SD	0.36	2.40	0.33
	MIN	7.5	22.7	1 9
	MAX	8.3	27.9	2.7
	N	4	4	4
3	MEAN	7.55	23.98 B^3	1.95
	SD	0.17	1.64	0.17
	MIN	7.4	22.1	1.8
	MAX	7.8	25.4	2 2
	N	4	4	4
4	MEAN	7.93	23.63 A^3	1.89
	SD	0.38	3.06	0.13
	MIN	7.6	19.5	1.8
	MAX	8.3	26.4	2 1
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 13
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	PT (Sec)	APTT (Sec)	FIB (g/L)
1	MEAN	7.83	26.95	2.20
	SD	0.21	2.03	0.27
	MIN	7.5	23.6	1 9
	MAX	8.1	29.2	2.7
	N	8	8	8
2	MEAN	7.75	24.85 A^3	2.21
	SD	0.27	2.22	0.23
	MIN	7.5	22.7	1 9
	MAX	8.3	27.9	2.7
	N	8	8	8
3	MEAN	7.64	24.16 B^3	2.05
	SD	0.23	1.46	0.21
	MIN	7.4	22.1	1.8
	MAX	8.0	25.8	2.4
	N	8	8	8
4	MEAN	7.85	24.75 A^3	2.01
	SD	0.32	2.68	0.21
	MIN	7.5	19.5	1.8
	MAX	8.3	27.9	2.4
	N	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 34
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	PT (Sec)	APTT (Sec)	FIB (g/L)
1	MEAN	7.90	22.28	2.02
	SD	0.29	2.20	0.43
	MIN	7.6	19.4	1.5
	MAX	8.2	24.1	2.6
	N	4	4	4
2	MEAN	8.03 A^3	22.88	1.83
	SD	0.35	4.20	0 24
	MIN	7.6	18.2	1.6
	MAX	8.4	27.5	2.1
	N	4	4	4
3	MEAN	8.20 C^3	21.48	2.02
	SD	0.32	2.66	0.42
	MIN	7.8	17.8	1.6
	MAX	8.5	23.9	2.4
	N	4	4	4
4	MEAN	8.25 A^3	21.23	1.63
	SD	0.34	2.71	0.08
	MIN	7.8	18.8	1.5
	MAX	8.6	25.1	1.7
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 34
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	PT (Sec)	APTT (Sec)	FIB (g/L)
1	MEAN	7.88	21.63	2.00
	SD	0.24	2.57	0 58
	MIN	7.7	19.4	1.6
	MAX	8.2	24.7	2.9
	N	4	4	4
2	MEAN	8.28 A^3	23.58	1 59
	SD	0.35	5.14	0 19
	MIN	7.9	20.4	1.3
	MAX	8.7	31.2	1.8
	N	4	4	4
3	MEAN	8.53 C^3	22.23	1 35
	SD	0.17	1.55	0 17
	MIN	8.3	20.7	1.2
	MAX	8.7	24.3	1.6
	N	4	4	4
4	MEAN	8.05 A^3	22.15	1.78
	SD	0.49	2.06	0 37
	MIN	7.5	19.6	1.3
	MAX	8.7	24.1	2.1
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 34
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	PT (Sec)	APTT (Sec)	FIB (g/L)
1	MEAN	7.89	21.95	2.01
	SD	0.25	2.25	0.47
	MIN	7.6	19.4	1.5
	MAX	8.2	24.7	2.9
	N	8	8	8
2	MEAN	8.15 A^3	23.23	1.71
	SD	0.35	4.36	0 24
	MIN	7.6	18.2	1.3
	MAX	8.7	31.2	2.1
	N	8	8	8
3	MEAN	8.36 C^3	21.85	1.68
	SD	0.29	2.05	0.47
	MIN	7.8	17.8	1.2
	MAX	8.7	24.3	2.4
	N	8	8	8
4	MEAN	8.15 A^3	21.69	1.70
	SD	0.41	2.28	0 26
	MIN	7.5	18.8	1.3
	MAX	8.7	25.1	2.1
	N	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (t-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (t-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	FIB (g/L)
1	MEAN	2.20
	SD	0.30
	MIN	2.0
	MAX	2.6
	N	4
2	MEAN	2.03
	SD	0.14
	MIN	1.9
	MAX	2.2
	N	4
3	MEAN	2.09
	SD	0.32
	MIN	1.8
	MAX	2.4
	N	4
4	MEAN	1.88
	SD	0.11
	MIN	1.8
	MAX	2.0
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	FIB (g/L)
1	MEAN	2.01
	SD	0.31
	MIN	1.8
	MAX	2.5
	N	4
2	MEAN	1.89
	SD	0.12
	MIN	1.7
	MAX	2.0
	N	4
3	MEAN	1.65
	SD	0.17
	MIN	1.5
	MAX	1.9
	N	4
4	MEAN	1.83
	SD	0.21
	MIN	1.6
	MAX	2.1
	N	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 46

(b) (4)

COAGULATION - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	FIB (g/L)
1	MEAN	2.11
	SD	0.30
	MIN	1.8
	MAX	2.6
	N	8
2	MEAN	1.96
	SD	0.14
	MIN	1.7
	MAX	2.2
	N	8
3	MEAN	1.87
	SD	0.33
	MIN	1.5
	MAX	2.4
	N	8
4	MEAN	1.86
	SD	0.16
	MIN	1.6
	MAX	2.1
	N	8

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (t-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (t-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (t-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (t-test)

TABLE NO. 47

(b) (4)

BUCCAL MUCOSAL BLEEDING TIME - SUMMARY
MEASUREMENT TIME (min)
F1 GENERATION - PUPPIES - POST WEANING
WEEK 34

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		MALES*	FEMALES*	SEX COMBINED
1	MEAN	> 27.25	> 24.00	> 25.63
	SD	5.50	7.12	6.14
	MIN	19.0	16.0	16.0
	MAX	30.0 Ω	30.0 Ω	30.0 Ω
	N	4	4	8
2	MEAN	22.13	16.75	19.44
	SD	8.89	4.27	7.07
	MIN	9.5	11.0	9.5
	MAX	30.0	20.0	30.0
	N	4	4	8
3	MEAN	> 17.38	> 14.88	> 16.13
	SD	10.13	10.73	9.75
	MIN	8.0	7.0	7.0
	MAX	30.0 Ω	30.0 Ω	30.0 Ω
	N	4	4	8
4	MEAN	15.75	> 15.00	> 15.38
	SD	8.65	10.11	8.72
	MIN	6.5	8.5	6.5
	MAX	27.0	30.0 Ω	30.0 Ω
	N	4	4	8

* - No statistical comparisons were performed

Significant difference when compared to group 1: a - $p \leq 0.05$, b - $p \leq 0.01$, c - $p \leq 0.001$ (Peto)

TABLE NO. 48

(b) (4)

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 13
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	72.50	1.0278	5.63
	SD	46.05	0.0083	0.25
	MIN	38.0	1.016	5.5
	MAX	140.0	1.035	6.0
	N	4	4	4
2	MEAN	29.95	1.0433 B^1	5.38 B^1
	SD	26.23	0.0189	0.25
	MIN	5.8	1.022	5.0
	MAX	67.0	1.068	5.5
	N	4	4	4
3	MEAN	31.25	1.0340	5.50 B^1
	SD	7.04	0.0080	0.00
	MIN	21.0	1.026	5.5
	MAX	37.0	1.045	5.5
	N	4	4	4
4	MEAN	46.25	1.0373 B^1	5.63
	SD	18.30	0.0120	0.25
	MIN	32.0	1.020	5.5
	MAX	73.0	1.047	6.0
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 48

(b) (4)

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 13
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	49.25	1.0298	5.38
	SD	16.32	0.0093	0.25
	MIN	26.0	1.020	5.0
	MAX	62.0	1.042	5.5
	N	4	4	4
2	MEAN	25.25	1.0448 B^1	5.38 B^1
	SD	9.81	0.0054	0.25
	MIN	13.0	1.038	5.0
	MAX	37.0	1.050	5.5
	N	4	4	4
3	MEAN	25.75	1.0360	5.50 B^1
	SD	5.19	0.0042	0.00
	MIN	21.0	1.033	5.5
	MAX	32.0	1.042	5.5
	N	4	4	4
4	MEAN	32.50	1.0473 B^1	5.50
	SD	18.43	0.0180	0.00
	MIN	14.0	1.024	5.5
	MAX	58.0	1.068	5.5
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 48

[redacted] (b) (4)

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 13
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	60.88	1.0288	5.50
	SD	34.32	0.0083	0.27
	MIN	26.0	1.016	5.0
	MAX	140.0	1.042	6.0
	N	8	8	8
2	MEAN	27.60	1.0440 B^1	5.38 B^1
	SD	18.50	0.0129	0.23
	MIN	5.8	1.022	5.0
	MAX	67.0	1.068	5.5
	N	8	8	8
3	MEAN	28.50	1.0350	5.50 B^1
	SD	6.44	0.0060	0.00
	MIN	21.0	1.026	5.5
	MAX	37.0	1.045	5.5
	N	8	8	8
4	MEAN	39.38	1.0423 B^1	5.56
	SD	18.52	0.0151	0.18
	MIN	14.0	1.020	5.5
	MAX	73.0	1.068	6.0
	N	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 48

[redacted] (b) (4)

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 34
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	38.75	1.0403	6.00
	SD	22.65	0.0083	0.00
	MIN	22.0	1.029	6.0
	MAX	71.0	1.047	6.0
	N	4	4	4
2	MEAN	54.67	1.0463 B^1	5.67 B^1
	SD	9.45	0.0121	0.29
	MIN	44.0	1.037	5.5
	MAX	62.0	1.060	6.0
	N	3	3	3
3	MEAN	103.75	1.0460	5.63 B^1
	SD	119.48	0.0205	0.25
	MIN	18.0	1.020	5.5
	MAX	280.0	1.070	6.0
	N	4	4	4
4	MEAN	59.25	1.0450 B^1	5.88
	SD	30.65	0.0076	0.48
	MIN	23.0	1.034	5.5
	MAX	98.0	1.050	6.5
	N	4	4	4

Significant differences against group 1 across sexes and occasions: $A^1 - p \leq 0.1$, $B^1 - p \leq 0.05$, $C^1 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: $A^2 - p \leq 0.1$, $B^2 - p \leq 0.05$, $C^2 - p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: $A^3 - p \leq 0.1$, $B^3 - p \leq 0.05$, $C^3 - p \leq 0.01$ (*t*-test)
Significant differences against group 1: $A^4 - p \leq 0.1$, $B^4 - p \leq 0.05$, $C^4 - p \leq 0.01$ (*t*-test)

TABLE NO. 48

[redacted] (b) (4)

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 34
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	46.75	1.0443	5.88
	SD	11.18	0.0049	0.25
	MIN	36.0	1.038	5.5
	MAX	61.0	1.050	6.0
	N	4	4	4
2	MEAN	43.25	1.0433 B^1	5.63 B^1
	SD	17.23	0.0071	0.25
	MIN	26.0	1.033	5.5
	MAX	63.0	1.048	6.0
	N	4	4	4
3	MEAN	52.00	1.0415	5.38 B^1
	SD	48.19	0.0048	0.25
	MIN	9.0	1.037	5.0
	MAX	120.0	1.047	5.5
	N	4	4	4
4	MEAN	54.00	1.0580 B^1	5.63
	SD	6.38	0.0054	0.48
	MIN	45.0	1.050	5.0
	MAX	60.0	1.062	6.0
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 48

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
WEEK 34
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	42.75	1.0423	5.94
	SD	17.08	0.0067	0.18
	MIN	22.0	1.029	5.5
	MAX	71.0	1.050	6.0
	N	8	8	8
2	MEAN	48.14	1.0446 B^1	5.64 B^1
	SD	14.68	0.0088	0.24
	MIN	26.0	1.033	5.5
	MAX	63.0	1.060	6.0
	N	7	7	7
3	MEAN	77.88	1.0438	5.50 B^1
	SD	88.76	0.0140	0.27
	MIN	9.0	1.020	5.0
	MAX	280.0	1.070	6.0
	N	8	8	8
4	MEAN	56.63	1.0515 B^1	5.75
	SD	20.69	0.0092	0.46
	MIN	23.0	1.034	5.0
	MAX	98.0	1.062	6.5
	N	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

(b) (4)

TABLE NO. 48

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	55.63	1.0340	5.81
	SD	21.66	0.0083	0.13
	MIN	30.0	1.023	5.8
	MAX	82.0	1.041	6.0
	N	4	4	4
2	MEAN	36.20	1.0475 B^1	5.50 B^1
	SD	23.38	0.0156	0.20
	MIN	5.8	1.032	5.3
	MAX	62.5	1.068	5.8
	N	4	4	4
3	MEAN	67.50	1.0400	5.56 B^1
	SD	60.31	0.0120	0.13
	MIN	25.5	1.023	5.5
	MAX	157.0	1.051	5.8
	N	4	4	4
4	MEAN	52.75	1.0411 B^1	5.75
	SD	18.40	0.0075	0.20
	MIN	30.5	1.033	5.5
	MAX	70.0	1.049	6.0
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 48

(b) (4)

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	48.00	1.0370	5.63
	SD	12.36	0.0043	0.14
	MIN	33.0	1.035	5.5
	MAX	60.0	1.044	5.8
	N	4	4	4
2	MEAN	34.25	1.0440 B^1	5.50 B^1
	SD	7.04	0.0040	0.20
	MIN	28.5	1.041	5.3
	MAX	44.5	1.049	5.8
	N	4	4	4
3	MEAN	38.88	1.0388	5.44 B^1
	SD	22.28	0.0025	0.13
	MIN	18.5	1.036	5.3
	MAX	70.5	1.042	5.5
	N	4	4	4
4	MEAN	43.25	1.0526 B^1	5.56
	SD	11.09	0.0089	0.24
	MIN	29.5	1.043	5.3
	MAX	56.5	1.064	5.8
	N	4	4	4

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 48

[redacted] (b) (4)

URINALYSIS - SUMMARY - F1 GENERATION - PUPPIES - POST WEANING
COMBINED DAYS
COMBINED SEXES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	VOL (mL)	SG	pH
1	MEAN	51.81	1.0355	5.72
	SD	16.83	0.0063	0.16
	MIN	30.0	1.023	5.5
	MAX	82.0	1.044	6.0
	N	8	8	8
2	MEAN	35.23	1.0458 B^1	5.50 B^1
	SD	16.02	0.0107	0.19
	MIN	5.8	1.032	5.3
	MAX	62.5	1.068	5.8
	N	8	8	8
3	MEAN	53.19	1.0394	5.50 B^1
	SD	44.79	0.0080	0.13
	MIN	18.5	1.023	5.3
	MAX	157.0	1.051	5.8
	N	8	8	8
4	MEAN	48.00	1.0469 B^1	5.66
	SD	14.95	0.0098	0.23
	MIN	29.5	1.033	5.3
	MAX	70.0	1.064	6.0
	N	8	8	8

Significant differences against group 1 across sexes and occasions: A^1 - $p \leq 0.1$, B^1 - $p \leq 0.05$, C^1 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across occasions: A^2 - $p \leq 0.1$, B^2 - $p \leq 0.05$, C^2 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1 across sexes: A^3 - $p \leq 0.1$, B^3 - $p \leq 0.05$, C^3 - $p \leq 0.01$ (*t*-test)
Significant differences against group 1: A^4 - $p \leq 0.1$, B^4 - $p \leq 0.05$, C^4 - $p \leq 0.01$ (*t*-test)

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F0 GENERATION – GESTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Days 0 to 6	Days 7 to 13	Days 14 to 20	Days 21 to 27	Days 28 to 34
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	5	5	5	5	5
2	MEAN	156.781	191.567	138.738	88.373	83.959
	SD	15.340	16.837	26.080	25.218	20.153
	MIN	130.61	175.31	112.50	47.60	65.77
	MAX	170.23	219.76	178.71	110.82	112.72
	N	5	5	5	5	5
3	MEAN	229.058	324.745	234.625	167.194	202.772
	SD	48.987	58.048	52.310	40.033	87.221
	MIN	176.52	252.00	184.48	115.79	108.53
	MAX	281.63	386.99	309.34	216.71	301.30
	N	5	5	5	5	5
4	MEAN	464.138	749.502	495.416	313.187	289.247
	SD	172.881	108.786	170.823	59.410	189.859
	MIN	282.60	581.51	241.94	240.35	105.08
	MAX	697.74	883.93	636.13	382.74	547.67
	N	5	5	5	5	5

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F0 GENERATION – GESTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Days 35 to 41	Days 42 to 48	Days 49 to 55	Days 56 to 62
1	MEAN	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00
	N	5	5	5	5
2	MEAN	158.037	156.706	138.496	131 525
	SD	13.628	40.612	31.611	22.794
	MIN	135 27	116.43	95.96	97.12
	MAX	171.07	205.32	179.88	159 28
	N	5	5	5	5
3	MEAN	304.340	283.671	266.331	224 257
	SD	78.196	31.412	36.873	80.591
	MIN	229 31	230.51	211.00	137 39
	MAX	434 16	307.21	301.56	333 54
	N	5	5	5	5
4	MEAN	562.529	654.179	435.021	310 954
	SD	253.955	138.191	172.989	55.531
	MIN	211 19	538.94	128.88	226 91
	MAX	838 37	880.71	545.57	381 52
	N	5	5	5	5

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F0 GENERATION - LACTATION - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Days 0 to 6	Days 7 to 13	Days 14 to 20	Days 21 to 27	Days 28 to 34
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	5	5	5	5	5
2	MEAN	209.852	352.321	371.503	414.998	419.622
	SD	126.354	44.586	54.795	42.125	56.387
	MIN	0.37	300.54	296.39	360.85	336.82
	MAX	303.13	408.04	427.91	459.15	458.64
	N	5	4	4	4	4
3	MEAN	378.339	625.242	801.247	838.068	915.333
	SD	216.054	83.673	145.328	94.972	90.384
	MIN	113.84	542.71	695.77	743.76	794.18
	MAX	701.76	740.32	1014.99	952.75	1005.17
	N	5	4	4	4	4
4	MEAN	799.752	1162 251	1417.365	1610.404	1680.543
	SD	332.730	176.368	73.593	134.744	151.637
	MIN	474.49	956.68	1316.93	1489.46	1492.14
	MAX	1125.00	1379 32	1481.74	1803.26	1810.49
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F0 GENERATION - LACTATION - FEMALES
F1 GENERATION - PUPPIES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Days 35 to 41	Days 42 to 48	Days 49 to 55
1	MEAN	0.000	0.000	0.000
	SD	0.000	0.000	0.000
	MIN	0.00	0.00	0.00
	MAX	0.00	0.00	0.00
	N	5	5	5
2	MEAN	257.611	267.978	259.996
	SD	10.861	10.047	23.477
	MIN	248.97	257.42	237.60
	MAX	273.28	280.91	282.53
	N	4	4	4
3	MEAN	525.130	532.654	494.379
	SD	21.690	41.951	8.135
	MIN	509.53	482.47	488.62
	MAX	557.21	584.89	505.93
	N	4	4	4
4	MEAN	1136.630	1122 582	1021.185
	SD	51.833	108.235	61.445
	MIN	1076.95	994.06	946.83
	MAX	1201.61	1236.89	1083.76
	N	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES – CAGES (MALES AND FEMALES)
WEEKS 1 AND 2

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 1	Week 2
1	MEAN	0.000	0.000
	SD	0.000	0.000
	MIN	0.00	0.00
	MAX	0.00	0.00
	N	4	4
2	MEAN	281.390	347.176
	SD	19.819	20.070
	MIN	252.83	323.05
	MAX	297.57	366.36
	N	4	4
3	MEAN	485.575	651.098
	SD	49.763	75.187
	MIN	414.48	545.43
	MAX	530.04	718.77
	N	4	4
4	MEAN	1250.880	1368.947
	SD	155.916	76.231
	MIN	1130.63	1285.03
	MAX	1478.78	1443.09
	N	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 3	Week 4	Week 5	Week 6	Week 7
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	288.896	294.453	313.527	314.073	300.542
	SD	40.093	38.981	35.955	28.162	38.115
	MIN	258.30	258.45	271.59	277.89	271.00
	MAX	345.62	348.73	354.46	346.66	356.42
	N	4	4	4	4	4
3	MEAN	559.604	555.574	569.005	580.449	546.737
	SD	53.912	49.874	34.212	50.409	28.770
	MIN	493.54	510.39	524.66	518.24	516.16
	MAX	620.01	616.22	607.63	641.20	573.69
	N	4	4	4	4	4
4	MEAN	1215.318	1265 177	1269.571	1297.113	1285.422
	SD	81.498	124.178	65.596	38.776	84.012
	MIN	1138.24	1153.40	1186.16	1250.48	1162.65
	MAX	1302.80	1436 90	1344.87	1344.77	1353.10
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 8	Week 9	Week 10	Week 11	Week 12
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	295.527	283.592	279.121	259.498	235.966
	SD	26.815	26.045	26.706	21.227	20.280
	MIN	265.11	245.80	249.19	237.48	207.76
	MAX	318.88	302.60	305.92	283.58	254.39
	N	4	4	4	4	4
3	MEAN	548.787	501.979	503.037	469.000	474.922
	SD	29.290	23.057	16.720	17.367	32.546
	MIN	506.19	477.52	479.94	449.68	438.52
	MAX	572.67	533.13	516.58	491.39	508.53
	N	4	4	4	4	4
4	MEAN	1161.030	1130 303	1119.001	1049.563	1062.712
	SD	67.219	60.385	149.899	25.489	49.641
	MIN	1089.18	1058.42	903.97	1030.26	1004.23
	MAX	1240.96	1202.04	1252.45	1086.65	1109.52
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 13	Week 14	Week 15	Week 16	Week 17
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	227.327	221.865	231.320	208.599	216.091
	SD	26.198	23.188	15.600	26.743	22.307
	MIN	204.69	206.45	214.51	183.50	189.46
	MAX	258.88	256.03	251.82	245.15	237.02
	N	4	4	4	4	4
3	MEAN	464.237	419.720	427.206	389.857	394.814
	SD	40.209	16.437	32.736	34.604	4.572
	MIN	408.89	405.23	398.85	352.87	388.29
	MAX	501.13	435.15	470.80	425.38	398.99
	N	4	4	4	4	4
4	MEAN	1012.483	933.838	917.744	878.538	857.388
	SD	73.853	94.045	75.406	47.661	107.707
	MIN	923.27	819.50	815.83	808.86	759.51
	MAX	1076.80	1012 37	994.31	910.29	1000.74
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 18	Week 19	Week 20	Week 21	Week 22
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	198.609	195.881	182.514	182.690	175.236
	SD	16.514	23.950	18.525	10.590	21.995
	MIN	182.14	161.48	162.93	169.91	157.89
	MAX	214.86	217.12	200.89	195.49	207.44
	N	4	4	4	4	4
3	MEAN	361.277	394.288	364.268	333.895	334.664
	SD	15.647	21.398	10.761	17.503	20.896
	MIN	340.63	374.03	355.11	316.62	315.14
	MAX	378.47	424.33	379.73	357.76	361.26
	N	4	4	4	4	4
4	MEAN	853.302	825.075	762.457	762.395	740.668
	SD	50.647	102.866	61.550	94.199	95.232
	MIN	799.55	718.83	703.74	675.86	630.43
	MAX	899.52	958.07	847.40	888.23	862.65
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 23	Week 24	Week 25	Week 26
1	MEAN	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00
	N	4	4	4	4
2	MEAN	168.121	172.784	162.435	150 158
	SD	24.901	18.874	17.256	20.325
	MIN	134 38	147.21	148.36	122.66
	MAX	194 27	192.76	187.54	171 29
	N	4	4	4	4
3	MEAN	321.346	350.154	299.671	286.726
	SD	19.689	23.965	21.964	18.078
	MIN	292 51	331.73	278.57	267 31
	MAX	336 93	384.22	328.29	310.61
	N	4	4	4	4
4	MEAN	693.243	686.801	635.881	612.730
	SD	72.844	72.113	89.499	99.788
	MIN	616 52	613.19	564.16	504 20
	MAX	789 24	755.95	764.89	746.06
	N	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 3	Week 4	Week 5	Week 6	Week 7
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	288.241	315.909	324.965	321.696	299.814
	SD	32.597	42.157	38.246	25.350	21.804
	MIN	245.24	274.38	285.80	300.32	268.07
	MAX	322.90	367.65	377.44	355.11	315.90
	N	4	4	4	4	4
3	MEAN	488.582	534.654	545.401	570.296	555.610
	SD	97.948	37.017	36.881	22.288	18.335
	MIN	394.71	489.96	497.87	539.91	542.79
	MAX	597.84	578.71	583.71	589.03	582.82
	N	4	4	4	4	4
4	MEAN	1189.028	1326.716	1308.831	1326.911	1287.713
	SD	105.452	126.819	45.009	95.154	62.263
	MIN	1056.22	1184 95	1243.11	1238.57	1204.43
	MAX	1301.11	1444.74	1344.72	1461.80	1355.29
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 8	Week 9	Week 10	Week 11	Week 12
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	294.872	289.387	281.098	261.387	248.061
	SD	20.097	25.944	24.480	24.214	17.275
	MIN	273.13	261.95	257.14	226.85	225.32
	MAX	314.67	315.54	315.17	282.39	267.14
	N	4	4	4	4	4
3	MEAN	528.051	514.119	512.340	479.611	456.515
	SD	18.190	46.881	33.444	14.883	19.848
	MIN	506.34	476.53	462.56	458.44	435.48
	MAX	550.36	580.27	534.01	490.95	473.82
	N	4	4	4	4	4
4	MEAN	1248.706	1201 184	1148.091	1124.851	1073.085
	SD	73.821	98.197	54.901	28.573	39.563
	MIN	1178.57	1069 37	1068.81	1086.08	1025.04
	MAX	1335.30	1298 53	1190.05	1152.66	1114.69
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 13	Week 14	Week 15	Week 16	Week 17
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	231.603	224.863	217.270	207.612	220.105
	SD	12.423	20.692	6.287	7.758	6.102
	MIN	214.43	207.85	211.07	200.31	214.14
	MAX	243.54	254.80	223.55	217.22	228.57
	N	4	4	4	4	4
3	MEAN	468.502	430.585	426.741	440.633	420.197
	SD	12.772	29.597	23.514	50.868	29.056
	MIN	450.22	393.67	391.50	383.26	393.31
	MAX	479.94	463.19	439.61	505.20	461.50
	N	4	4	4	4	4
4	MEAN	999.056	910.333	938.321	924.094	861.704
	SD	85.315	49.149	43.083	103.493	90.882
	MIN	917.43	853.57	902.41	855.52	768.04
	MAX	1103.90	957.49	1000.00	1076.08	971.98
	N	4	4	4	4	4

TABLE NO. 49 (b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 18	Week 19	Week 20	Week 21	Week 22
1	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	MEAN	206.997	200.027	186.893	182.877	171.811
	SD	23.996	12.094	21.480	16.718	21.992
	MIN	173.34	183.89	164.55	166.35	142.82
	MAX	228.59	213.16	214.04	199.62	189.04
	N	4	4	4	4	4
3	MEAN	394.522	398.976	356.651	370.483	362.084
	SD	28.202	33.562	9.506	26.377	12.352
	MIN	367.68	371.39	346.33	350.91	349.72
	MAX	434.19	446.14	368.64	407.73	375.00
	N	4	4	4	4	4
4	MEAN	808.927	858.216	758.173	730.045	713.647
	SD	52.022	32.983	11.608	89.550	76.775
	MIN	755.72	810.98	741.98	662.92	617.31
	MAX	876.41	881.82	769.58	855.56	796.22
	N	4	4	4	4	4

TABLE NO. 49

(b) (4)

ACHIEVED AOCED INTAKE SUMMARY
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.		Week 23	Week 24	Week 25	Week 26
1	MEAN	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00
	N	4	4	4	4
2	MEAN	182.022	175.729	180.481	162 548
	SD	15.011	6.086	11.934	16.699
	MIN	173 24	166.63	162.71	149.87
	MAX	204 50	179.39	188.45	186 59
	N	4	4	4	4
3	MEAN	334.022	331.457	328.739	313.076
	SD	31.853	32.101	49.302	14.729
	MIN	297 10	295.86	257.87	293 18
	MAX	363 33	367.60	368.44	324.81
	N	4	4	4	4
4	MEAN	680.930	722.768	670.552	606.842
	SD	57.001	82.857	60.600	60.356
	MIN	603 30	602.48	593.26	516.78
	MAX	728 19	792.30	727.67	641.88
	N	4	4	4	4

(b) (4)

APPENDICES
GENERAL

(b) (4)

APPENDIX NO. 1
CERTIFICATES OF ANALYSIS

(b) (4)

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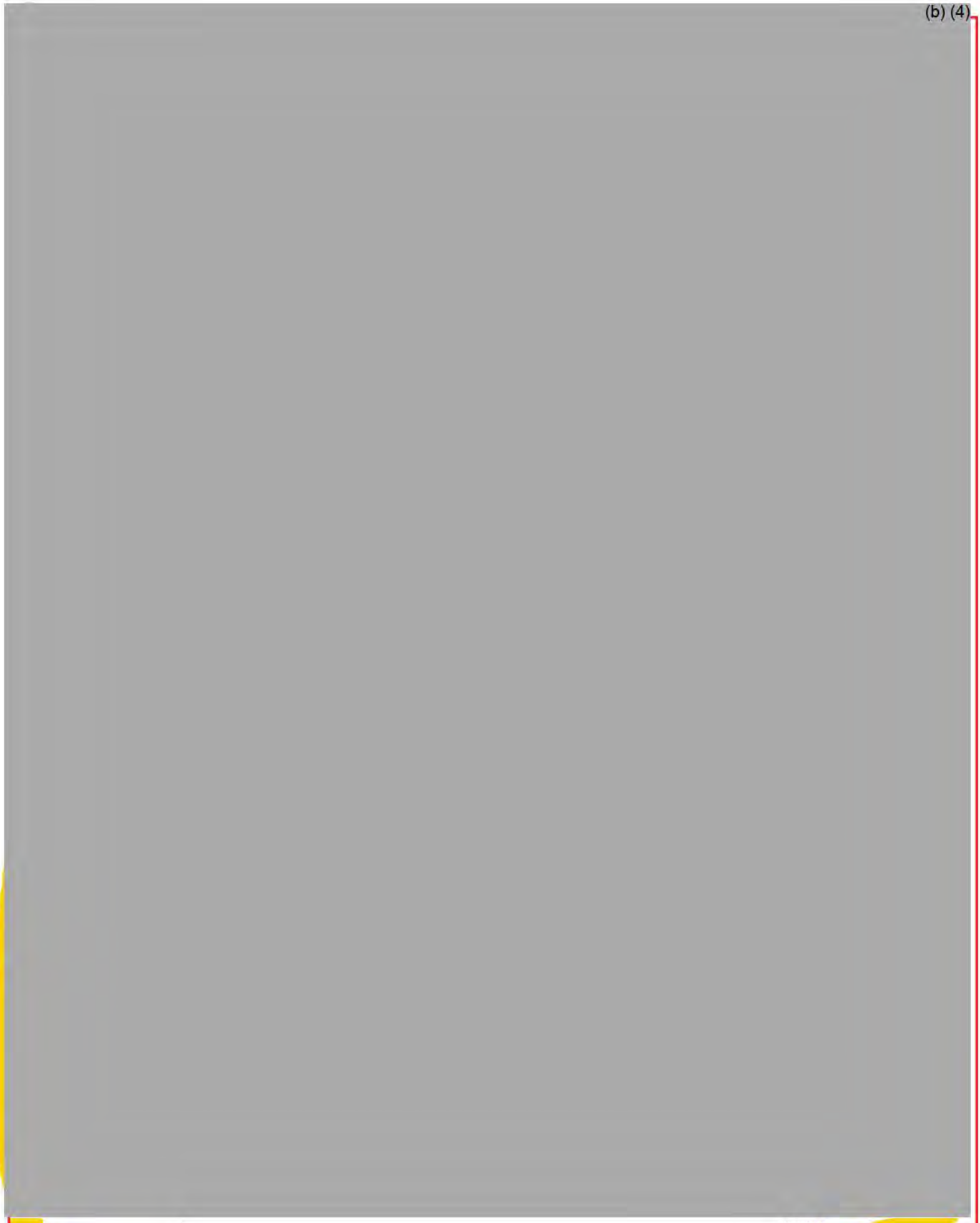
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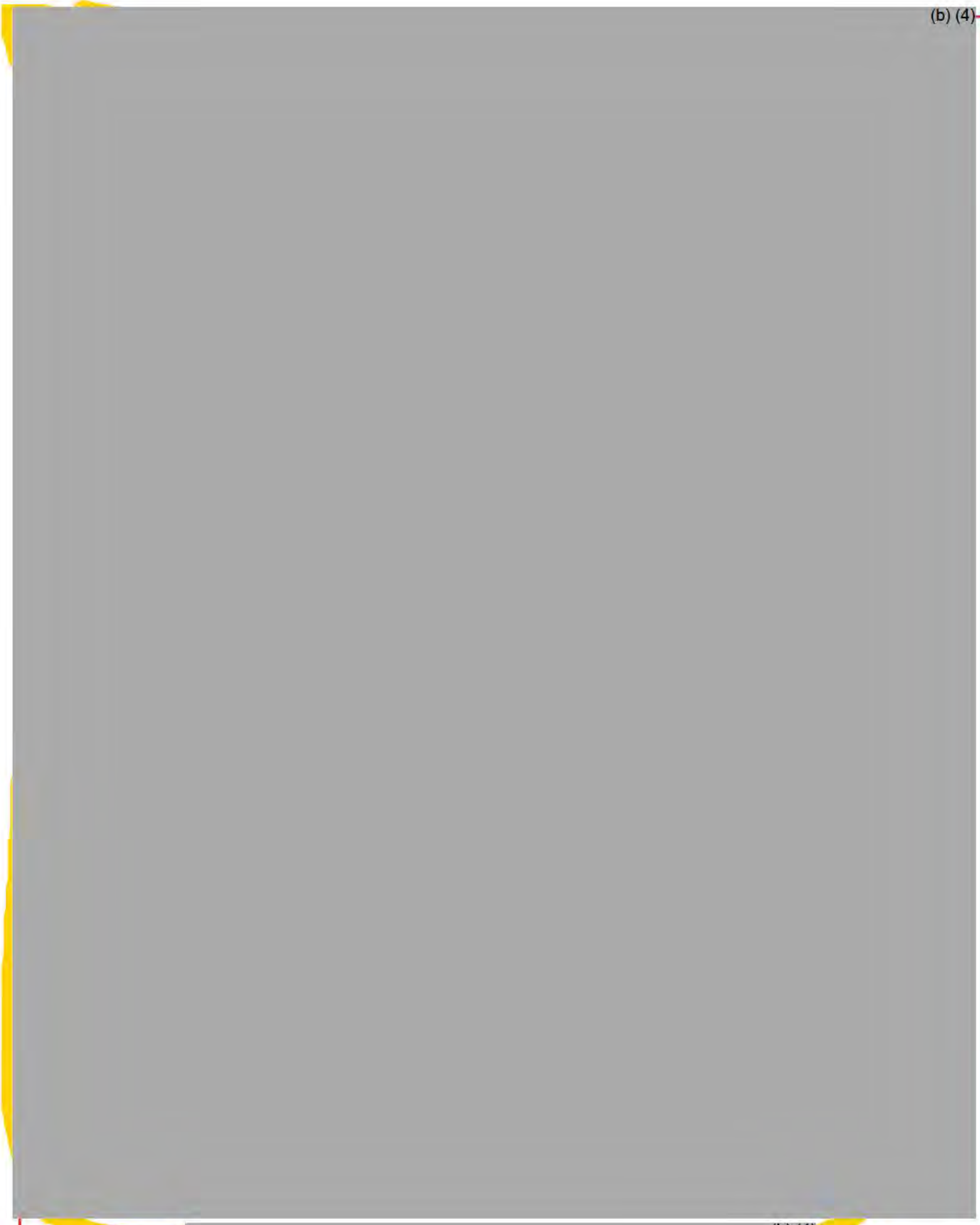
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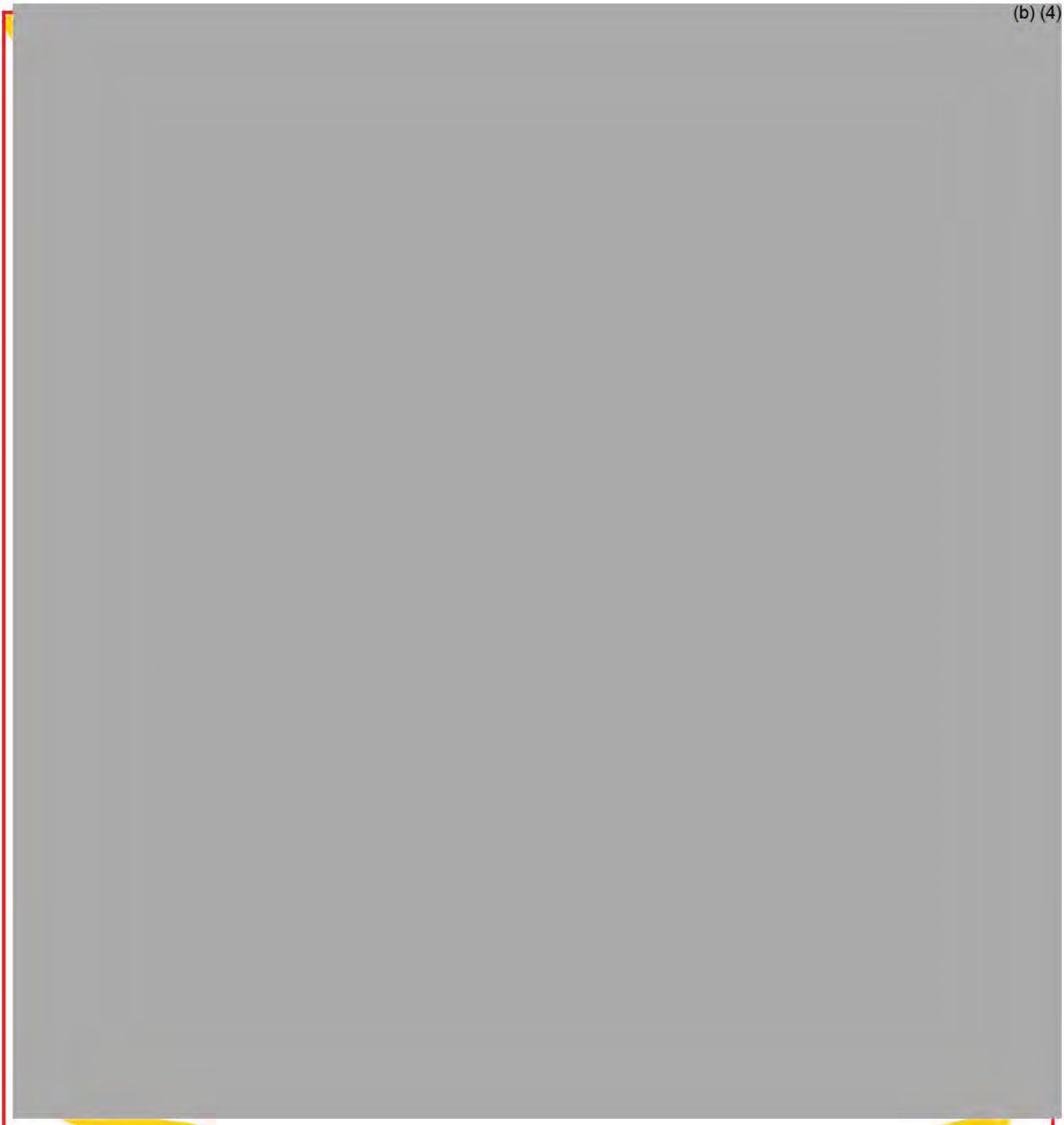
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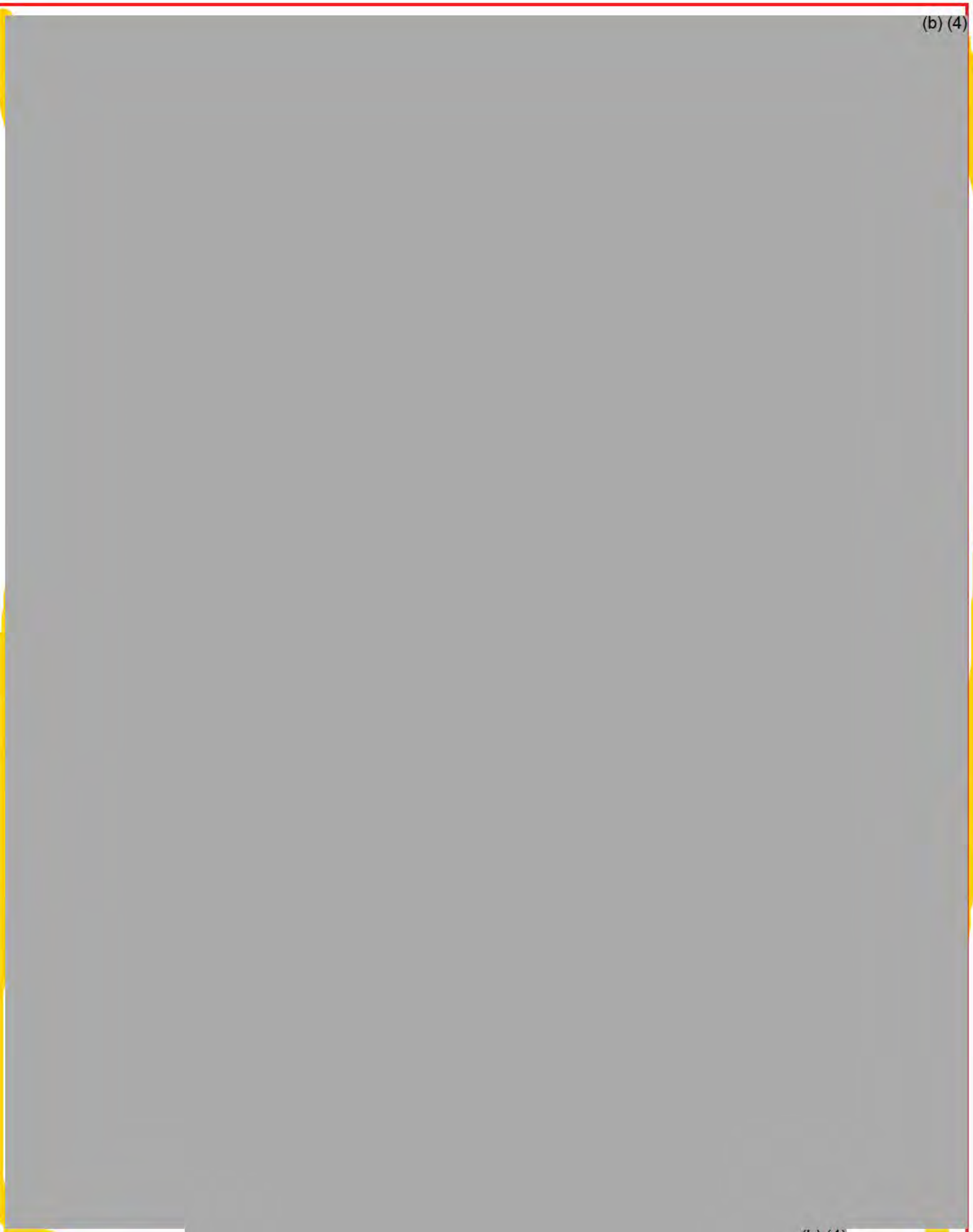
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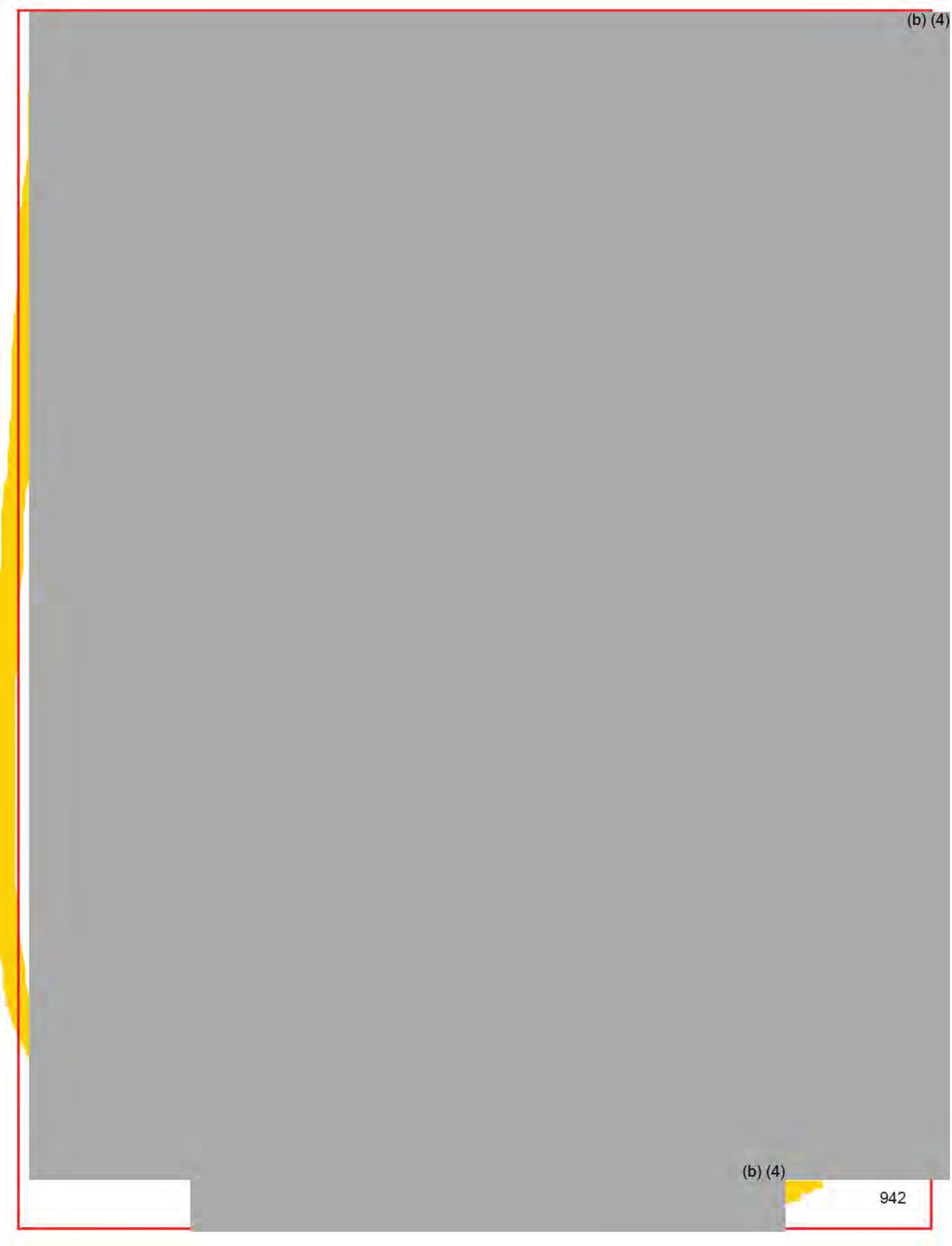
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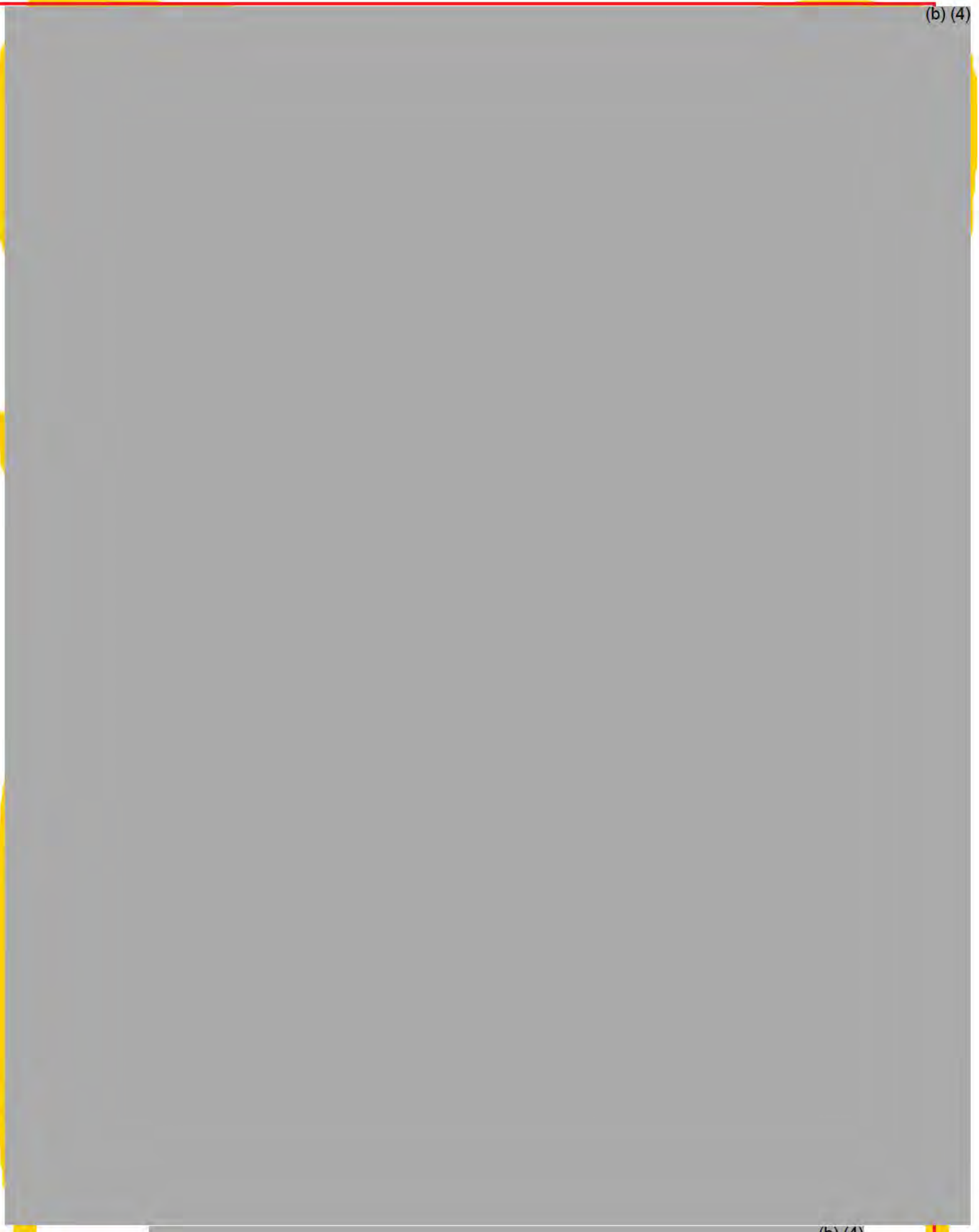
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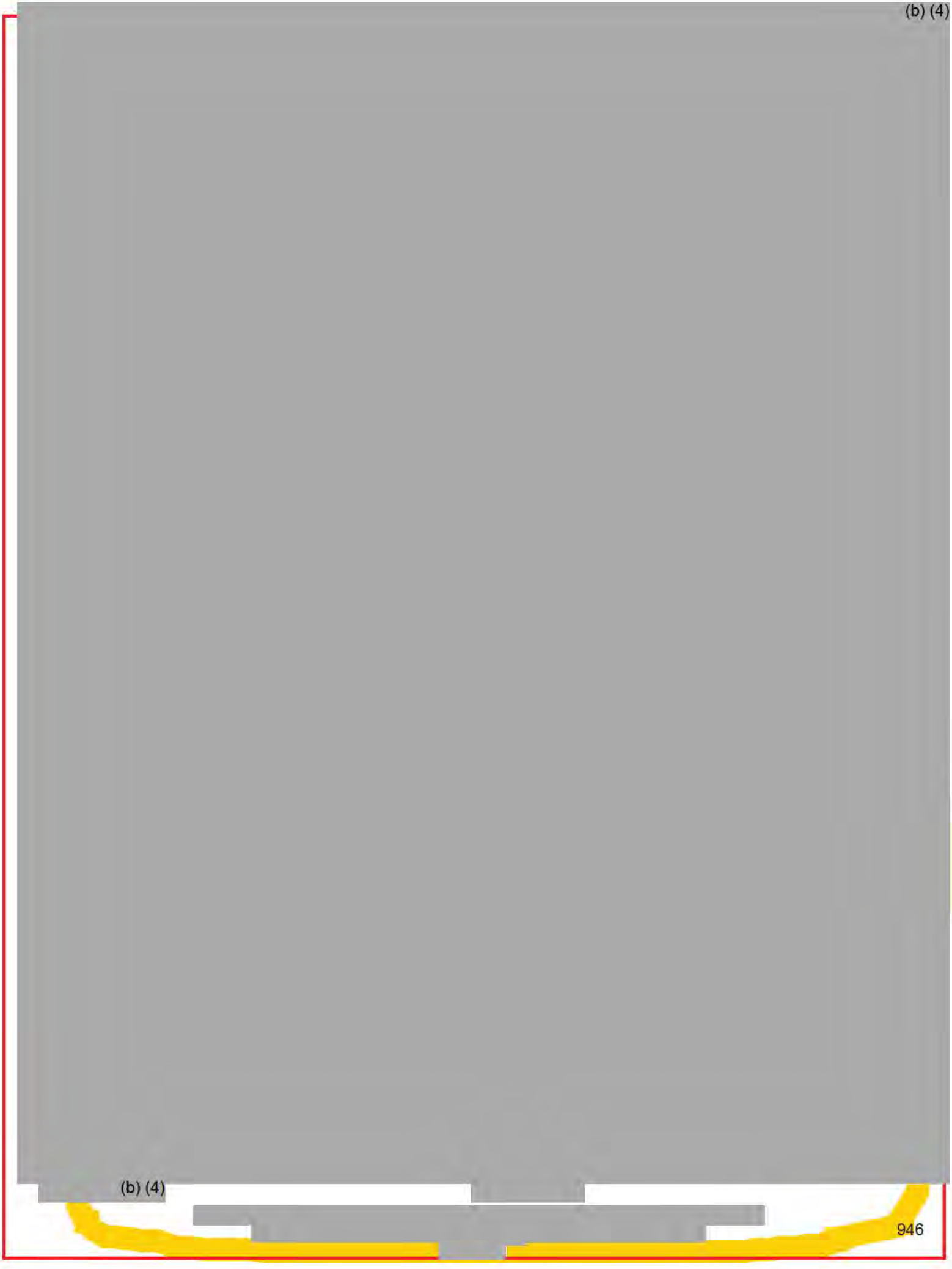
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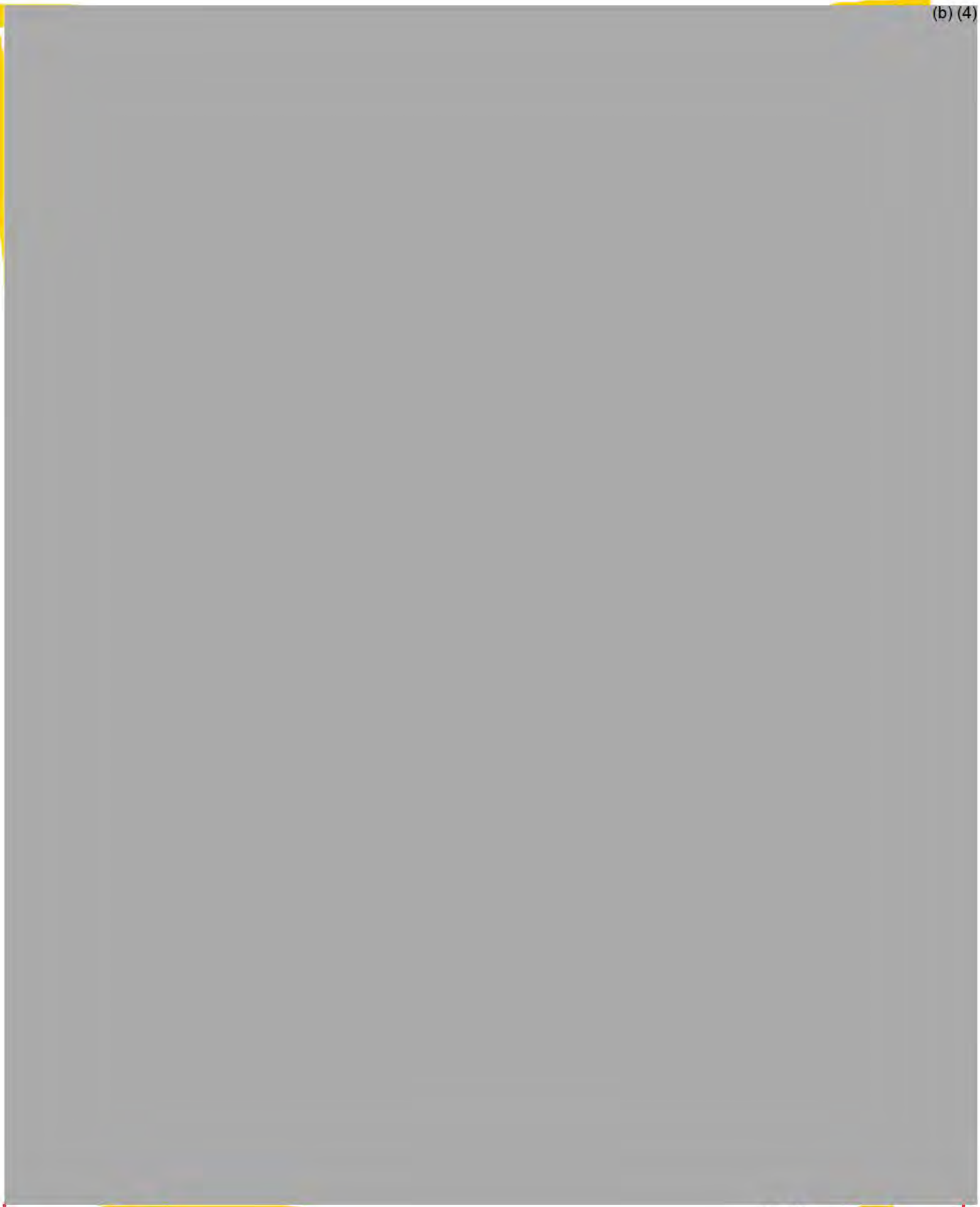

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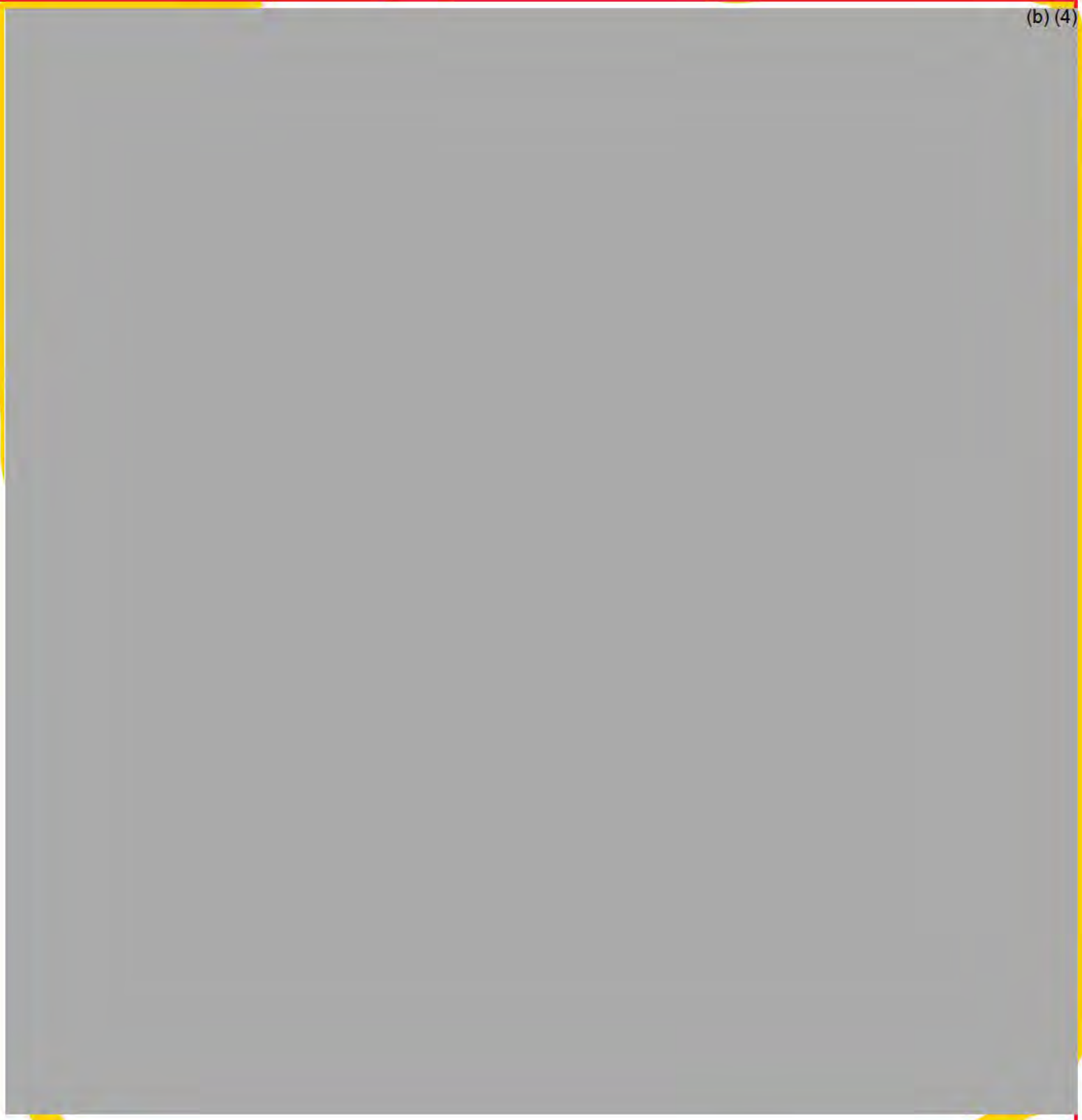
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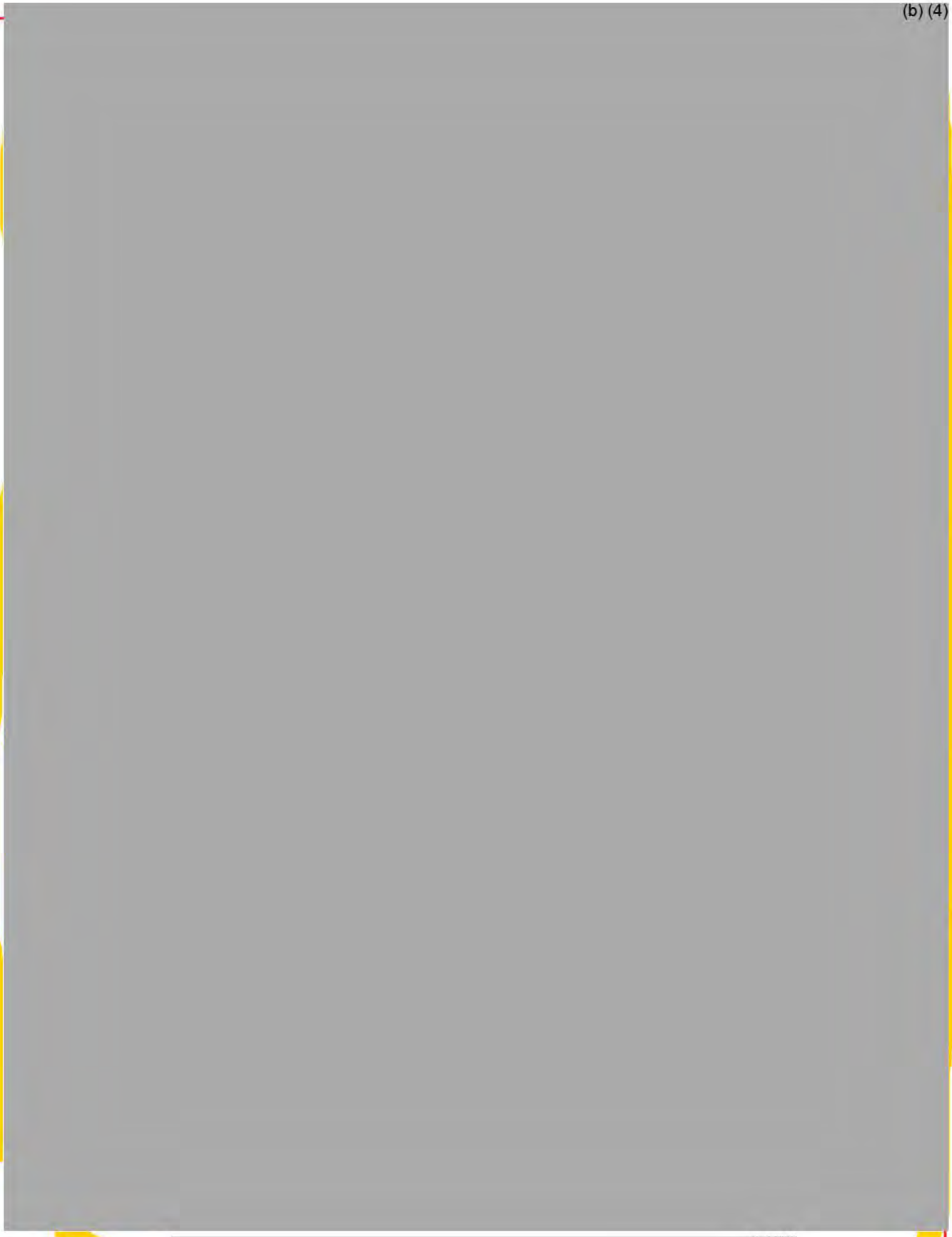



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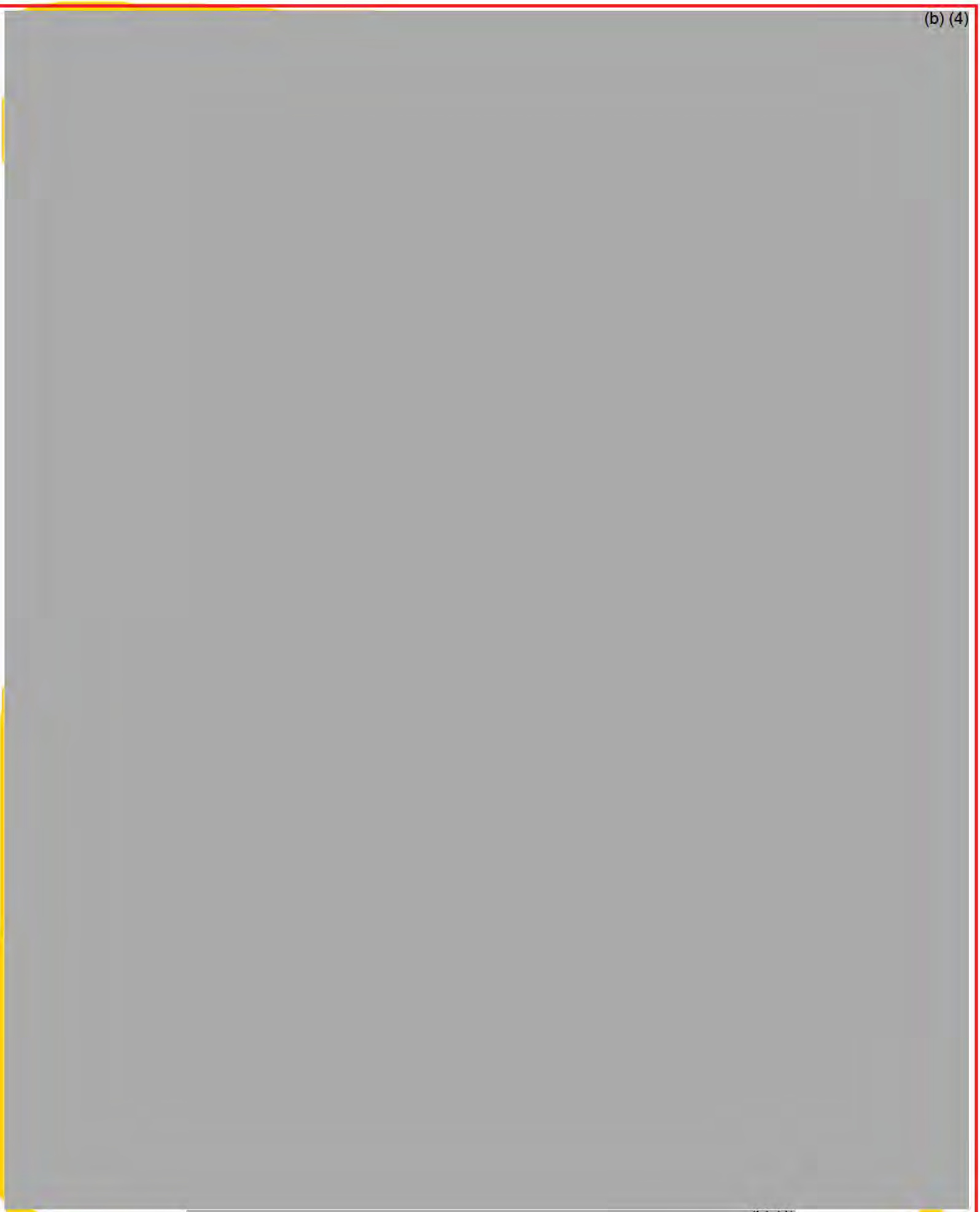
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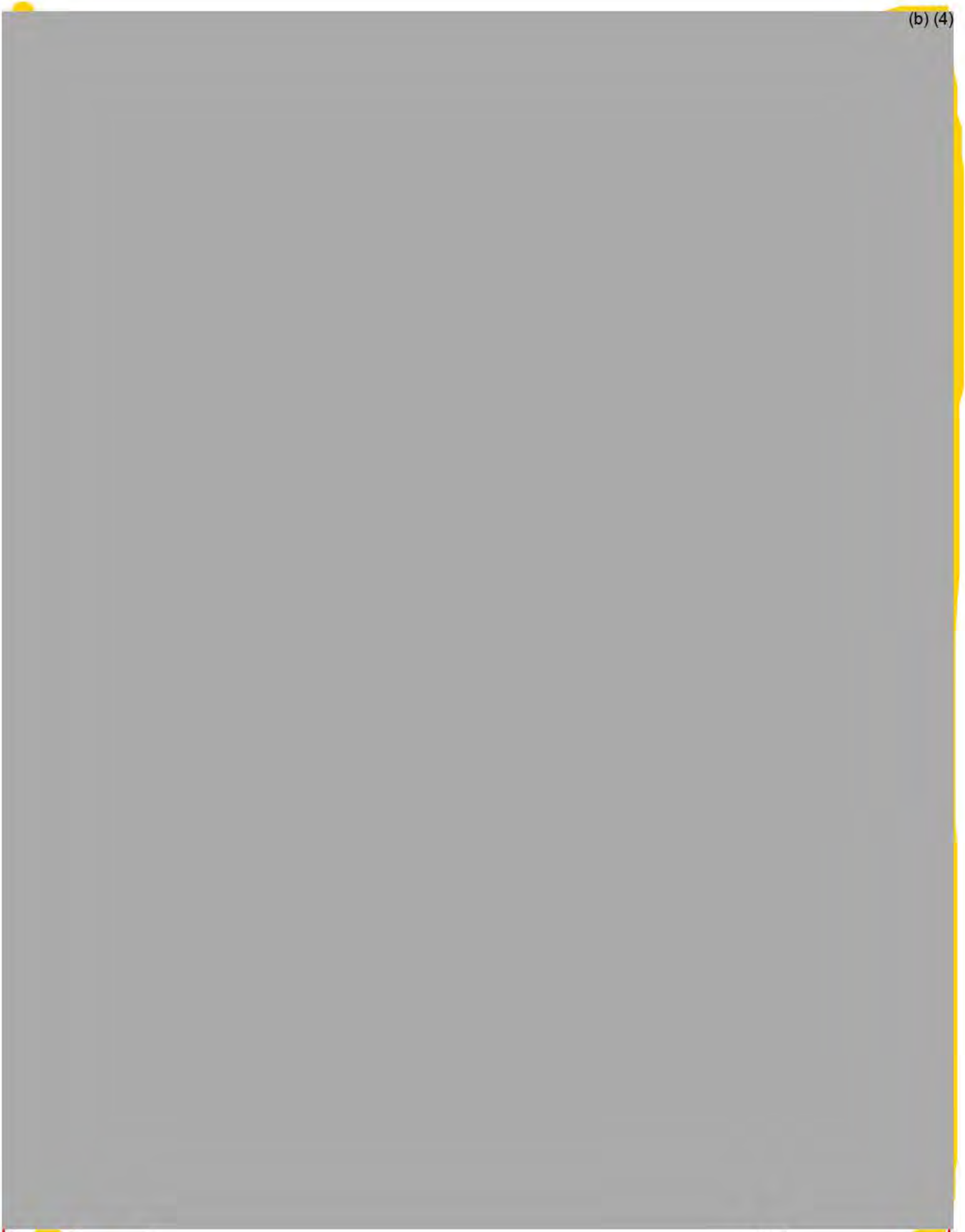

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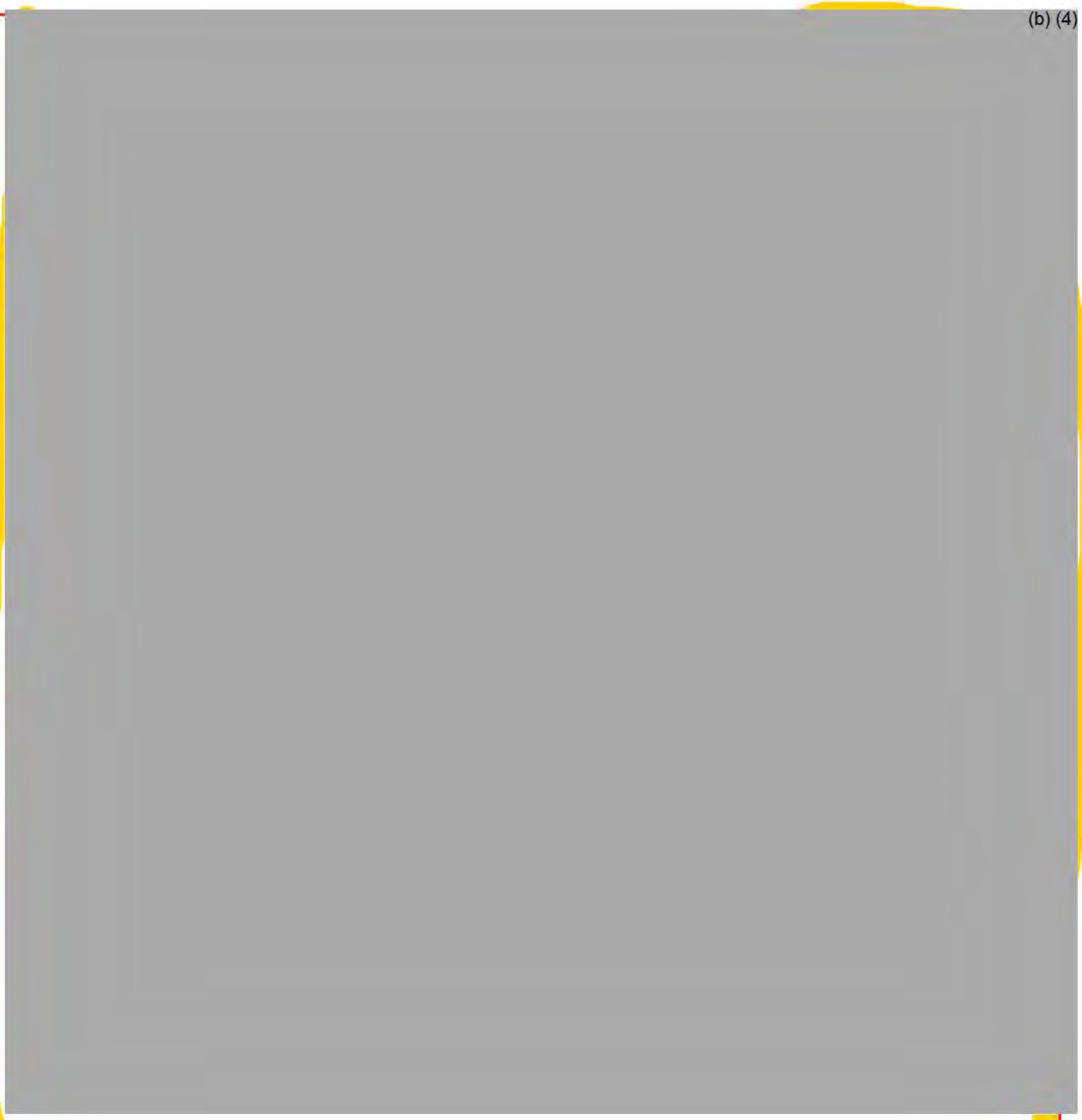

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APPENDIX NO. 2
ANALYTICAL CHEMISTRY REPORT

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies:

DOSE FORMULATION REPORT

SPONSOR

DSM
6480 Dobbin Rd.
Columbia, MD 21045, USA

STUDY FACILITY

(b) (4)

[redacted]

DIET ANALYSIS FACILITY

DSM Nutritional Products: (b) (4) nada

(b) (4), (b) (6)

[redacted]

Date: September 24, 2018

1. INTRODUCTION....3
1.1.1. Study Number....3
1.1.2. Study Title....3
1.1.3. Study Summary....3
1.1.4. Dose Formulation Analysis....3
1.1.5. Test Site....3
2. ANALYTE AND VEHICLE....3
3. STUDY DESIGN....4
3.1.1. Table 1: Study Design....4
3.1.2. Test substance....4
4. EXPERIMENTAL DIETS....5
4.1.1. Diet Preparations....5
4.1.2. Sample Receipt and Handling....5
5. SAMPLE ANALYSIS....5
5.1.1. Concentration Verification....6
5.1.2. Peroxide Value Determination....7
6. RESULTS....7
6.1.1. Initial Diet Analysis....7
6.1.2. Dose Confirmation....7
6.1.3. Peroxide Value (PV) Determination....10
7. REFERENCES:....10
8. APPENDIX....11
8.1.1. Eurofins Certificates of Analysis for Control and Dose Diets....11
8.1.2. DSM, Dartmouth, Canada SOP# [redacted] (b) (4) 31
9. SIGNATURES....45

1. INTRODUCTION

1.1.1. Study Number

(b) (4)

1.1.2. Study Title

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies: Dose Formulation Results.

1.1.3. Study Summary

The objective of this study is to evaluate safety and bioavailability of Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to Beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old). This report summarizes the results of the analysis of the DHA and EPA in the test diets to verify their concentrations in the formulations and the Peroxide Values (PVs) of the diets throughout the duration of the study. The formulation is considered successful if EPA+DHA concentrations in diets are within ± 15% of the targeted concentrations.

1.1.4. Dose Formulation Analysis

A dose formulation analysis was conducted in accordance with internal DSM SOPs (b) (4) (b) (4) (Appendix Section 7.1.2). The study was not conducted in compliance with GLP regulations.

1.1.5. Test Site

DSM Nutritional Products

(b) (4), (b) (6)

2. ANALYTE AND VEHICLE

Identification of Analyte and Vehicle

Analyte Name: Docosahexaenoic Acid (DHA)

Eicosapentaenoic Acid (EPA)

Vehicle Name: DSM prepared dried dog food diet

3. STUDY DESIGN

3.1.1. Table 1: Study Design

The test and reference items will be administered as a diet as shown below:

Table 1: Study Design

Study Design

Treatment Group	Dosage Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F0 Generation (dams)	F1 Generation (puppies)	
					F	M(Spare)	F(Spare)
1. Control diet*	0	0	0.11%	0.12%	5	4(1)	4(1)
2. AOCED	½ X	0.75%	0.41%**	0.44%	5	4(1)	4(1)
3. AOCED	1X	1.5%	0.77% **	0.83%	5	4(1)	4(1)
4. AOCED	2X	3.0%	1.55%**	1.69%	5	4(1)	4(1)

* Group 1 animals received the control diet, which was formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA level (0.11%) was achieved by using fish oil.

** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content was the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA).
Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.

*** Calculated based on dry matter basis (adjusted for moisture content).

M: male; F: female

3.1.2. Test substance

Identification

Test Substance: Algal Oil Containing EPA+DHA (AOCED)
Lot: (b) (4)
DHA+EPA CONTENT, mg/g oil: 525 mg/g
DHA CONTENT, mg/g oil: 400 mg/g
EPA CONTENT, mg/g oil: 125 mg/g
Manufacturing Date: September 04, 2016

A nominal content of DHA+EPA in AOCED is 50% but can vary depending on a manufacturing lot. The AOCED lot (b) (4) used for the test diets preparation contained DHA at 42.7 area% of total fatty acids (400.3 mg/g oil) and EPA at 13.6 area% of total fatty acids (124.7 mg/g oil). Therefore, the total DHA+EPA content was 525 mg/g oil.

4. EXPERIMENTAL DIETS

4.1.1. Diet Preparations

Experimental diets were manufactured at (b) (4) from May 15 to May 23, 2017. The diets, including the control, were formulated by DSM Nutritional Products, LLC to meet the AAFCO Dog Food Nutrient Profile for Growth and Reproduction (AAFCO, 2016). The dry kibble diets were manufactured using a Wenger X20 extruder and then dried in a Wenger dryer. They were cooled before coating with flavors and a mixture of chicken fat and fish oil (Control), or a mixture of chicken fat and AOCED (AOCED-containing diets). The diets were made isocaloric with the control diet. Sam les from each formulation were collected upon manufacture and shipped to (b) (4) for analysis. Certificates of Analysis (CoAs) of the diets can be found in the Appendix. Diet codes were CDS002, CDS003, CDS004, and CDS005 for the Control, Low-, Mid- and High-Dose AOCED diets, respectively.

4.1.2. Sample Receipt and Handling

Representative samples (approximatel 500 g in du licate of each diet formulation were taken from one bag at Day 1 (at (b) (4)), from Day 1 of dosing at (b) (4) on the day of the animal arrival, at two-month intervals throughout the study, and at the end of treatment. Samples were stored at room temperature and shipped after each collection point at room temperature to (b) (4), (b) (6) at DSM, Dartmouth, Canada for concentration and peroxide value determination.

At the end of the stud , the retention samples from each collection point were shipped to (b) (4), (b) (6) at DSM, Dartmouth, Canada at room temperature. The retention samples were homogenized using a food grinder upon recei t. A ortion of the homogenized sample was shipped at room temperature to (b) (4) for analysis.

5. SAMPLE ANALYSIS

Analysts:

Peroxide Values: (b) (4), (b) (6)
Phone (b) (4), (b) (6)
Email: (b) (4), (b) (6)

Potenc Verification: (b) (4), (b) (6)
Phone: (b) (4), (b) (6)
Email: (b) (4), (b) (6)

Table 2: Diet sample receipt and analysis dates at DSM, Canada and (b) (4)

Sample Code	Timepoint	Date shipped from (b) (4)	Date Received at DSM Dartmouth, Canada	Date of PV analysis (DSM, Dartmouth)	Date of Potency Analysis (DSM, Dartmouth)	Date retention sample shipped from DSM, Dartmouth	Date of Potency Analysis (b) (4)
CD907, CD165, CD049, CD610	Day 1	16-Aug-17	17-Aug-17	24-Aug-17	25-Aug-17	14-Aug-18	20-Aug-18
CD907, CD165, CD049, CD610	Animal Arrival	14-Sep-17	15-Sep-17	19-Sep-17	29-Sep-17	14-Aug-18	20-Aug-18
CD907, CD165	Month 2	24-Oct-17	26-Oct-17	8-Nov-17	28-Nov-17	14-Aug-18	20-Aug-18
CD049, CD610	Month 2	24-Oct-17	26-Oct-17	8-Nov-17	8-Dec-17	14-Aug-18	20-Aug-18
CD907, CD165	Month 4	4-Jan-18	9-Jan-18	15-Jan-18	16-Mar-18	14-Aug-18	20-Aug-18
CD049, CD610	Month 4	4-Jan-18	9-Jan-18	15-Jan-18	23-Mar-18	14-Aug-18	20-Aug-18
CD907, CD165, CD049, CD610	Month 6	26-Feb-18	1-Mar-18	19-Mar-18	20-Mar-18	14-Aug-18	21-Aug-18
CD907, CD165, CD049, CD610	Month 8	1-May-18	2-May-18	3-May-18	1-Jun-18	14-Aug-18	21-Aug-18
CD907, CD165, CD049, CD610	Last Day	29-May-18	1-Jun-18	4-Jun-18	19-Jun-18	14-Aug-18	21-Aug-18

5.1.1. Concentration Verification

A GC/FID method to quantitate the fatty acids in Omega-3 levels in fortified foods was developed at DSM Dartmouth, Canada. This method (b) (4) (b) (4) was used to analyze the dog diet samples.

- Approximately 80-100 grams of diet sample was placed on a freeze-dryer for 2 to 3 days until a constant weight was reached. Percent moisture loss was recorded for each sample. Samples are analyzed in triplicate and the average of the three results are reported.
- Approximately 80-100g (everything that was freeze dried) of representative dog diet was homogenized using a food grinder.
- Approximately 250 mg of homogenized sample was weighed into a glass test tube and the weight was recorded to the nearest 0.1 mg.
- (b) (4)
- Approximately 1mL of the top organic phase was transferred to a GC vial containing sodium sulfate and the samples were analyzed by gas-liquid chromatography (GLC).

Fatty acid concentrations were analyzed using gas chromatography (GC) with flame ionization detection on a Restek Famewax 30m x 0.32 mm x 0.25 µm column. Fatty acids were identified by comparison with a standard mixture of fatty acids (b) (4)

(b) (4) Fatty acid composition was expressed as a weight percent of total identified fatty acids based on potency determinations (milligram of fatty acid per gram of sample).
Recoveries of a total EPA + DHA content were calculated by dividing the measured EPA + DHA concentration at each time point by the EPA + DHA concentration reported by (b) (4) in the Certificates of Analysis for each respective diet.

5.1.2. Peroxide Value Determination

A method to quantitate peroxide values (PVs) of oils in fortified foods using the FoodLABfat analyzer was developed at DSM Dartmouth, Canada. The FoodLABfat analyzer uses a colorimetric assay to measure peroxide oxidized Fe2+ ions as a marker of lipid oxidation. This method was used to analyze PVs of the dog diet samples.

- 3-5g of dog diet was placed in a Swedish tube containing 3 stainless steel balls

(b) (4)

- The remaining oil was tested for PV using the FoodLABfat analyzer according to the manufacture's method.

6. RESULTS

6.1.1. Initial Diet Analysis

Diet formulations were verified by (b) (4) (See Appendix 7.1.1). Diet formulations were considered valid because their EPA+DHA levels (as % of total fatty acids) were within 15% of the targeted concentrations.

6.1.2. Dose Confirmation

Dietary samples were collected during the study to confirm that the diets potencies remained stable over the duration of the study. A fatty acid analysis of dietary samples was conducted at DSM Dartmouth, Canada. Samples were analyzed in triplicate and the average of the three results were reported.
Based on reported EPA and DHA concentrations, recoveries of a total EPA + DHA content were calculated. The acceptance criteria for the recoveries were set at ±15% of CoA values.

Fatty acid analysis of dietary samples collected throughout the study confirmed acceptable levels of EPA+DHA at Study Day 1 ((b) (4) at the arrival of animals to (b) (4) and at 2 and 6 months thereafter (refer to Table 1). At Month 4, a recovery of the Low dose diet (82%) was outside of the range ±15% of the CoA concentrations. At Month 8, recovery values for all diets, including the control, did not meet the acceptance criteria of ±15% of the CoA concentrations. The same was true for the

control and High dose diet at the study completion. However, recoveries for Low and Mid dose diets were ≥85% at the end of the study.

Table 1. DHA+EPA Potency Determination for Control and Dose Diets Analyzed at DSM, Dartmouth, Canada

Collection Timepoint	Diet	Diet Code	Expected EPA +DHA Concentration (%) (b) (4)	Measured EPA +DHA Concentration (%) *(DSM, Canada)*	% Of Target *(DSM, Canada)*
Day 1	Control	CD907	0.11	0.10	90
	Low Dose, 0.5X	CD165	0.41	0.41	99
	Mid Dose, 1X	CD049	0.77	0.73	95
	High Dose, 2X	CD610	1.55	1.44	93
Animal Arrival	Control	CD907	0.11	0.10	87
	Low Dose, 0.5X	CD165	0.41	0.39	95
	Mid Dose, 1X	CD049	0.77	0.87	114
	High Dose, 2X	CD610	1.55	1.43	93
Month 2	Control	CD907	0.11	0.11	98
	Low Dose, 0.5X	CD165	0.41	0.41	101
	Mid Dose, 1X	CD049	0.77	0.76	98
	High Dose, 2X	CD610	1.55	1.49	96
Month 4	Control	CD907	0.11	0.08	76
	Low Dose, 0.5X	CD165	0.41	0.34	82
	Mid Dose, 1X	CD049	0.77	0.72	94
	High Dose, 2X	CD610	1.55	1.37	88
Month 6	Control	CD907	0.11	0.10	92
	Low Dose, 0.5X	CD165	0.41	0.36	87
	Mid Dose, 1X	CD049	0.77	0.71	93
	High Dose, 2X	CD610	1.55	40	90
Month 8	Control	CD907	0.11	0.07	68
	Low Dose, 0.5X	CD165	0.41	0.32	78
	Mid Dose, 1X	CD049	0.77	0.65	84
	High Dose, 2X	CD610	1.55	1.19	76
Last Day	Control	CD907	0.11	0.08	70
	Low Dose, 0.5X	CD165	0.41	0.35	85
	Mid Dose, 1X	CD049	0.77	0.70	91
	High Dose, 2X	CD610	1.55	1.10	71

To determine a reason for low recoveries at Month 8 and higher recoveries observed at the study completion compare to Month 8 data, a decision to re-analyze samples at the lab performed the original analysis was made. The retention samples were sent to (b) (4) and were analyzed as one batch to determine DHA + EPA potencies (Table 2). Although recovery values at most timepoints were below original values determined shortly after samples collection (refer to Table 1), generally, they were above 80% and were consistent across different diets and timepoints. It should be mentioned that the acceptance criteria used by industry for solids is recovery values of 100±20% where recovery is measured by dividing the found concentration by the nominal value (Whitmire et al., 2010). The diets recoveries were above 80% either at the original analysis or re-analysis (or both) and, therefore, seem to be acceptable to ensure proper dosing of animals.

Table 2. DHA+EPA Potenc Determination for Control and Dose Diets Analyzed at (b) (4)

Collection Timepoint	Diet	Diet Code	Expected EPA +DHA Concentration (%) (b) (4)	Measured EPA +DHA Concentration (%) (b) (4)	% Of Target (b) (4)
Day 1	Control	CD907	0.11	0.08	73
	Low Dose, 0.5X	CD165	0.41	0.32	78
	Mid Dose, 1X	CD049	0.77	0.63	82
	High Dose, 2X	CD610	1.55	1.29	83
Animal Arrival	Control	CD907	0.11	0.09	82
	Low Dose, 0.5X	CD165	0.41	0.33	80
	Mid Dose, 1X	CD049	0.77	0.63	82
	High Dose, 2X	CD610	1.55	1.26	81
Month 2	Control	CD907	0.11	0.09	82
	Low Dose, 0.5X	CD165	0.41	0.33	80
	Mid Dose, 1X	CD049	0.77	0.60	78
	High Dose, 2X	CD610	1.55	1.32	85
Month 4	Control	CD907	0.11	.10	91
	Low Dose, 0.5X	CD165	0.41	0.34	83
	Mid Dose, 1X	CD049	0.77	0.65	84
	High Dose, 2X	CD610	1.55	1.27	82
Month 6	Control	CD907	0.11	0.09	82
	Low Dose, 0.5X	CD165	0.41	0.33	80
	Mid Dose, 1X	CD049	0.77	0.64	83
	High Dose, 2X	CD610	1.55	1.31	85
Month 8	Control	CD907	0.11	0.09	82

	Low Dose, 0.5X	CD165	0.41	0.33	80
	Mid Dose, 1X	CD049	0.77	0.67	87
	High Dose, 2X	CD610	1.55	1.28	83
Last Day	**Control**	CD907	0.11	0.09	82
	Low Dose, 0.5X	CD165	0.41	0.34	83
	Mid Dose, 1X	CD049	0.77	0.65	84
	High Dose, 2X	CD610	1.55	1.30	84

6.1.3. Peroxide Value (PV) Determination

Peroxide values were consistently below 10 mEq/Kg throughout the entire duration of the study (Table 3).

Table 3. Peroxide Value Determination for Control and Dose Diets in mEq/Kg

Diet	Day 1	Animal Arrival	Month 2	Month 4	Month 6	Month 8	Last Day
Control Diet	2	2	2	3	4	5	6
Low Dose, 0.5X	2	3	2	3	6	6	6
Mid Dose, 1X	2	3	3	3	4	5	6
High Dose, 2X	2	3	3	8	5	7	5

7. REFERENCES:

Whitmire ML, Bryan P, Henry TR, Holbrook J, Lehmann P, Mollitor T, Ohorodnik S, Reed D, and Wietgrefe HD (2010). NonClinical Dose Formulation Analysis Method Validation and Sample Analysis. The AAPS Journal, vol. 12, No. 4, pp 628-634

8. APPENDIX

(b) (4)

[redacted]

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CERTIFICATE OF ANALYSIS

(b) (4)

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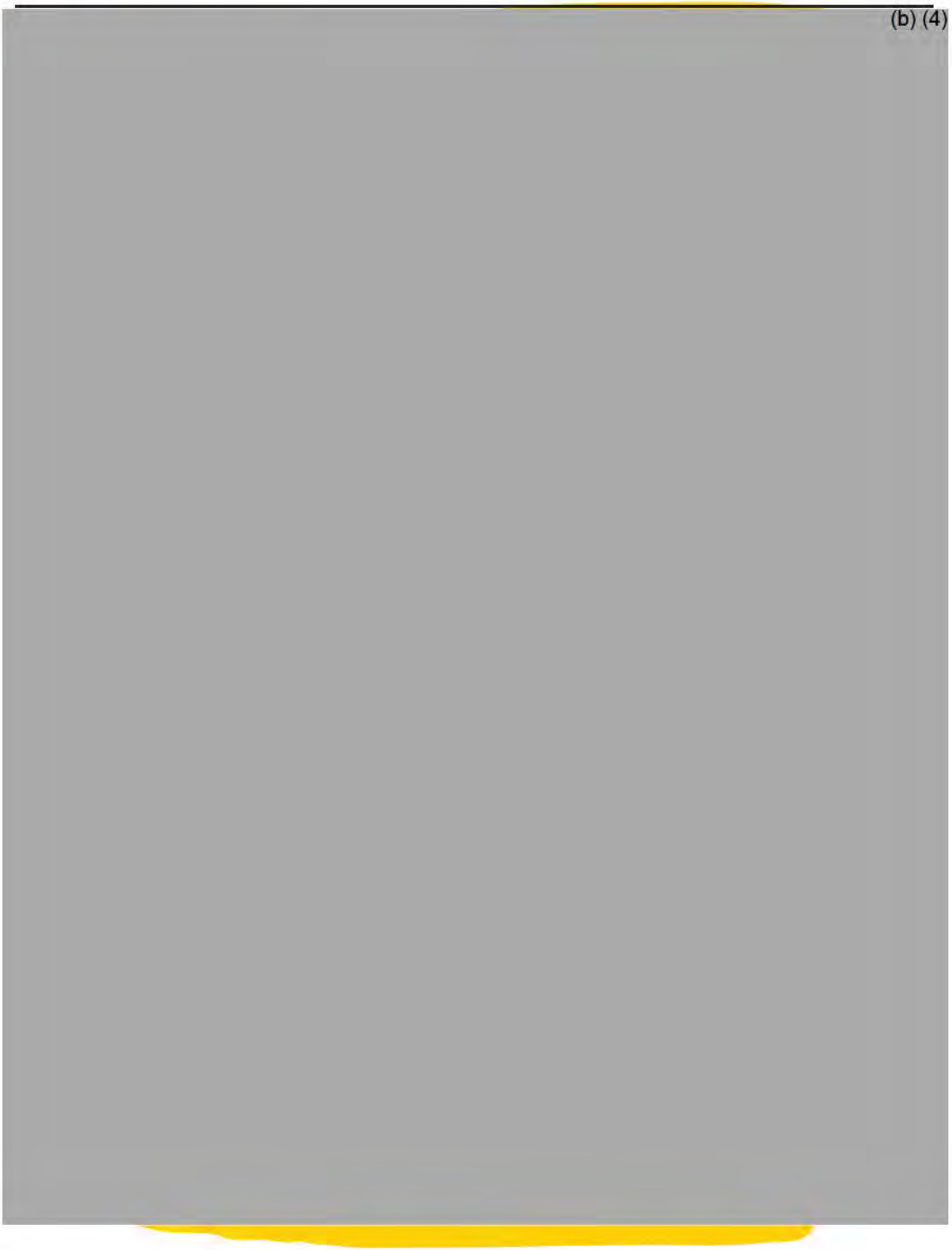

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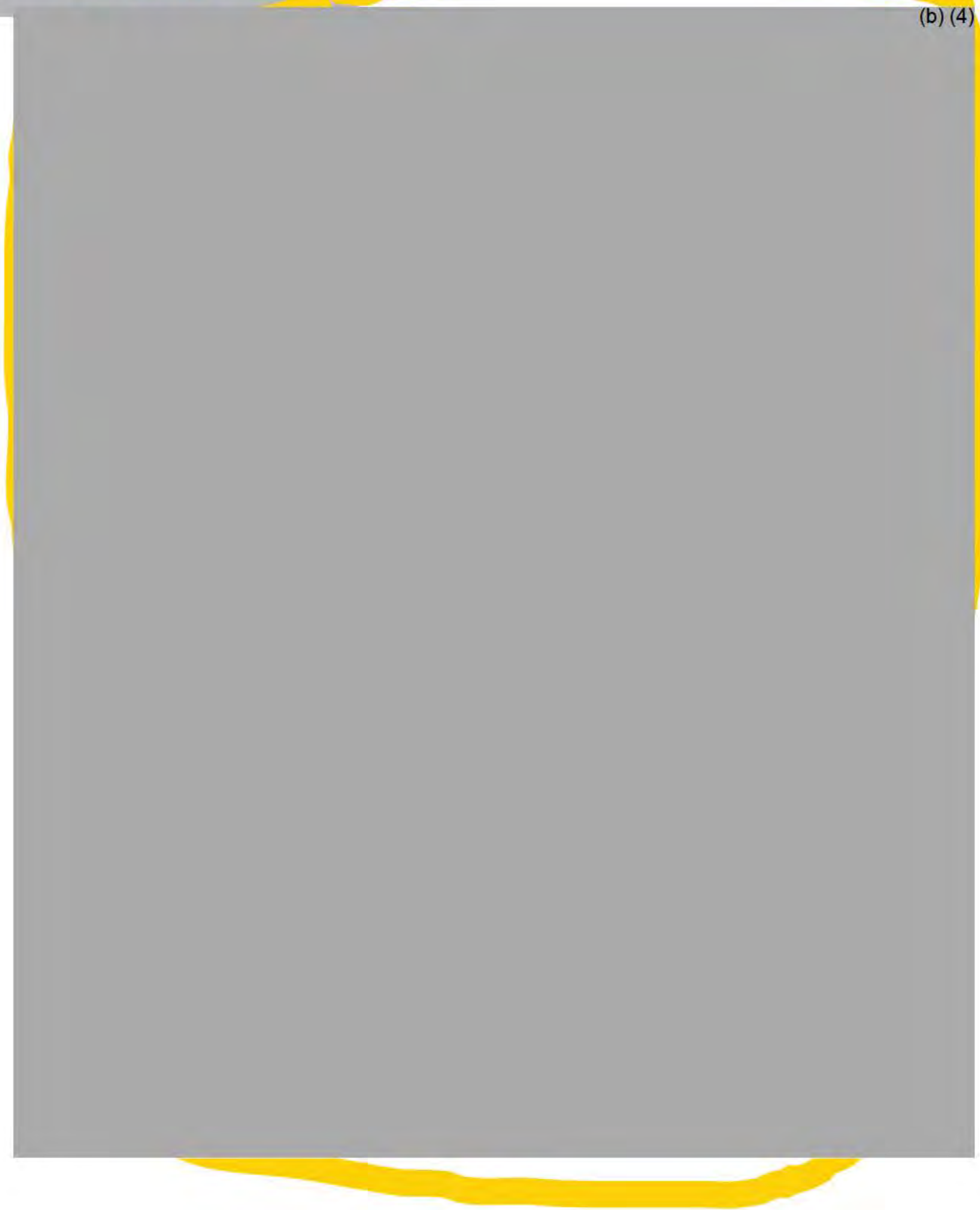

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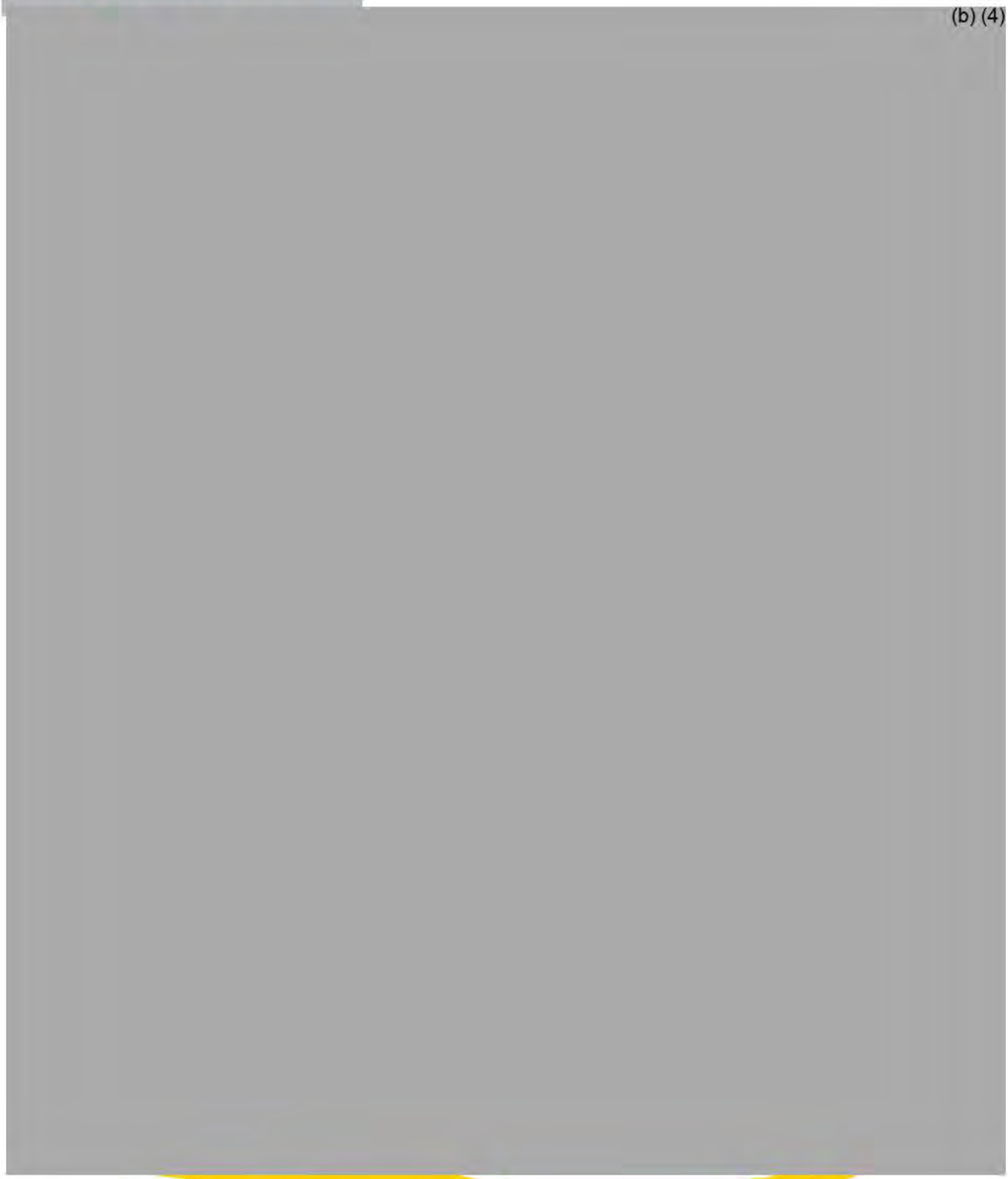

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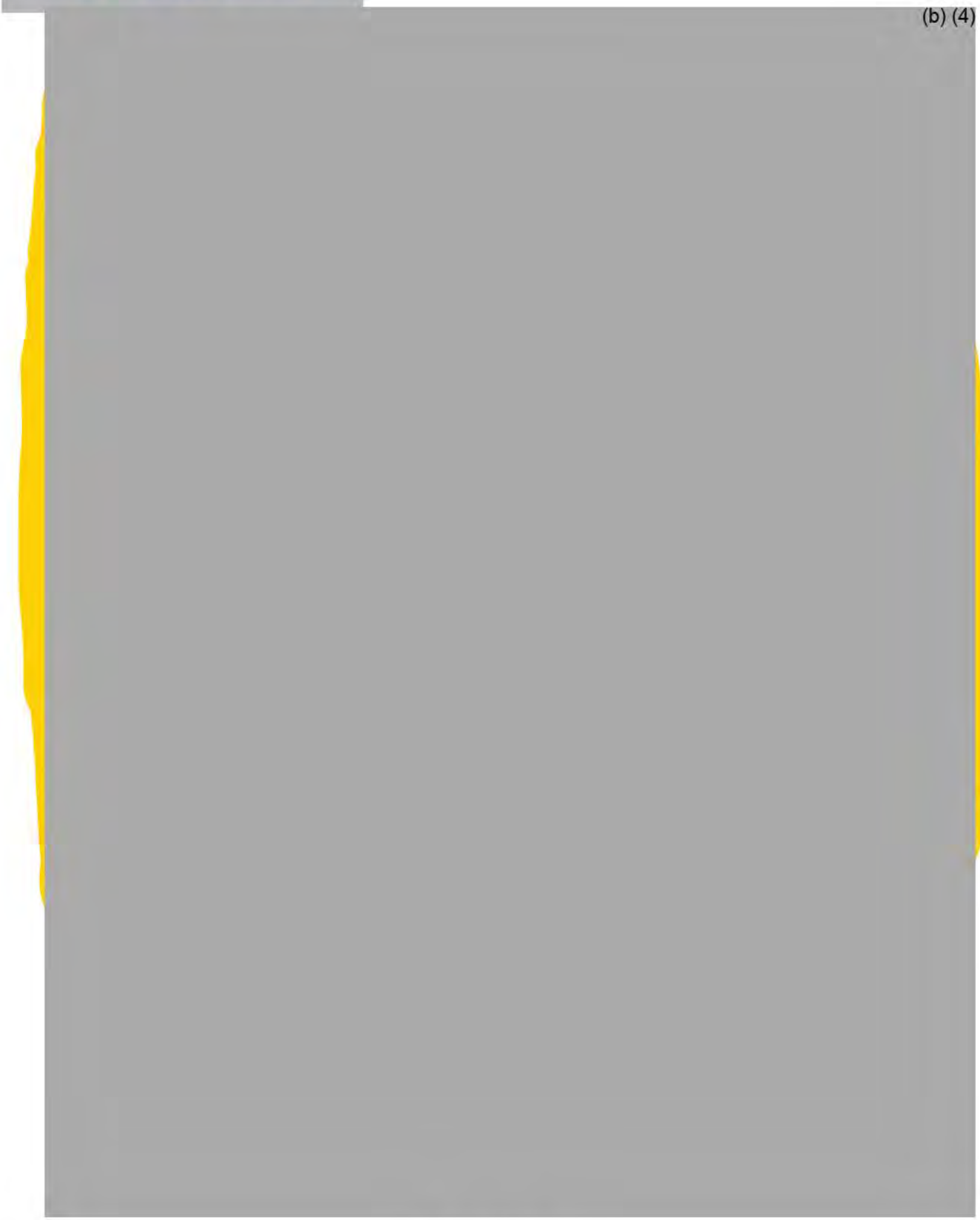

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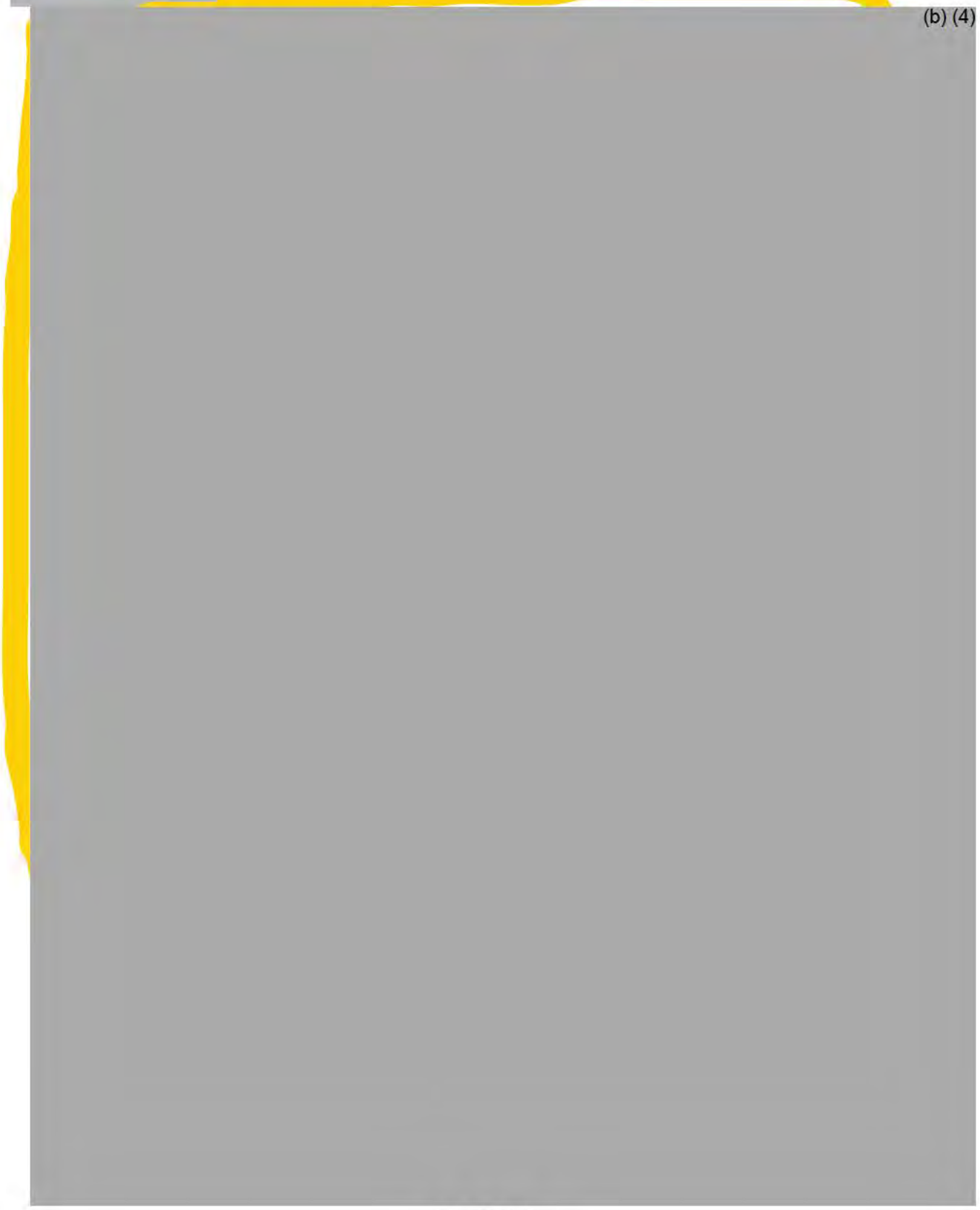

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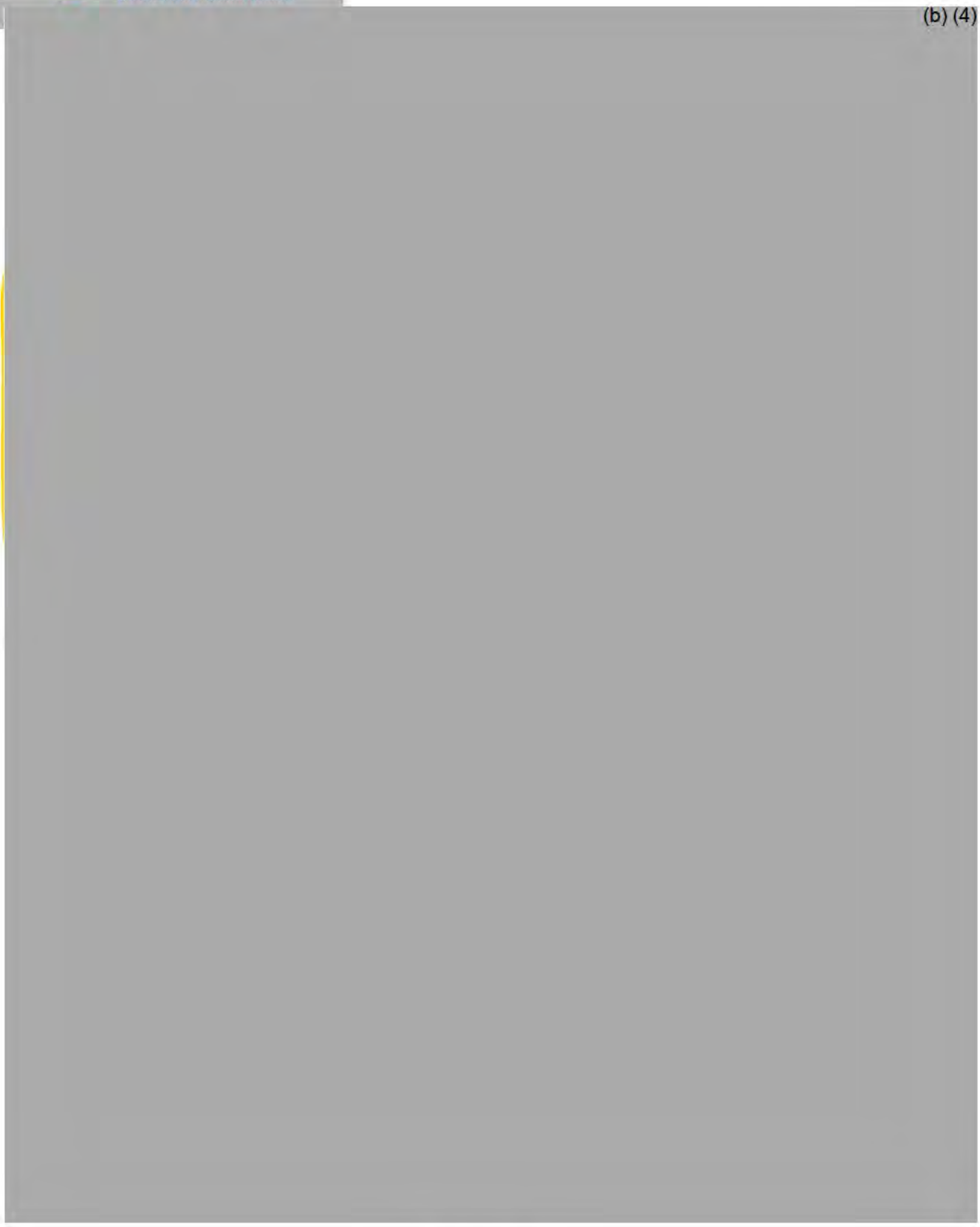

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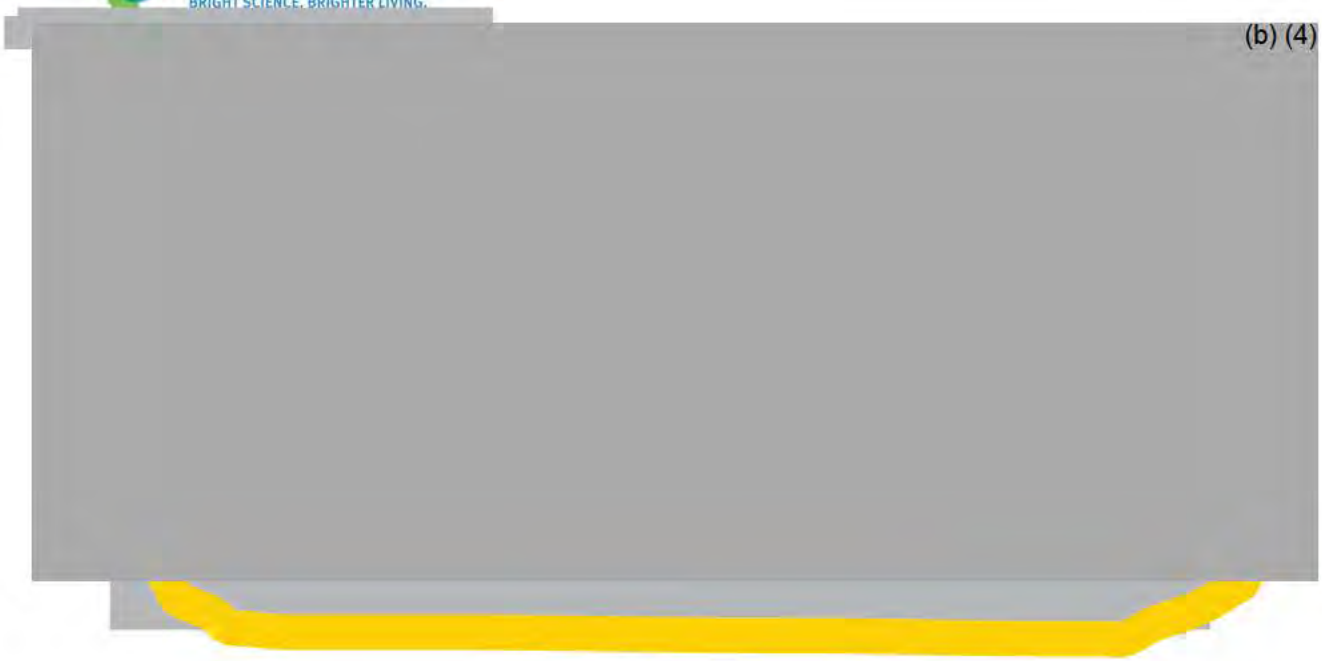

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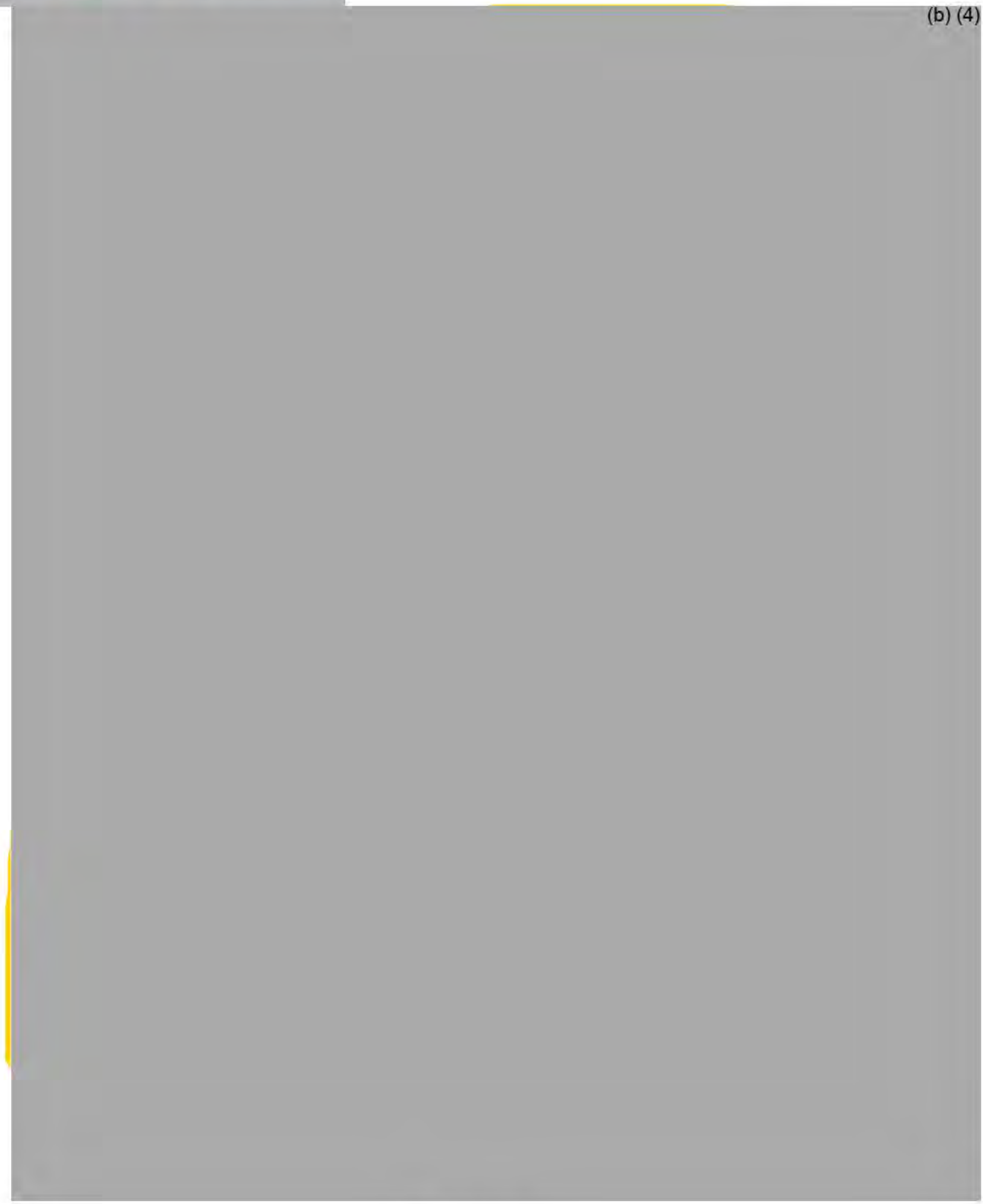

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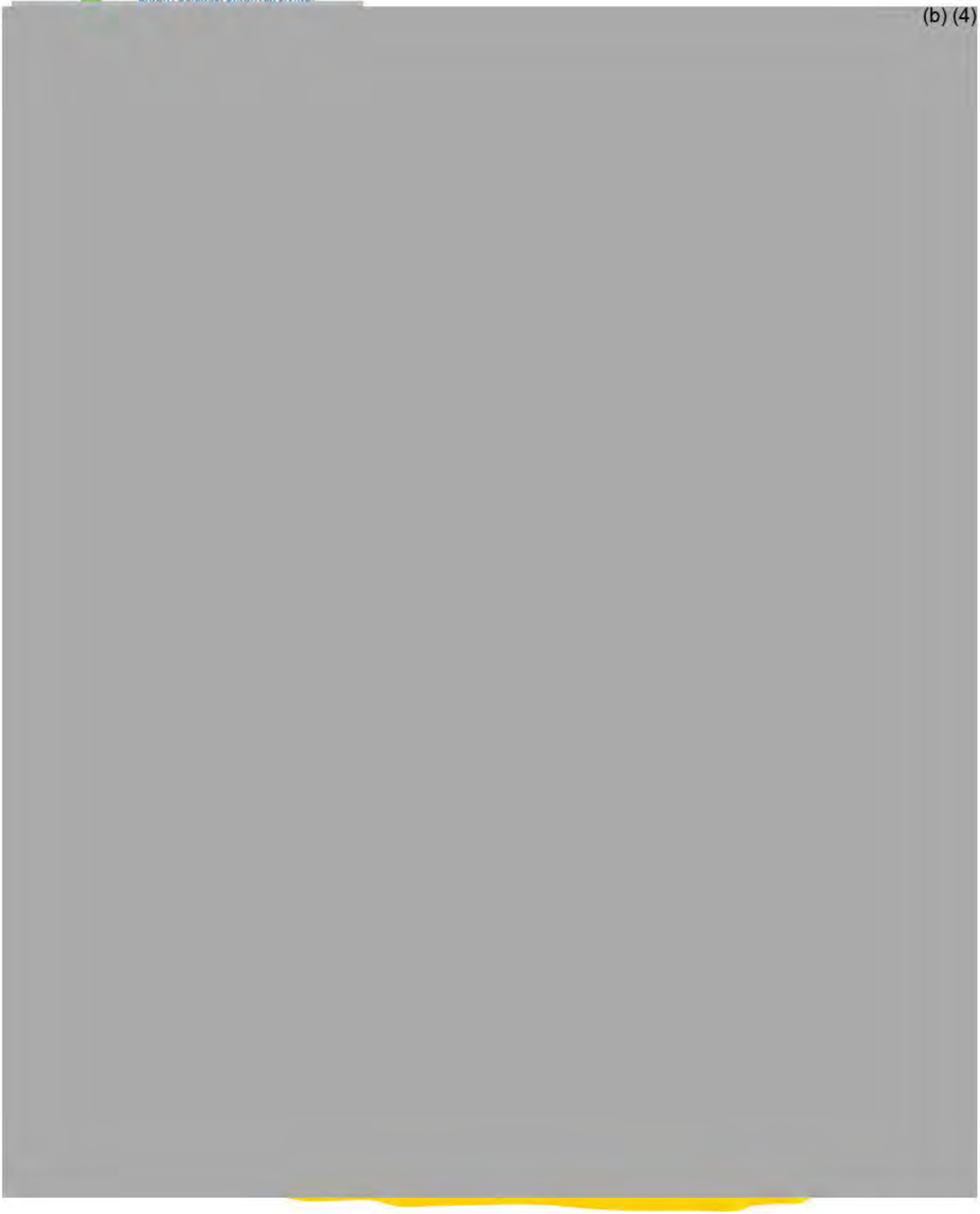

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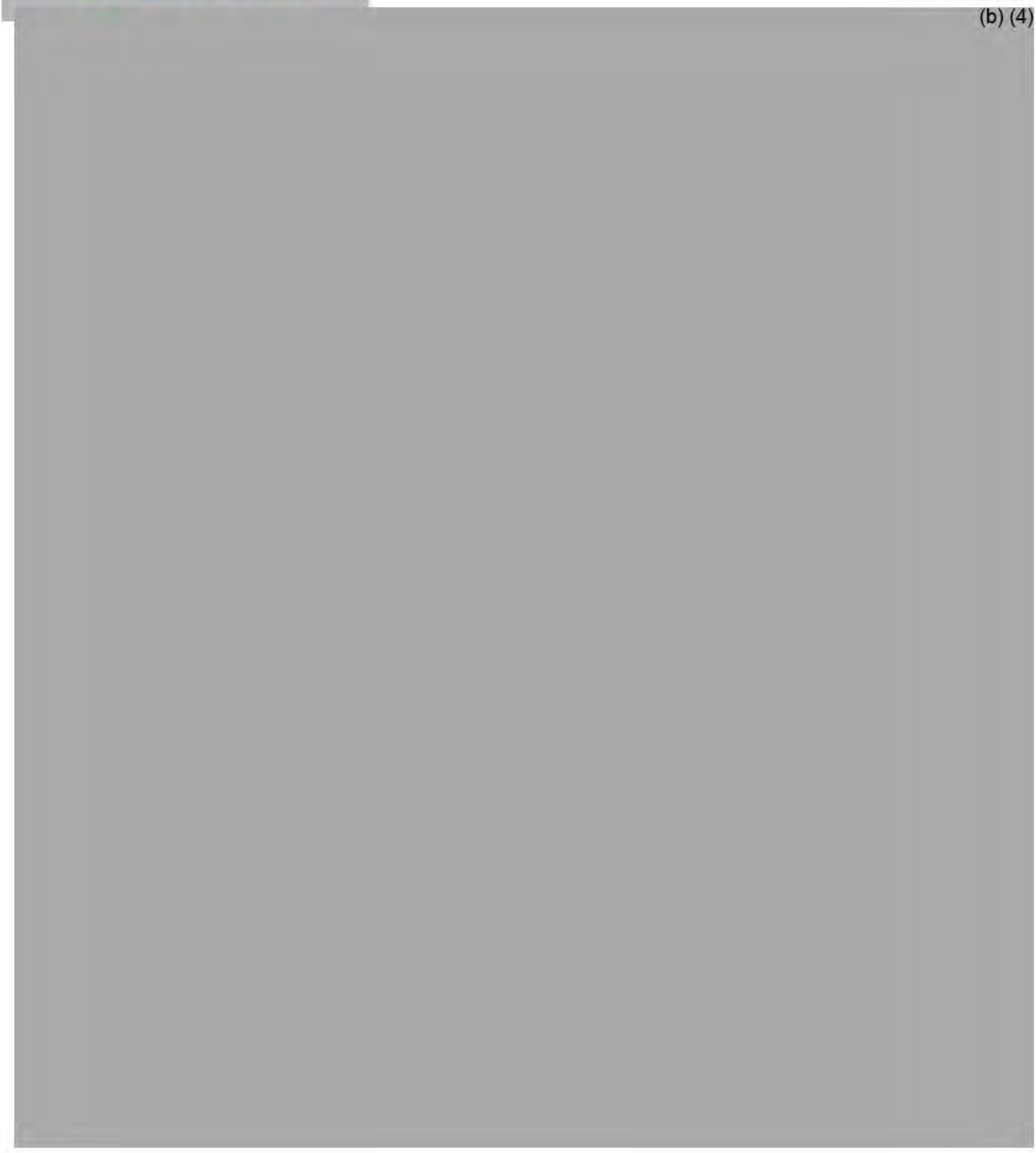

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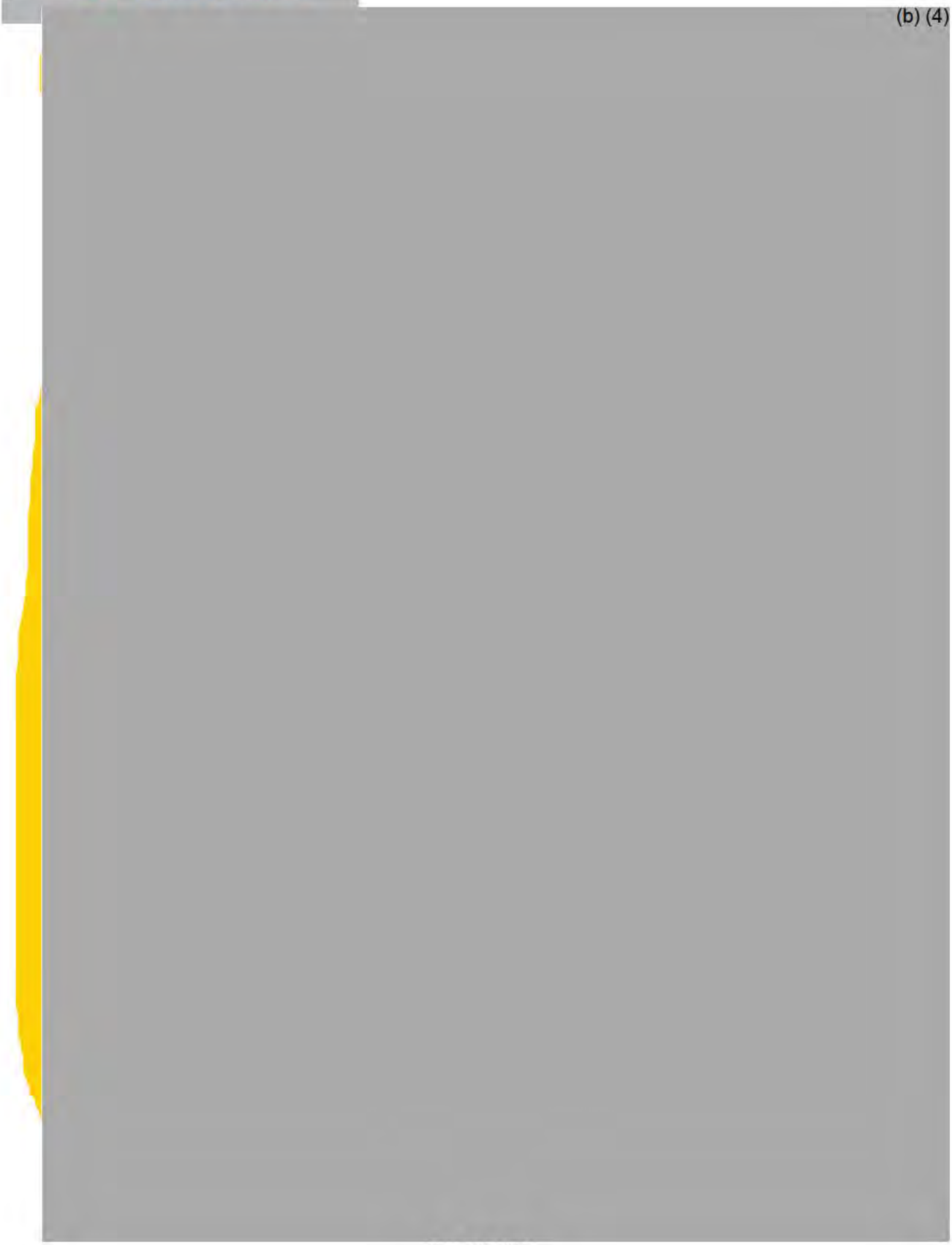

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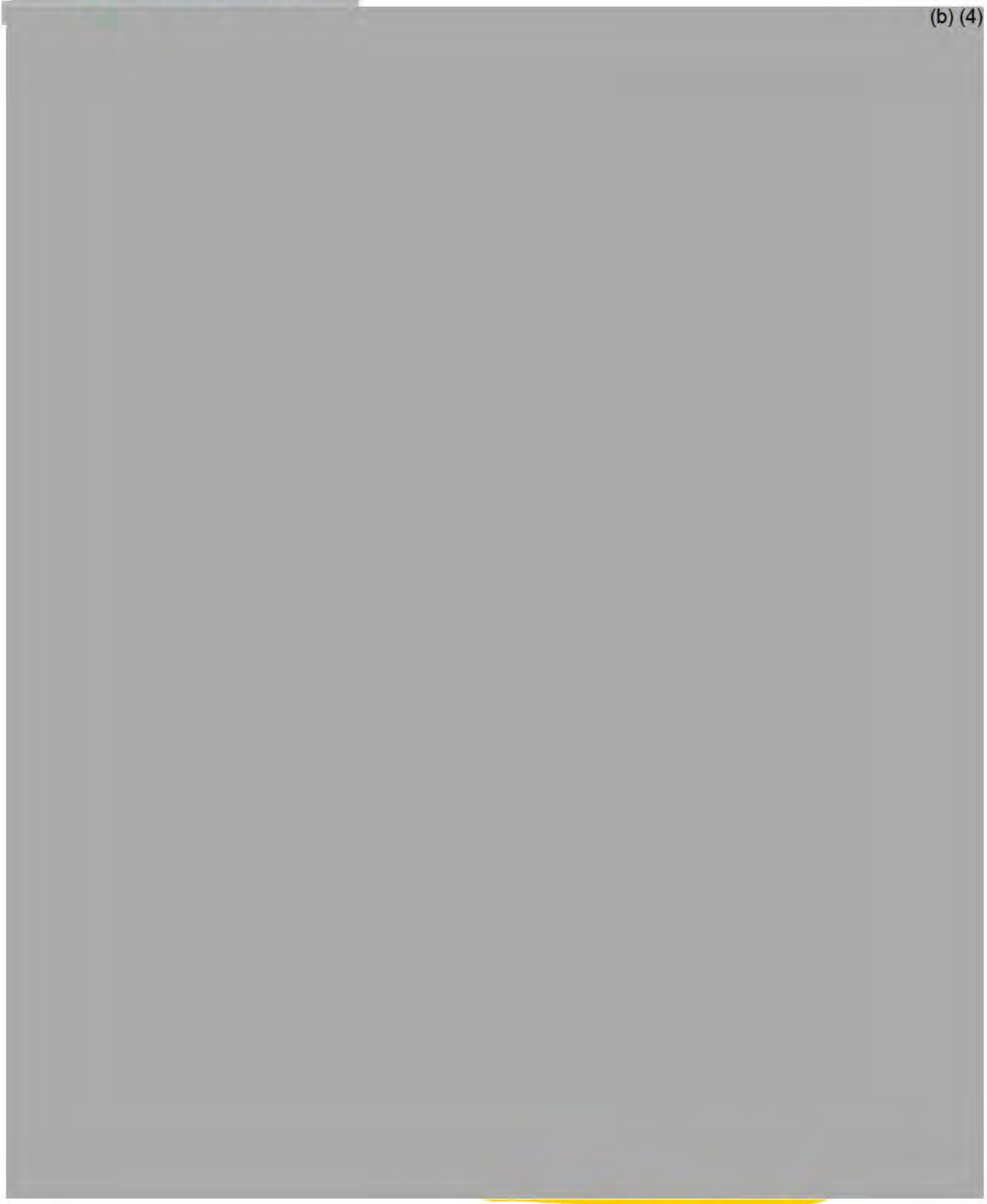

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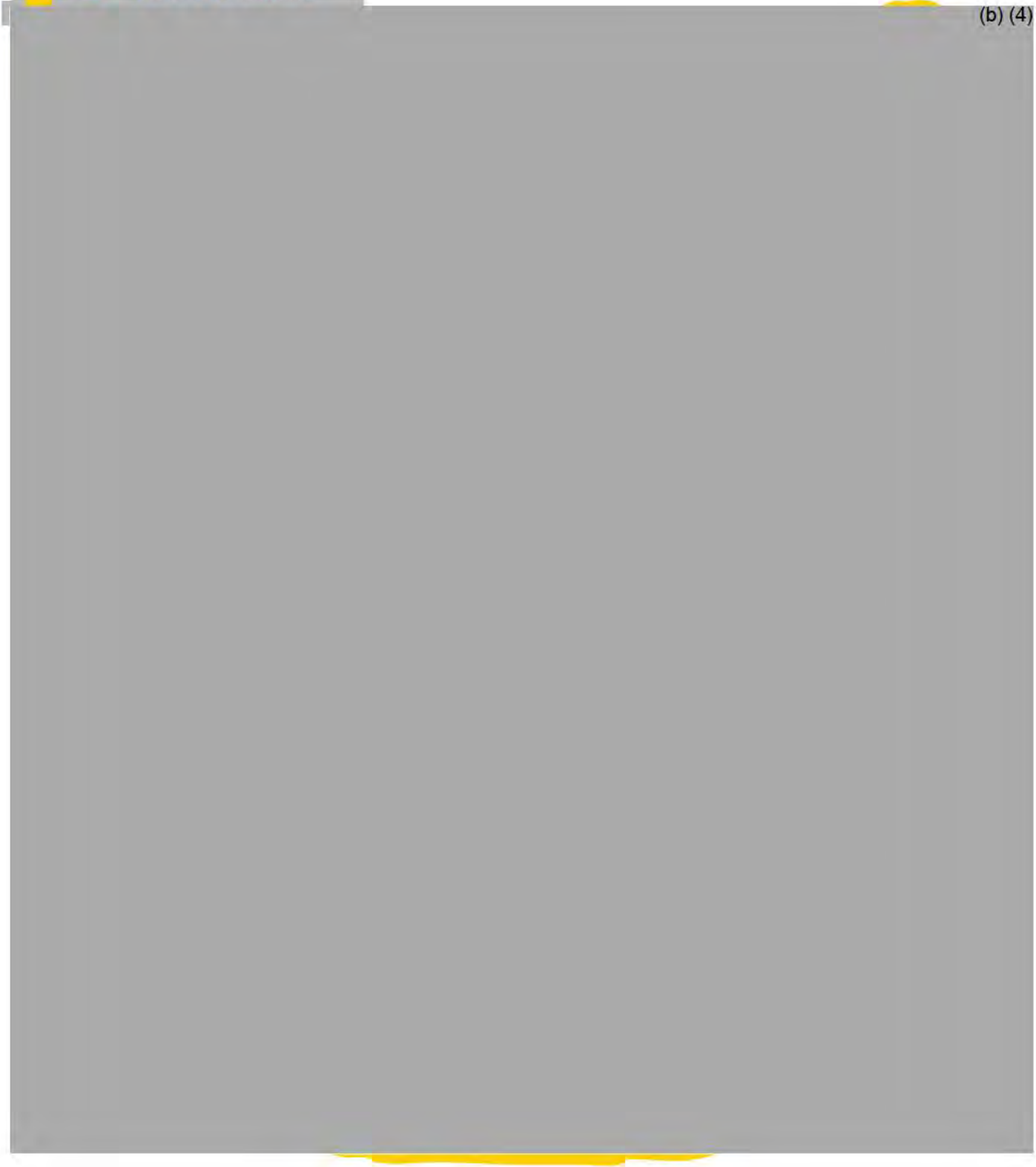

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8.1.2. DSM, Dartmouth, Canada (b) (4)

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Version: 1.0

Effective Date: 08-Sep-2017

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(b) (4), (b) (6)

Owner:

Authors:

Reviewed By

(b) (4), (b) (6)

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(b) (4) Version: 1.0, CURRENT Effective Date: 08/Sep/2017

Location: CA Dartmouth

Department: Research and Development: Analytical, Oil

Table of Contents

1 Purpose 2
2 Scope 2
3 Responsibilities 2
4 Definitions 2
5 SHE 2
6 Quality 2
7 References 2
8 List of attachments 2
9 Distribution 2
10 Procedure 3
11 Revision History 13

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10 Procedure

10.1 Background

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10.4 Procedure

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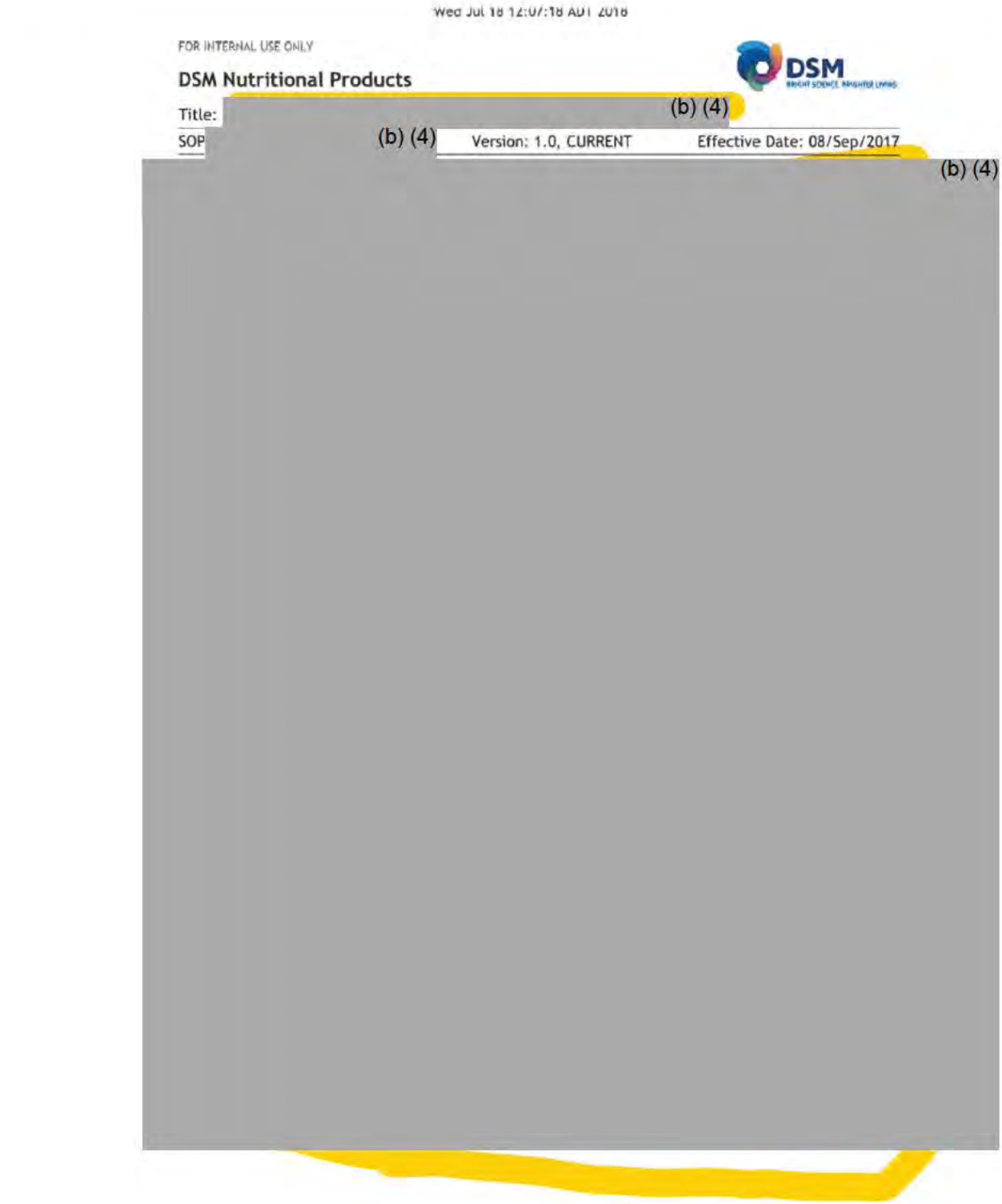
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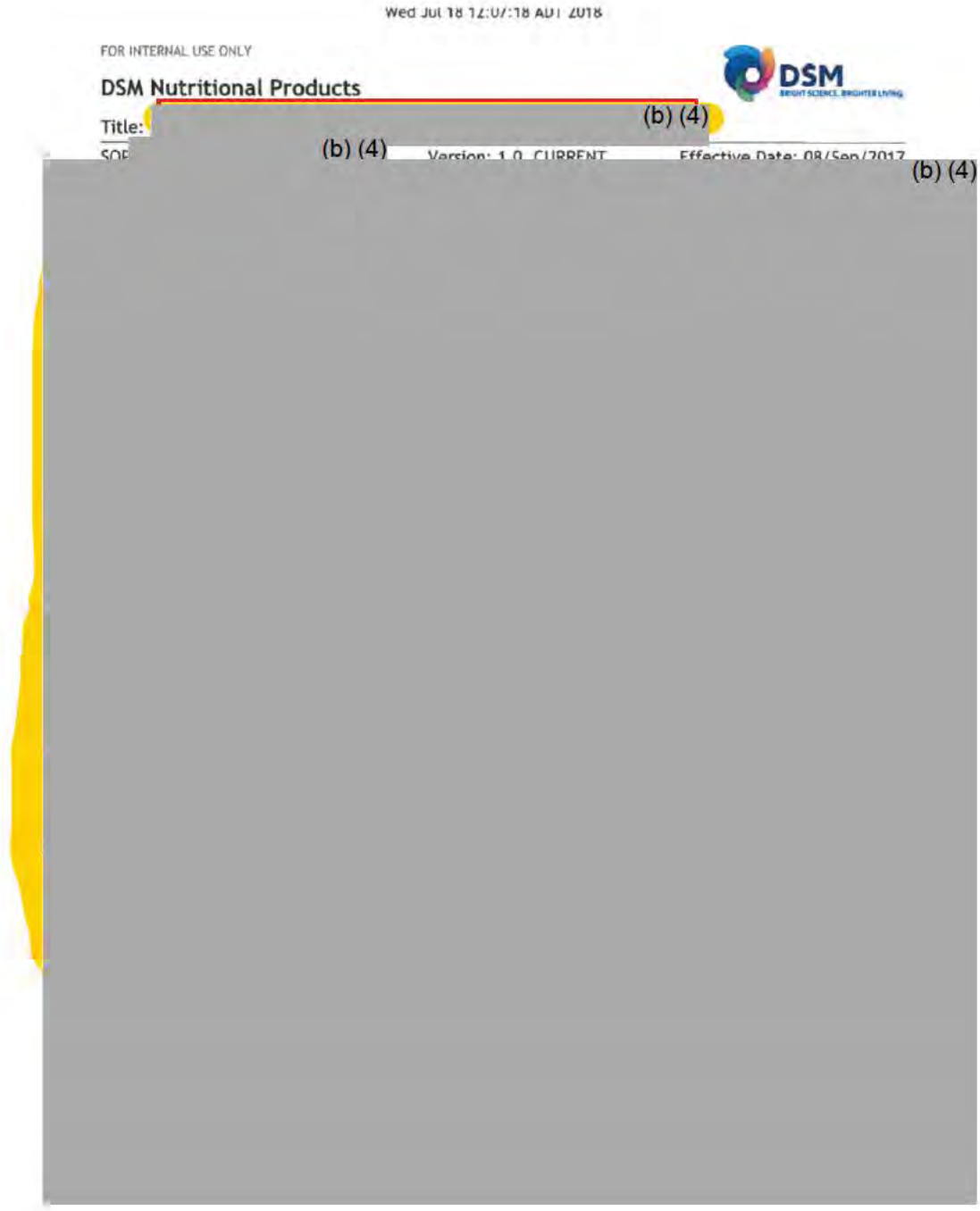
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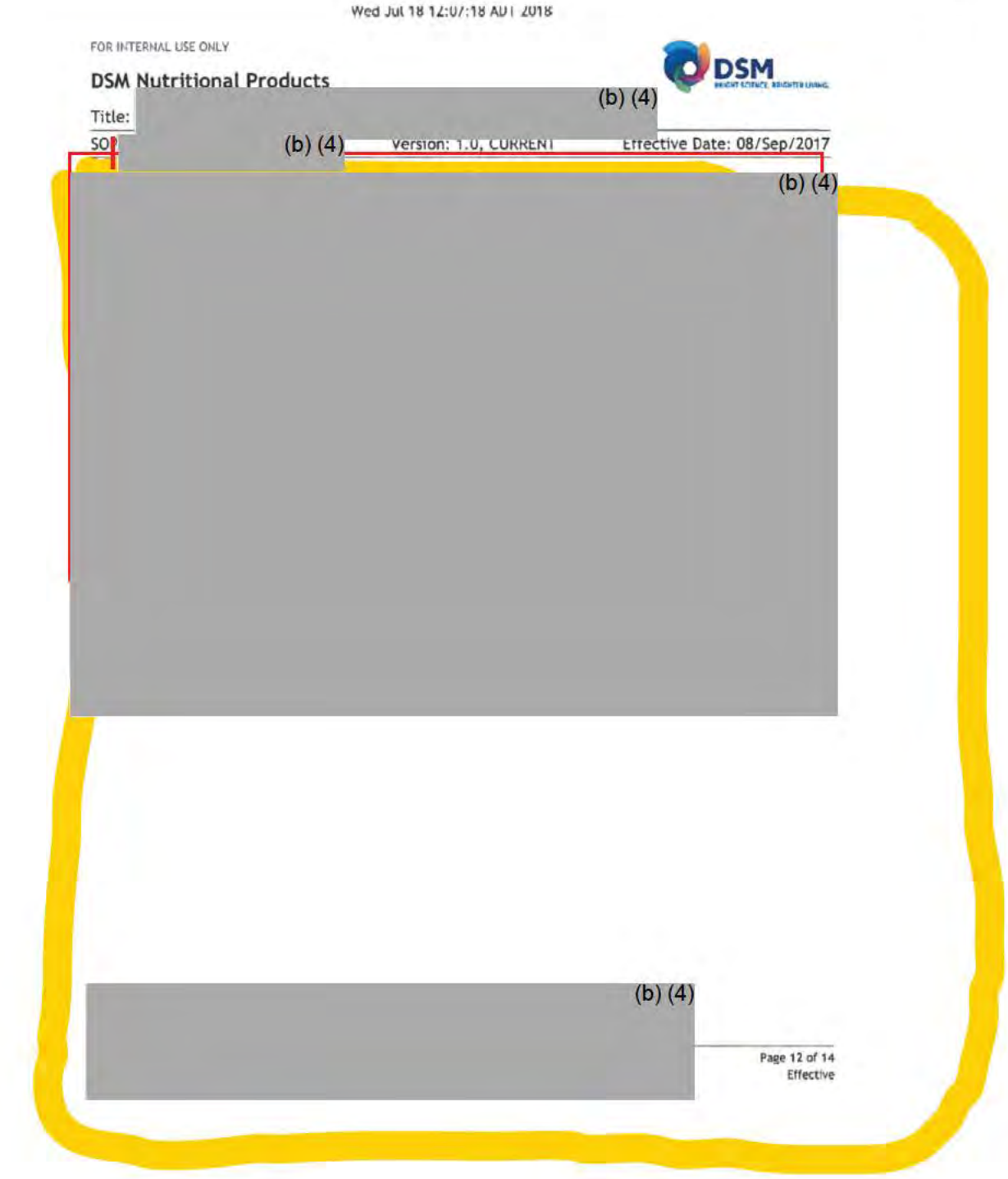
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Page 12 of 14
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Page 14 of 14
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9. SIGNATURES

Principal Investigator Approval

(b) (4), (b) (6)

09/28/2018
Date

10/03/2018
Date

Reviewer

APPENDIX NO. 3

EXPERIMENTAL DESIGN

(b) (4)

EXPERIMENTAL DESIGN

The test and reference items were administered as a diet as shown below:

Table 1: Study Design

Treatment Group [b]	Dosage Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F_0 Generation (dams)[@]	F_1 Generation (puppies) [a]	
					F	M(Spare)	F(Spare)
1. Control diet*	0	0	0.11%	0.12%	5	4(1)	4(1)
2. AOCED	½ X	0.75%	0.41%**	0.44%	5	4(1)	4(1)
3. AOCED	1X	1.5%	0.77% **	0.83%	5	4(1)	4(1)
4. AOCED	2X	3.0%	1.55%**	1.69%	5	4(1)	4(1)

* Group 1 animals received the control diet, which was formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA level (0.11%) have been achieved by using the chicken by-product meal as one of the ingredients.

** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content was the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA) and from the chicken by-product meal (0.11%). Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.

*** Calculated based on dry matter basis (adjusted for moisture content).

[a] Two puppies per litter (1 male and 1 female), randomly selected, the spare was randomly selected from any litter within each group.

[b] Since this study design include blinding to treatment groups, designations for individual animals was not revealed during the conduct of the study and only became available following the end of the data collection period and interpretation by the Study Director.

@ Six (6) females per group were mated, as an attempt to have at least 5 females per group confirmed pregnant at GD 28. Only confirmed pregnant females (up to a maximum of 5/group, randomly selected) were shipped to (b) (4)

M: male; F: female

APPENDIX NO. 4

(b) (4)

MEDICAL TREATMENT
F0 GENERATION / F1 GENERATION - PUPPY

The following footnotes have been used throughout the appendix.

*: Pupppies found dead Day 2 of Lactation

**: Puppies missing Day 63 of Gestation

APPENDIX NO. 4

(b) (4)

MEDICAL TREATMENT / SUPPORTIVE CARE

F0 GENERATION / F1 GENERATION - PUPPY

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TREATMENT	REASON FOR TREATMENT	STUDY GESTATION DAY
	DAMS			
2	(b) (4)	Cefazolin 334 mg/mL	Suspected Infection	61 and 62
		Solucal D 500 mg	Suspected Infection	61 and 62
		Baytril 50 mg/mL	Suspected Infection	61 and 62
		Ensure	Suspected Infection	61 and 62
		Buprenorphine 0.3 mg/mL	Suspected Infection	60 and 62
3		Iodine Solution 1%	Wound	42 to 46
		Clavamox 125 mg	Prophylactic Treatment	65 to 72
		Cefazolin 334 mg/mL	Suspected Fetus Retention	63
		Baytril 50 mg/mL	Suspected Fetus Retention	63
		Buprenorphine 0.3 mg/mL	Suspected Fetus Retention	0 (Lactation)
4		Lactated Ringer's and 5% Dextrose	Dehydration	56 to 58
		Baytril 50 mg/mL	Suspected GI Infection	56 to 58
		Clavamox 125 mg/tablet	Suspected GI Infection	56 to 58
		Ensure	Appetite Decrease	57
		Canned Food	Appetite Decrease	57
	PUPPY			
2	(b) (4)	Iodine Solution 1%	Wound	0 (Post Partum)

(b) (4)

APPENDICES
F0 GENERATION

APPENDIX NO. 5 (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - PRE-TREATMENT AND GESTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix

Only cage-side observations with abnormal findings are presented.

DCE: Detailed Clinical Examination

UNS: Unscheduled

AM: Ante Meridiem

PM: Post Meridiem

Severity Codes:

X=Present

1=Slight

2=Moderate

3=Severe

A=Absent

D=Decreased

©: See comment associated to Clinical Observation at the end of the appendix

P: Present

N: Not applicable

APPENDIX NO. 5

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY -8 DCE	-8 PM	-7 DCE	-7 PM	-6 AM	-6 DCE	-6 PM	-5 AM	-5 DCE	-5 PM	-4 AM	-4 DCE	-4 PM	-3 AM
1	[redacted]	No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	A	.	.	.	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Lump		.	.	N©	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	A	A	.	.	.	.	.	.	.	.	A
		No Abnormalities Detected		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	A	.	.	A	.
		Feces, Output		.	.	.	A	A	.	A	.	.	.	.	.	.	.
		Skin Lump	Forepaw Left	.	.	X	.	.	.	.	.	.	.	.	.	.	.
			Forepaw Right	.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY -3 PM	-2 AM	-2 PM	-1 AM	-1 DCE	-1 PM	0 AM	0 DCE	0 PM	1 AM	1 PM	2 AM	2 PM	3 AM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	X	.	.	.	.	.	.
		Feces, Output		A	.	.	A	.	.	A	.	.	A	A	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	A	.	A	.	.	.	.	A	.	.	.	A	.
		Lump		.	.	.	.	.	.	.	N©	.	.	.	.	.	.
		Feces, Output		.	A	.	A	.	.	.	.	.	A	A	A	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		A	.	.	.	.	.	A	.	.	.	A	.	.	.
		Feces, Output		.	.	A	.	.	A	A	.	A	.	A	.	A	.
		Skin Lump	Forepaw Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 5

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 3 PM	4 AM	4 PM	5 AM	5 PM	6 AM	6 PM	7 AM	7 DCE	7 PM	8 AM	8 PM	9 AM	9 PM
1	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	.	A	A	.	A	.	.	A	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	.	.	A	.	A	.	.	.	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	A	A	.	A	.	A	.	.	A	.	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		A	.	A	.	.	.	A	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	A	.	A	.	.	A	.	A	.	A
		Skin Lump	Forepaw Right	.	.	.	.	.	.	.	.	X	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 10 AM	10 PM	11 AM	11 PM	12 AM	12 PM	13 AM	13 PM	14 AM	14 DCE	14 PM	15 AM	15 PM	16 AM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	.	.	.	A	A	.	.	.	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces, Output		.	A	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		A	A	.	A	.	.	A	.	.	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	A	.	.	.	.	.	A	.
		Feces, Output		.	A	.	A	.	A	.	A	A	.	A	.	.	.
		Skin Lump	Forepaw Right	.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 PM	17 AM	17 PM	18 AM	18 PM	19 AM	19 PM	20 AM	20 PM	21 AM	21 DCE	21 PM	22 AM	22 PM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	.	A	.	A	.	A	.	A	.	.	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	A	A	.	A	.	A	.	.	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Liquid		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	A	.	A	.	A	.	A	.	.	A	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Liquid		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	.	.	.	A	.	.	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	.	A	.	A	.	A	.	A	.	.	A	.	A

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 23 AM	23 PM	24 AM	24 PM	25 AM	25 PM	26 AM	26 PM	27 AM	27 PM	28 AM	28 DCE	28 PM	29 AM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		A	A	.	A	A	A	.	A	A	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	A	.	.	.	A	.	A	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	A	.	.	.	A	.	A	.	A	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	A	.	.	.	A	.	A	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	A	.	A	.	A	.	A	.	A	.	.	A	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM	34 AM	34 UNS	34 PM	35 AM	35 DCE
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	.	A	A	A	.	.	.	A	A	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	A	.	.	A	.	A	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	A	.	A	A	.	.	.	.	A	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	A	.	A	.	.	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	.	A	.	A	.	A	.	A	.	.	A	A	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 35 PM	36 AM	36 UNS	36 PM	37 AM	37 PM	38 AM	38 PM	39 AM	39 PM	40 AM	40 UNS	41 AM	41 UNS
1	[redacted] (b) (4)	Feces Liquid		.	.	.	.	X	.	X	.	X	.	.	.	.	.
		Feces, Output		A	.	.	A	.	A	.	A	.	.	.	.	.	.
		Feces, Output		.	A	.	.	A	.	D	.	.	.	D	.	.	.
		Feces Liquid		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 41 PM	42 AM	42 DCE	42 PM	43 AM	43 PM	44 AM	45 AM	45 UNS	45 PM	46 PM	47 AM	47 PM	48 AM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	D	.	.	.	.	.	D
		Discharge, White	Vulva	.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	A	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 48 PM	49 AM	49 UNS	49 PM	50 AM	50 PM	51 AM	51 UNS	51 UNS 2	51 PM	52 AM	52 UNS	52 PM	53 AM
1	[redacted] (b) (4)	Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	.	A
		Feces Liquid		.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				53 UNS	53 PM	54 AM	54 UNS	54 UNS 2	54 PM	55 AM	55 UNS	55 PM	56 AM	56 UNS	56 PM	57 AM	57 UNS
1	[redacted] (b) (4)	Feces, Output		.	.	A	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 58 AM	58 PM	59 AM	59 UNS	59 PM	60 AM	60 UNS	60 PM	61 AM	61 PM	62 AM	62 UNS	62 UNS 2	62 PM
1	[redacted] (b) (4)	Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	X

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 63 AM	63 UNS	63 PM	64 AM	64 UNS	64 PM	65 AM	65 PM	66 AM	66 UNS	67 AM	67 UNS	68 UNS	69 UNS
1	[redacted] (b) (4)	Littered		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Material Liquid Green		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	X	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Littered		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 70 PM	DAY 72 UNS
1	[redacted] (b) (4)	Feces Loose		X	.
		Littered		.	X

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY -8 DCE	-8 PM	-7 DCE	-7 PM	-6 AM	-6 DCE	-6 PM	-5 AM	-5 DCE	-5 PM	-4 AM	-4 DCE	-4 PM	-3 AM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	A
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	A	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces, Output		.	A	.	.	.	.	.	.	.	A	A	.	.	A

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY -3 PM	-2 AM	-2 PM	-1 AM	-1 DCE	-1 PM	0 AM	0 DCE	0 PM	1 AM	1 PM	2 AM	2 PM	3 AM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	.	.	.	.	A	A	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		A	.	.	.	.	.	.	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	.	A	.	.	A	.	.	A	A	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	.	A	.	.	A	A	.	A	.	A	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	X	.	.	.	.	.	.
		Feces, Output		A	.	A	.	.	.	A	.	A	.	A	.	A	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 3 PM	4 AM	4 PM	5 AM	5 PM	6 AM	6 PM	7 AM	7 DCE	7 PM	8 AM	8 PM	9 AM	9 PM
2	[redacted] (b) (4)	o Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		eces Liquid		.	X	.	.	.	X	.	.	.	.	.	.	.	.
		eces, Output		.	.	A	A	.	.	.	.	.	.	.	A	.	A
		o Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		eces, Output		A	.	.	.	A	.	A	.	.	A	.	.	.	.
		o Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		eces Soft		.	.	.	X	.	X	.	.	.	.	.	.	.	.
		eces, Output		A	A	.	.	A	.	A	A	.	A	.	.	.	A
		o Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		eces, Output		.	.	A	.	A	.	A	.	.	A	.	A	.	A
		o Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		eces Liquid		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		eces, Output		.	.	A	.	A	.	A	.	.	.	.	.	.	A

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 10 AM	10 PM	11 AM	11 PM	12 AM	12 PM	13 AM	13 PM	14 AM	14 DCE	14 PM	15 AM	15 PM	16 AM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Liquid		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	A	.	A	.	.	.	.	.	.	A	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	A	.	.	.	A	.	.	.	.	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	X
		Feces Liquid		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	A	.	.	.	.	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	A	.	A	.	A	.	A	.	.	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	A	.	A	.	A	A	A	.	.	A	.	A	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 PM	17 AM	17 PM	18 AM	18 PM	19 AM	19 PM	20 AM	20 PM	21 AM	21 DCE	21 PM	22 AM	22 PM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	.	A	.	.	.	A	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Feces, Output		A	A	A	.	A	.	A	.	A	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	A	.	A	.	A	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	.	A	.	.	.	A	.	.	.	.	A	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		A	.	.	.	.	.	A	.	.	.	.	.	.	A

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 23 AM	23 PM	24 AM	24 PM	25 AM	25 PM	26 AM	26 PM	27 AM	27 PM	28 AM	28 DCE	28 PM	29 AM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	A	.	A	.	.	A	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		A	.	A	A	.	.	.	A	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	A	.	A	A	.	.	A	.	A	.	.	A	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	A	.	A	.	A	.	A	.	A	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	.	.	.	X	.	.	X	.	.	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	X	.	.	X
		Feces, Output		.	A	.	A	.	.	.	A	.	.	.	.	A	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM	34 AM	34 UNS	34 PM	35 AM	35 DCE
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces, Output		A	.	.	A	A	.	.	.	A	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	A	.	.	A	A	.	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	X	.	.	.	X	.	X	.	.	.	.
		Feces, Output		A	.	A	.	.	.	A	.	A	.	.	A	.	.
		Circling		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		A	.	.	.	A	.	A	.	A	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		.	X	.	.	.	X	.	.	.	X	.	.	.	.
		Feces, Output		A	.	A	.	A	.	A	.	A	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 35 PM	36 AM	36 UNS	36 PM	37 AM	37 PM	38 AM	38 PM	39 AM	39 PM	40 AM	40 UNS	41 AM	41 UNS
2	[redacted] (b) (4)	Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	X	.	X	X	.	X	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	A	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	.	A	A	.	A	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	.	.	A	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Material Mucoid Brown		.	.	.	.	.	.	.	.	.	.	.	1	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 41 PM	42 AM	42 DCE	42 PM	43 AM	43 PM	44 AM	45 AM	45 UNS	45 PM	46 PM	47 AM	47 PM	48 AM
2	[redacted] (b) (4)	ischarge, Clear	Eye Left	.	.	1	.	.	.	.	.	.	.	.	.	.	.
			Eye Right	.	.	1	.	.	.	.	.	.	.	.	.	.	.
		welling Soft	Vulva	.	.	1	.	.	.	.	.	.	.	.	.	.	.
		o Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		o Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		eces Soft		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		eces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		o Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		eces, Output		.	.	.	.	.	.	.	.	.	.	.	.	.	D
		o Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		eces Soft		.	.	.	.	.	X	.	.	.	.	.	.	X	X

631 of 1567

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 48 PM	49 AM	49 UNS	49 PM	50 AM	50 PM	51 AM	51 UNS	51 UNS 2	51 PM	52 AM	52 UNS	52 PM	53 AM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Material Mucoid Yellow		.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Sclera Red	Left	.	.	.	.	.	X	.	.	.	.	.	.	.	.
			Right	.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Liquid		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Material Liquid Red		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Material Liquid Yellow		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Material Mucoid Red		.	.	.	.	.	.	.	.	1	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 53 UNS	53 PM	54 AM	54 UNS	54 UNS 2	54 PM	55 AM	55 UNS	55 PM	56 AM	56 UNS	56 PM	57 AM	57 UNS
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Material Liquid Yellow		1	.	.	.	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Brown		2	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 58 AM	58 PM	59 AM	59 UNS	59 PM	60 AM	60 UNS	60 PM	61 AM	61 PM	62 AM	62 UNS	62 UNS 2	62 PM
2	[redacted] (b) (4)	Feces Loose		.	X	.	.	.	.	.	X	.	.	.	.	.	X
		Feces Loose		.	.	.	.	.	.	.	.	.	X	X	.	.	.
		Feces Soft		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Brown		.	.	.	.	.	.	.	.	.	.	.	.	.	1
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Littered		.	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 63 AM	63 UNS	63 PM	64 AM	64 UNS	64 PM	65 AM	65 PM	66 AM	66 UNS	67 AM	67 UNS	68 UNS	69 UNS
2	[redacted] (b) (4)	Littered		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	X	X	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		.	.	.	.	.	.	X	X	.	.	.	.	.	.
		Material Mucoid Brown		.	.	.	.	.	.	.	.	1	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		.	.	X	.	.	.	.	.	X	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	.	.	X

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY -8 DCE	-8 PM	-7 DCE	-7 PM	-6 AM	-6 DCE	-6 PM	-5 AM	-5 DCE	-5 PM	-4 AM	-4 DCE	-4 PM	-3 AM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	X	.	X	X
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	A	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	A

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY -3 PM	-2 AM	-2 PM	-1 AM	-1 DCE	-1 PM	0 AM	0 DCE	0 PM	1 AM	1 PM	2 AM	2 PM	3 AM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		A	.	A	.	.	.	.	.	.	.	A	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		A	.	.	.	.	A	A	.	.	.	A	.	A	A
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	A	A	.	.	A	A	.	.	.	A	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	A	.	A	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		.	A	A	.	.	A	.	.	A	.	A	A	.	.

637 of 1567

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 3 PM	4 AM	4 PM	5 AM	5 PM	6 AM	6 PM	7 AM	7 DCE	7 PM	8 AM	8 PM	9 AM	9 PM
3	[redacted] (b) (4)	Feces, Output		A	.	.	.	A	A	.	.	.	A	.	A	.	A
		Broken Nail/Claw	Forepaw Left	.	.	.	.	.	.	.	.	X	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	A	.	.	.	.	.	.	A	A	A	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Liquid		.	.	X	.	.	X	X	.	.	.	X	.	X	.
		Feces, Output		.	.	.	.	A	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	A	.	.	.	A	.	.	.	.	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		A	.	A	.	A	.	A	.	.	A	.	A	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 10 AM	10 PM	11 AM	11 PM	12 AM	12 PM	13 AM	13 PM	14 AM	14 DCE	14 PM	15 AM	15 PM	16 AM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	.	.	.	A	.	A	.	.	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	A	A	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	A	.	.	.	A	.	A	A	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	.	.	.	.	A	A	A	.	.	A	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	A	.	.	.	.	.	.	.	A	.	.	.

APPENDIX NO. 5

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 PM	17 AM	17 PM	18 AM	18 PM	19 AM	19 PM	20 AM	20 PM	21 AM	21 DCE	21 PM	22 AM	22 PM
3		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	A	A	.	A	.	A	.	A	.	.	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	.	.	A	.	.	.	.	A	A	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	X	.
		Feces Liquid		.	.	.	X	.	X	.	X	.	.	.	.	.	.
		Feces, Output		.	.	.	.	A	.	A	.	.	.	.	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	.	A	.	A	.	A	.	.	.	.	A	.	A
	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	A	A	.	.	.	A	.	A	.	.	.	.	A

640 of 1567

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 23 AM	23 PM	24 AM	24 PM	25 AM	25 PM	26 AM	26 PM	27 AM	27 PM	28 AM	28 DCE	28 PM	29 AM
3	[redacted]	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	A	.	A	.	A	.	A	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		A	A	.	A	.	.	.	A	.	.	.	.	A	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		.	.	.	.	.	X	.	.	.	.	X	.	.	.
		Feces, Output		.	A	.	A	.	.	.	A	.	A	.	.	A	.
		Feces, Output		.	A	A	A	A	.	A	A	.	A	A	.	A	.
		Skin Lump	Vulva	.	.	.	.	.	.	.	.	.	.	.	X	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	A	.	.	A	.	.	A	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM	34 AM	34 UNS	34 PM	35 AM	35 DCE
3	[redacted]	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		A	.	A	.	A	.	.	.	A	A	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	.	A	.	A	A	A	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		X	.	X	X	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	.	.	A	.	A	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	.	A	.	.	A	A	.	.	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		.	.	.	.	.	.	.	.	X	X	.	.	.	.
		Feces, Output		.	.	A	.	A	A	.	.	.	.	.	A	.	.

[redacted] (b) (4)

642 of 1567

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 35 PM	36 AM	36 UNS	36 PM	37 AM	37 PM	38 AM	38 PM	39 AM	39 PM	40 AM	40 UNS	41 AM	41 UNS
3	[redacted] (b) (4)	Feces, Output		A	.	.	A	.	A	.	.	A	.	.	.	.	.
		Skin Wound with Discharge	Hindpaw Left	.	.	.	.	.	.	.	.	.	.	.	.	.	2
		Feces, Output		.	.	.	A	.	.	A	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	X	.	.	.	.
		Feces Liquid		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	A	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	X	.	.	X	X	X	.	X	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	A	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 41 PM	42 AM	42 DCE	42 PM	43 AM	43 PM	44 AM	45 AM	45 UNS	45 PM	46 PM	47 AM	47 PM	48 AM
3	[redacted] (b) (4)	Fur Thin	Hindpaw Left	.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Right	.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Swelling Soft	Vulva	.	.	1	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	X	.	.	.
		Material Mucoid Brown		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	D	.	.
		Material Mucoid Clear		.	.	.	.	.	.	.	.	.	1	.	.	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Dry Red		.	.	.	.	.	.	.	.	1	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 48 PM	49 AM	49 UNS	49 PM	50 AM	50 PM	51 AM	51 UNS	51 UNS 2	51 PM	52 AM	52 UNS	52 PM	53 AM
3	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	X	.	.	.	.	X	.	.
		Feces Loose		.	X	.	.	X	.	.	.	.	X	.	.	.	X
		Material Mucoid Red		.	.	.	.	.	.	.	.	.	.	.	2	.	.
		Material Mucoid Yellow		.	.	.	.	.	.	.	.	.	.	.	1	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	D	.	.	D

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 53 UNS	53 PM	54 AM	54 UNS	54 UNS 2	54 PM	55 AM	55 UNS	55 PM	56 AM	56 UNS	56 PM	57 AM	57 UNS
3	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	X	.
		Feces, Output		.	.	.	.	.	.	.	.	.	A	.	.	.	.
		Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 58 AM	58 PM	59 AM	59 UNS	59 PM	60 AM	60 UNS	60 PM	61 AM	61 PM	62 AM	62 UNS	62 UNS 2	62 PM
3	[redacted] (b) (4)	Feces, Output		.	.	.	.	.	.	.	.	A	.	.	.	.	.
		Feces Loose		.	X	X	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	X	X	.	.	.	.	.	X	X	.	.	.	.
		Material Liquid Green		.	.	.	.	.	.	.	.	.	.	.	.	.	I
		Material Mucoid Brown		.	.	.	I	.	.	.	.	.	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 63 AM	63 UNS	63 PM	64 AM	64 UNS	64 PM	65 AM	65 PM	66 AM	66 UNS	67 AM	67 UNS	68 UNS	69 UNS
3	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Material Frothy Yellow		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		X	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Brown		.	.	.	.	.	.	.	.	1	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Littered		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Littered		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				-8 DCE	-8 PM	-7 DCE	-7 PM	-6 AM	-6 DCE	-6 PM	-5 AM	-5 DCE	-5 PM	-4 AM	-4 DCE	-4 PM	-3 AM
4	[redacted] (b) (4)	Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	.
		Skin Lump	Forepaw Right	.	.	.	.	.	.	.	.	.	.	.	X	.	.
		No Abnormalities Detected		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	.	.	.	.	.	A	.	.	.	.	.	A	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	A	.	.	.	.	.	A	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	A	.	.	A
		No Abnormalities Detected		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	A	.	.	.	.	A	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY -3 PM	-2 AM	-2 PM	-1 AM	-1 DCE	-1 PM	0 AM	0 DCE	0 PM	1 AM	1 PM	2 AM	2 PM	3 AM
4	[redacted] (b) (4)	Lump		.	.	.	.	.	.	.	N©	.	.	.	.	.	.
		Feces, Output		.	.	A	.	.	.	.	.	A	A	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		.	.	A	.	.	A	A	.	.	A	A	A	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	.	.	A	A	.	.	.	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		.	A	.	A	.	A	A	.	A	.	A	.	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	X	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		A	.	.	.	.	A	A	.	A	A	.	.	.	.

650 of 1567

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 3 PM	4 AM	4 PM	5 AM	5 PM	6 AM	6 PM	7 AM	7 DCE	7 PM	8 AM	8 PM	9 AM	9 PM
4	[redacted]	Lump		.	.	.	.	.	.	.	.	N©	.	.	.	.	.
		Feces, Output		A	.	.	.	.	.	A	.	.	A	.	A	.	.
		Feces, Output		A	A	A	.	A	.	A	.	.	A	.	.	.	.
		Material Frothy Clear		.	.	.	.	.	.	.	.	I	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	A	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	A	A	A	A	.	.	.	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Liquid		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	.	A	.	A	.	.	A	.	.	.	A

(b) (4)

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 10 AM	10 PM	11 AM	11 PM	12 AM	12 PM	13 AM	13 PM	14 AM	14 DCE	14 PM	15 AM	15 PM	16 AM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	A	.	.	.	.	A	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	.	.	.	A	A	A	.	.	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	A	.	.	.	.	.	.	A	.	A	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		A	.	A	.	.	A	.	.	.	.	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces, Output		.	A	A	A	.	A	.	A	.	.	A	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 PM	17 AM	17 PM	18 AM	18 PM	19 AM	19 PM	20 AM	20 PM	21 AM	21 DCE	21 PM	22 AM	22 PM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	A	.	.	A	.	A	.	A	A	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	.	A	.	A	.	A	.	A	.	.	A	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	.	A	.	A	.	A	.	A	.	.	A	.	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		A	.	.	A	.	.	.	.	.	.	.	A	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces, Output		.	.	A	.	A	.	A	.	A	.	.	A	A	A

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 23 AM	23 PM	24 AM	24 PM	25 AM	25 PM	26 AM	26 PM	27 AM	27 PM	28 AM	28 DCE	28 PM	29 AM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		A	.	A	A	.	A	.	A	A	.	A	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	A	.	A	.	.	.	.	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	A	.	A	.	A	.	A	.	A	.	.	A	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	A	A	A	.	.	.	.	A	A	.	.	A	A
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	X	.	.	X
		Feces, Output		.	A	.	A	.	A	.	A	.	A	.	.	A	.

APPENDIX NO. 5

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM	34 AM	34 UNS	34 PM	35 AM	35 DCE
4		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		.	.	.	.	.	.	.	.	.	X	.	.	X	.
		Feces, Output		.	A	.	A	A	A	A	.	A	.	.	A	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		A	.	.	.	A	.	.	.	A	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		A	.	.	.	A	.	.	.	A	.	.	A	.	.
		Feces, Output		.	A	A	.	A	A	A	.	A	A	.	.	.	.
	(b) (4)	Feces Liquid		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces, Output		A	A	A	.	A	.	A	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 35 PM	36 AM	36 UNS	36 PM	37 AM	37 PM	38 AM	38 PM	39 AM	39 PM	40 AM	40 UNS	41 AM	41 UNS
4	[redacted] (b) (4)	Feces Liquid		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		A	A	.	A	.	A	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Feces, Output		A	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	A	A	D	.	D	.	A	.
		Feces, Output		.	.	.	.	A	.	D	.	.	.	.	.	A	.
		Material Mucoid Brown		.	.	1	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 41 PM	42 AM	42 DCE	42 PM	43 AM	43 PM	44 AM	45 AM	45 UNS	45 PM	46 PM	47 AM	47 PM	48 AM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	X	X	.	.	X	.	X	.	.	.
		Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	D	.	.	.	.	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	D	.	.	D	.	D	.	.	.	.	.	.	A
		No Abnormalities Detected		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	D	.	.	A	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 48 PM	49 AM	49 UNS	49 PM	50 AM	50 PM	51 AM	51 UNS	51 UNS 2	51 PM	52 AM	52 UNS	52 PM	53 AM
4	(b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	X
		Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	A	.	.	.
		Material Liquid Red		.	.	.	.	.	.	.	.	.	I	.	.	.	.
		Feces, Output		.	.	.	.	D	.	A	.	.	.	.	.	.	.
		Feces, Output		D	.	.	.	D	.	A	.	.	.	.	.	.	A
		Feces, Output		.	D	.	.	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Brown		.	.	.	.	.	.	.	.	.	.	I	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 53 UNS	53 PM	54 AM	54 UNS	54 UNS 2	54 PM	55 AM	55 UNS	55 PM	56 AM	56 UNS	56 PM	57 AM	57 UNS
4	[redacted] (b) (4)	Circling		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Retching		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Discharge, Brown	Vulva	.	.	.	.	1	1	.	.	.	.	.	.	.	.
		Discharge, Green	Vulva	.	.	.	.	.	.	.	.	.	.	.	1	.	.
		Discharge, Red	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Sclera Red	Left	.	.	.	.	.	X	.	.	.	.	.	.	.	.
			Right	.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Black		X	.	X	.	.	.	X	.	X	X	.	.	.	X
		Feces Loose		X	.	X	.	.	.	X	.	X	.	.	.	.	X
		Feces Liquid		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	.
		Material Dry Black		1	.	.	.	.	.	.	.	.	.	.	.	.	.
		Material Dry Green		1	.	1	.	.	.	.	.	.	.	.	.	.	.
		Material Dry Red		.	.	.	.	.	.	1	.	.	.	.	.	.	.
		Material Liquid Black		.	.	.	.	.	.	.	.	.	.	2	.	.	.
		Material Liquid Brown		.	.	.	.	1	1	.	.	.	.	.	.	.	.
		Material Liquid Clear		.	.	.	.	.	.	.	.	.	.	1	.	.	.
		Material Liquid Green		.	.	.	.	.	.	.	.	.	2	2	.	.	.
		Material Liquid Red		.	.	.	1	.	1	.	.	.	.	.	.	.	.
		Activity Decreased		.	.	.	.	.	.	.	.	.	.	2	.	.	.
		Tremors		.	.	.	.	.	.	.	.	.	.	2	.	.	.
		Capillary refill time		.	.	.	.	.	.	.	.	.	.	3	.	.	.
		Skin Pallor		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	X	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.

[redacted] (b) (4)

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				53 UNS	53 PM	54 AM	54 UNS	54 UNS 2	54 PM	55 AM	55 UNS	55 PM	56 AM	56 UNS	56 PM	57 AM	57 UNS
4	[redacted] (b) (4)	Feces, Output		.	.	.	.	.	.	D	.	.	.	.	.	A	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces, Output		.	.	A	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 58 AM	58 PM	59 AM	59 UNS	59 PM	60 AM	60 UNS	60 PM	61 AM	61 PM	62 AM	62 UNS	62 UNS 2	62 PM
4	[redacted] (b) (4)	Feces Black		X	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Green		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	A	.	.	A	.	.	.	.	.
		Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Littered		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces, Output		A	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Red		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Material Mucoid Brown		.	.	.	.	.	.	.	.	.	.	.	.	.	1

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 63 AM	63 UNS	63 PM	64 AM	64 UNS	64 PM	65 AM	65 PM	66 AM	66 UNS	67 AM	67 UNS	68 UNS	69 UNS
4	[redacted] (b) (4)	Feces Black		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	D	.	.	.	.	.	.	.	.	.	.
		Littered		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Littered		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Littered		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	STUDY DAY	TIME SLOT	CLINICAL SIGN	COMMENT
1	[redacted] (b) (4)	-7	DCE	Lump	Other: Lump Interdigital cyst, Location not recorded
		0	DCE	Lump	Other: Lump Interdigitial cyst, Location not recorded
4		0	DCE	Lump	Other: Lump Interdigital cyst, Location Not recorded
		7	DCE	Lump	Other: Lump Interdigital cyst, location not recorded

APPENDIX NO. 5

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

					Day numbers relative to Start Date						
Group	Sex	Animal	Clinical Sign	Site	35 DCE	42 DCE	60	62	63 Unscheduled	64	64 Unscheduled
1	f	(b) (4)	Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	P	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	P	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	P	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	P	.	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	X
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

					Day numbers relative to Start Date					
Group	Sex	Animal	Clinical Sign	Site	65 Unscheduled	66 Unscheduled	67 Unscheduled	68 Unscheduled	69 Unscheduled	72 Unscheduled
1	f	[redacted] (b) (4)	Released		.	X	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	X
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	X	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	X	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	35 DCE	42 DCE	60	62	63 Unscheduled	64	64 Unscheduled
2		[redacted] (b) (4)	Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	X	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.

APPENDIX NO. 5

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

					Day numbers relative to Start Date					
Group	Sex	Animal	Clinical Sign	Site	65 Unscheduled	66 Unscheduled	67 Unscheduled	68 Unscheduled	69 Unscheduled	72 Unscheduled
2	f	(b) (4)	Released		X	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	X	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	X	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	X	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.

APPENDIX NO. 5

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

					Day numbers relative to Start Date						
Group	Sex	Animal	Clinical Sign	Site	35 DCE	42 DCE	60	62	63 Unscheduled	64	64 Unscheduled
3	f	[redacted]	Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	X
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	X	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	X	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

					Day numbers relative to Start Date					
					65	66	67	68	69	72
Group	Sex	Animal	Clinical Sign	Site	Unscheduled	Unscheduled	Unscheduled	Unscheduled	Unscheduled	Unscheduled
3	f	[redacted] (b) (4)	Released		.	.	X	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	X	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	35 DCE	42 DCE	60	62	63 Unscheduled	64	64 Unscheduled
4	f	[redacted] (b) (4)	Released		.	.	.	.	X	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	X	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	X	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.
			Released		.	.	.	.	.	.	X
			Direct Pupillary Reflex	Left	.	P	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	P	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	P	.	.	.	.	.

APPENDIX NO. 5

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
VETERINARY EXAM
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

					Day numbers relative to Start Date					
Group	Sex	Animal	Clinical Sign	Site	65 Unscheduled	66 Unscheduled	67 Unscheduled	68 Unscheduled	69 Unscheduled	72 Unscheduled
4	f	[redacted] (b) (4)	Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	X	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.
			Released		.	.	.	.	.	.
			Direct Pupillary Reflex	Left	.	.	.	.	.	.
			Direct Pupillary Reflex	Right	.	.	.	.	.	.
			Consensual Pupillary Reflex	Left	.	.	.	.	.	.
			Consensual Pupillary Reflex	Right	.	.	.	.	.	.

APPENDIX NO. 6

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix

Only cage-side observations with abnormal findings are presented.

DCE: Detailed Clinical Examination

UNS: Unscheduled

AM: Ante Meridiem

PM: Post Meridiem

Rx: Dose

Severity Codes:

X=Present

1=Slight

2=Moderate

A=Absent

D=Decreased

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 0 AM	0 DCE	0 UNS 2	0 UNS 3	0 UNS 4	1 AM	1 UNS	1 UNS 2	1 UNS 3	1 PM	2 AM	2 DCE	3 AM	3 PM
1	[redacted]	Discharge, Red	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	1	.	.	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Fur Stained Brown	Hindlimb Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindlimb Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindpaw Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindpaw Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Tail	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	A	.	.	.
		Discharge, Red	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	D	.
		Material Dry Red		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Swelling Soft	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Fur Stained Brown	Hindpaw Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindpaw Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Tail	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	X	.	.	.
	[redacted] (b) (4)	No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	D	.	.	.	.	.	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 4 AM	4 PM	5 AM	5 DCE	6 PM	7 AM	7 PM	8 AM	11 AM	12 UNS	13 AM	14 AM	15 AM	16 AM
1	[redacted] (b) (4)	Feces, Output		.	.	.	.	.	A	.	.	.	.	.	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Dry Red		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces, Output		D	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 UNS	17 UNS	18 AM	19 AM	20 AM	21 AM	21 PM	22 AM	22 UNS	23 AM	23 PM	24 AM	25 AM	26 AM
1	[redacted] (b) (4)	Feces Soft		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Material Liquid Red		.	.	.	.	.	.	.	.	.	.	.	1	.	.

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 26 PM	27 AM	28 AM	28 DCE	29 AM	29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM
1		No Abnormalities Detected		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Hindlimb Left	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Hindlimb Right	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Brown		.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Feces Loose		.	X	X	.	.	.	.	.	X	.	X	.	.	X
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Lower Jaw	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Mouth	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Pinna Left	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Pinna Right	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Swelling Soft	Lower Jaw	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Skin Wound with Discharge	Lower Jaw	.	.	.	1	.	.	.	.	.	.	.	.	.	.
	(b) (4)	Material Dry Red		.	.	.	.	.	.	.	.	.	.	.	1	.	.
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 34 PM	35 AM	35 PM	36 AM	36 PM	38 AM	38 PM	39 AM	39 PM	40 AM	44 PM	45 AM	47 AM	52 PM
1	(b) (4)	Feces Yellow		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 55 UNS	DAY 56 DCE
1	[redacted] (b) (4)	Material Mucoid Brown		1	.
		Skin Red	Abdominal	.	X
		Skin Red	Abdominal	.	X
		No Abnormalities Detected		.	X
		Skin Red	Abdominal	.	X
			Pinna Left	.	X
			Pinna Right	.	X
		Discharge, Brown	Ear Canal Left	.	1
			Ear Canal Right	.	1
		Discharge, Red	Vulva	.	1
		Skin Red	Abdominal	.	X

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 0 AM	0 DCE	0 UNS 2	0 UNS 3	0 UNS 4	1 AM	1 UNS	1 UNS 2	1 UNS 3	1 PM	2 AM	2 DCE	3 AM	3 PM
2	[redacted] (b) (4)	Fur Dull	Hindlimb Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindlimb Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Urogenital	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Fur Stained Brown	Hindpaw Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindpaw Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	D	.	.	.	.	.	.	.	.
		Thin		.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Skin Red	Abdominal	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Material Dry Red		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Swelling Soft	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	.	2	2	2	.	.	.	2	2	.	2	.	.
		Discharge, Yellow	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Eye Conjunctiva Red	Left	.	X	X	X	.	.	.	.	X	X	.	X	.	.
			Right	.	X	X	X	.	.	.	.	X	X	.	X	.	.
		Fur Dull	Tail	.	.	.	X	.	.	.	.	X	X	.	X	.	.
			Urogenital	.	X	X	X	.	.	.	.	X	X	.	X	.	.
		Fur Loss		.	1	1	1	.	.	.	.	1	1	.	1	.	.
		Fur Stained Red	Forepaw Left	.	.	.	.	.	.	.	.	.	.	.	X	.	.
			Forepaw Right	.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Liquid		.	.	.	.	X	X	.	.	.	.	.	.	.	.

APPENDIX NO. 6

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 0 AM	0 DCE	0 UNS 2	0 UNS 3	0 UNS 4	1 AM	1 UNS	1 UNS 2	1 UNS 3	1 PM	2 AM	2 DCE	3 AM	3 PM
2	[redacted]	Material Liquid Red		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Material Vomitus Brown	During Rx	.	.	.	.	.	.	.	.	.	.	.	1	.	.
		Activity Decreased		.	.	.	1	.	.	.	.	1	1	.	.	.	.
		Tremors		.	.	1	1	.	.	.	.	2	2	.	.	.	.
		Warm to Touch		.	.	X	X	.	.	.	.	X	X	.	.	.	.
		Weak		.	.	.	1	.	.	.	.	1	1	.	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 UNS	17 UNS	18 AM	19 AM	20 AM	21 AM	21 PM	22 AM	22 UNS	23 AM	23 PM	24 AM	25 AM	26 AM
2	[redacted] (b) (4)	Feces Soft		.	.	.	.	X	.	.	.	.	.	.	X	.	X
		Feces, Output		.	.	.	.	.	.	.	A	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	A	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.

681 of 1567

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 26 PM	27 AM	28 AM	28 DCE	29 AM	29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM
2	[redacted] (b) (4)	Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	X	.
		Backbone Prominent		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Thin		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Skin Red	Vulva	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	X	X	X	X
		Thin		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Teeth Broken		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Tremors		.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Skin Red	Abdominal	.	.	.	.	.	.	.	.	.	X	.	.	.	.
			Tail	.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 34 PM	35 AM	35 PM	36 AM	36 PM	38 AM	38 PM	39 AM	39 PM	40 AM	44 PM	45 AM	47 AM	52 PM
2	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 55 UNS	DAY 56 DCE
2	(b) (4)	Thin		.	1
		No Abnormalities Detected		.	X
		Skin Red	Abdominal	.	X
		Teeth Broken		.	X
		Skin Red	Abdominal	.	X

(b) (4)

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 0 AM	0 DCE	0 UNS 2	0 UNS 3	0 UNS 4	1 AM	1 UNS	1 UNS 2	1 UNS 3	1 PM	2 AM	2 DCE	3 AM	3 PM
3	(b) (4)	Skin Red	Vulva	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		D	.	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Vulva	.	1	.	.	.	.	.	.	.	.	1	.	.	.
		Fur Stained Brown	Forepaw Left	.	X	.	.	.	.	.	.	.	.	X	.	.	.
			Forepaw Right	.	X	.	.	.	.	.	.	.	.	X	.	.	.
			Hindpaw Left	.	X	.	.	.	.	.	.	.	.	X	.	.	.
			Hindpaw Right	.	X	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces, Output		.	.	.	.	.	D	.	.	.	.	.	.	.	.
		Tremors		.	.	.	.	.	.	1	.	.	.	1	.	.	.
		Skin Red	Abdominal	.	X	.	.	.	.	.	.	.	.	X	.	.	.
		Fur Stained Red	Hindlimb Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindlimb Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Tail	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	D	.	.	.
		Thin		.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Fur Stained Green	Hindlimb Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindlimb Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Urogenital	.	X	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 4 AM	4 PM	5 AM	5 DCE	6 PM	7 AM	7 PM	8 AM	11 AM	12 UNS	13 AM	14 AM	15 AM	16 AM
3	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Discharge, Brown	Ear Canal Left	.	.	.	1	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Feces Loose		X	X	.	.	.	.	.	.	.	.	.	.	.	X
		Material Liquid Red		.	.	.	.	.	1	1	1	.	.	.	.	.	1
		Backbone Prominent		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Thin		.	.	.	.	.	.	.	.	.	2	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 UNS	17 UNS	18 AM	19 AM	20 AM	21 AM	21 PM	22 AM	22 UNS	23 AM	23 PM	24 AM	25 AM	26 AM
3	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Material Dry Red		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	X	.	X	.	X	.	.	X	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	X
		Material Mucoid Red		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Yellow		.	.	.	.	.	.	.	.	.	.	.	.	1	.
		Material Liquid Red		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	.	.	.	.	A	.	.	.	A	.	.	.	.

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 26 PM	27 AM	28 AM	28 DCE	29 AM	29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM
3		Material Dry Red		.	.	.	.	1	.	.	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	X	X	.	X	X	.	.	.	.	X	X	X	.
		Thin		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	2	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	2	.	.	.	.	.	.	.	.	.	.
		Discharge, Clear	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Fur Thin	Cervical Ventral	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Thin		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Skin Dry	Cervical Ventral	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Cervical Ventral	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Swelling Soft	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	X	.	.	.	.	.	.	.	.	.	.
	(b) (4)	Feces Soft		.	.	.	.	X	.	.	.	.	.	.	.	.	.
	(4)	Feces Loose		X	X	X	.	.	.	X	.	.	.	X	X	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 34 PM	35 AM	35 PM	36 AM	36 PM	38 AM	38 PM	39 AM	39 PM	40 AM	44 PM	45 AM	47 AM	52 PM
3	[redacted] (b) (4)	Feces Soft		.	.	.	X	.	.	X	.	.	.	.	.	.	.
		Material Dry Red		1	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose		.	X	.	X	X	.	X	.	.	.	.	X	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 55 UNS	DAY 56 DCE
3	[redacted] (b) (4)	Skin Red	Abdominal	.	X
			Pinna Right	.	X
		Skin Red	Abdominal	.	X
		Discharge, Brown	Ear Canal Left	.	1
			Ear Canal Right	.	1
		Skin Red	Abdominal	.	X
		Swelling Soft	Vulva	.	1
		Skin, Brown	Abdominal	.	X
		Skin Red	Abdominal	.	X

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 0 AM	0 DCE	0 UNS 2	0 UNS 3	0 UNS 4	1 AM	1 UNS	1 UNS 2	1 UNS 3	1 PM	2 AM	2 DCE	3 AM	3 PM
4		Discharge, Brown	Ear Canal Right	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Fur Loss		.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	X	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	X	.	.	.
		Tremors		.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	1	.	.	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Fur Dull	Hindlimb Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Hindlimb Right	.	X	.	.	.	.	.	.	.	.	.	.	.	.
			Tail	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Fur Stained Brown	Hindlimb Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Material Dry Red		.	.	.	.	.	.	.	.	.	.	1	.	.	.
	(b) (4)	Discharge, Red	Vulva	.	1	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 4 AM	4 PM	5 AM	5 DCE	6 PM	7 AM	7 PM	8 AM	11 AM	12 UNS	13 AM	14 AM	15 AM	16 AM
4		Feces Loose		.	X	.	.	X	X	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	D	.
		Feces, Output		.	.	D	.	.	.	.	.	.	.	.	.	.	.
	(b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces, Output		.	.	.	.	.	A	.	A	.	.	.	.	.	.
		Material Dry Red		1	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 6

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 16 UNS	17 UNS	18 AM	19 AM	20 AM	21 AM	21 PM	22 AM	22 UNS	23 AM	23 PM	24 AM	25 AM	26 AM
4	(b) (4)	Feces Soft		.	X	.	.	X	.	.	.	X	X	.	.	.	.
		Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.

693 of 1567

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 26 PM	27 AM	28 AM	28 DCE	29 AM	29 PM	30 AM	30 PM	31 AM	31 PM	32 AM	32 PM	33 AM	33 PM
4	[redacted] (b) (4)	Discharge, Brown	Ear Canal Right	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Fur Dull	Tail	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	X
		Skin Red	Abdominal	.	.	.	X	.	.	.	.	.	.	.	.	.	.
			Thoracic Ventral	.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	1	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Discharge, Red	Vulva	.	.	.	1	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 34 PM	35 AM	35 PM	36 AM	36 PM	38 AM	38 PM	39 AM	39 PM	40 AM	44 PM	45 AM	47 AM	52 PM
4	[redacted] (b) (4)	Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Material Mucoid Red		.	.	.	.	.	1	.	1	.	.	.	.	.	.
		Feces, Output		.	A	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 6

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL - LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 55 UNS	DAY 56 DCE
4	[redacted] (b) (4)	Skin Red	Abdominal	.	X
		Fur Dull	Tail	.	X
		Skin, Brown	Abdominal	.	X
		Skin Red	Abdominal	.	X
		Skin Red	Abdominal	.	X
			Thoracic Ventral	.	X
		Discharge, Brown	Ear Canal Left	.	1
			Ear Canal Right	.	1

(b) (4)

BODY TEMPERATURE
PRE-TREATMENT AND GESTATION
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

NA: Not Applicable

--: No data

T: Technical Oversight

^: Activity performed at Rectal region

NOTE:

Pre-Treatment Period = Day -8 to -1

Gestation Period = Day 0 to 42

APPENDIX NO. 7

(b) (4)

BODY TEMPERATURE
AXILLARY (Degree Celsius)
PRE-TREATMENT AND GESTATION - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day -8	Day -7	Day -6	Day -5	Day -4	Day -1	Day 0	PRE-TREATMENT AVERAGE (Day -8 to 0)
1	(b) (4)								38.6 38.1 38.3 38.9 38.3
	MEAN	38.89	38.22	39.33	--	38.22	38.33	38.31	38.42
	SD	NA	0.16	NA	--	NA	NA	0.22	0.30
	MIN	38.9	38.1	39.3	--	38.2	38.3	38.0	38.1
	MAX	38.9	38.3	39.3	--	38.2	38.3	38.5	38.9
	N	1	2	1	--	1	1	5	5
2	(b) (4)								38.7 38.4 38.3 38.7 38.8
	MEAN	39.22	38.83	--	39.00	38.28	38.56	38.49	38.58
	SD	NA	NA	--	NA	0.08	NA	0.07	0.21
	MIN	39.2	38.8	--	39.0	38.2	38.6	38.4	38.3
	MAX	39.2	38.8	--	39.0	38.3	38.6	38.6	38.8
	N	1	1	--	1	2	1	5	5
3	(b) (4)								38.3 38.3 38.3 38.6 38.9
	MEAN	--	--	--	38.44	38.67	--	38.43	38.48
	SD	--	--	--	0.38	0.47	--	0.19	0.26
	MIN	--	--	--	38.2	38.3	--	38.3	38.3
	MAX	--	--	--	38.9	39.0	--	38.8	38.9
	N	--	--	--	3	2	--	5	5
4	(b) (4)								38.5 38.1 38.0 38.5 38.9
	MEAN	--	--	38.53	38.44	38.61	--	38.37	38.39
	SD	--	--	0.27	NA	NA	--	0.47	0.35
	MIN	--	--	38.3	38.4	38.6	--	37.9	38.0
	MAX	--	--	38.7	38.4	38.6	--	39.1	38.9
	N	--	--	2	1	1	--	5	5

APPENDIX NO. 7

(b) (4)

BODY TEMPERATURE
AXILLARY (Degree Celsius)
PRE-TREATMENT AND GESTATION - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
1	(b) (4)						
	MEAN	38.38	38.43	38.42	38.60	38.26	37.93
	SD	0.42	0.39	0.46	0.41	0.49	0 25
	MIN	37.8	38.0	37.8	38.2	37.9	37.6
	MAX	38.8	39.0	38.9	39.1	39.1	38.2
	N	5	5	5	5	5	4
2	(b) (4)						
	MEAN	38.41	38.56	38.65	38.52	38.24	38.00
	SD	0.31	0.45	0.59	0.41	0.28	0 10
	MIN	38.2	38.1	37.9	37.9	38.0	37.9
	MAX	38.9	39.3	39.4	39.0	38.6	38.1
	N	5	5	4	5	4	5
3	(b) (4)						
	MEAN	38.42	38.59	38.46	38.34	38.21	37.88
	SD	0.18	0.20	0.33	0.17	0.17	0 25
	MIN	38.2	38.3	37.9	38.1	38.0	37.5
	MAX	38.7	38.9	38.7	38.6	38.4	38.1
	N	5	5	5	5	5	5
4	(b) (4)						
	MEAN	38.27	38.39	38.67	38.42	38.19	37.70
	SD	0.25	0.15	0.47	0.33	0.37	0 25
	MIN	38.0	38.2	38.3	38.0	37.9	37.5
	MAX	38.6	38.6	39.4	38.9	38.6	38.1
	N	5	5	5	5	3	5

APPENDIX NO. 7

(b) (4)

BODY TEMPERATURE
RECTAL (Degree Celsius)
PRE-TREATMENT AND GESTATION - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS (7 to 42)
1	(b) (4)	
	MEAN	38.34
	SD	0.33
	MIN	38.0
	MAX	38.8
	N	5
2	(b) (4)	
	MEAN	38.37
	SD	0.31
	MIN	38.1
	MAX	38.8
	N	5
3	(b) (4)	
	MEAN	38.32
	SD	0.13
	MIN	38.1
	MAX	38.4
4	(b) (4)	
	MEAN	38.29
	SD	0.19
	MIN	38.1
	MAX	38.6
	N	5

APPENDIX NO. 8

(b) (4)

BODY TEMPERATURE - LACTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation
MIN: Minimum
MAX: Maximum
N: Number of Animals
NA: Not Applicable
--: No data

APPENDIX NO. 8

(b) (4)

BODY TEMPERATURE - LACTATION PERIOD
BODY TEMPERATURE (RECTAL) (Degree Celsius)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0	Day 2	Day 5	Day 28	Day 56
1	(b) (4)					
	SD	0.41	--	--	0.38	0.60
	MIN	37.8	--	--	37.8	37.3
	MAX	38.9	--	--	38.8	38.8
	N	5	--	--	5	5
2	(b) (4)					
	MEAN	38.68	38.40	--	38.58	38.23
	SD	0.97	NA	--	0.22	0.48
	MIN	37.9	38.4	--	38.4	37.8
	MAX	40.3	38.4	--	38.9	38.9
	N	5	1	--	4	4
3	(b) (4)					
	MEAN	38.16	--	38.50	38.20	38.23
	SD	0.38	--	NA	0.18	0.21
	MIN	37.5	--	38.5	38.0	38.0
	MAX	38.4	--	38.5	38.4	38.5
	N	5	--	1	4	4
4	(b) (4)					
	MEAN	38.58	--	--	38.13	38.35
	SD	0.22	--	--	0.26	0.17
	MIN	38.3	--	--	37.9	38.2
	MAX	38.8	--	--	38.4	38.6
	N	4	--	--	4	4

APPENDIX NO. 8 (b) (4)

BODY TEMPERATURE - LACTATION PERIOD
BODY TEMPERATURE (RECTAL) (Degree Celsius)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS (0, 28 and 56)
1	(b) (4)	
	MEAN	38.23
	SD	0.33
	MIN	37.9
	MAX	38.8
	N	5
2	(b) (4)	
	MEAN	38.75
	SD	0.89
	MIN	38.1
	MAX	40.3
	N	5
3	(b) (4)	
	MEAN	38.21
	SD	0.07
	MIN	38.1
	MAX	38.3
	N	5
4	(b) (4)	
	MEAN	38.35
	SD	0.13
	MIN	38.2
	MAX	38.5
	N	4

(b) (4)

APPENDIX NO. 9

HEART RATE
PRE-TREATMENT AND GESTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

NA: Not Applicable

--: No data

*: Suspected cardiac anomalie

NOTE:

Pre-Treatment Period = Day -8 to -1

Gestation Period = Day 0 to 42

APPENDIX NO. 9

(b) (4)

HEART RATE
HEART RATE (Beats/min)
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day -8	Day -7	Day -6	Day -5	Day -4	Day -1	Day 0	PRE-TREATMENT AVERAGE (Day -8 to 0)	Day 7	Day 14	Day 21
1												(b) (4)
	MEAN	80.0	100.0	80.0	--	120.0	110.0	96.0	97.7	98.0	110.0	114.0
	SD	NA	14.1	NA	--	NA	NA	13.4	14.5	8.4	21.2	18.2
	MIN	80	90	80	--	120	110	80	80	90	80	90
	MAX	80	110	80	--	120	110	110	115	110	130	130
	N	1	2	1	--	1	1	5	5	5	5	5
2												(b) (4)
	MEAN	130.0	120.0	--	100.0	95.0	100.0	102.0	103.3	99.2	95.2	105.2
	SD	NA	NA	--	NA	7.1	NA	14.8	12.0	21.1	11.2	6.7
	MIN	130	120	--	100	90	100	80	85	76	80	96
	MAX	130	120	--	100	100	100	120	117	130	110	110
	N	1	1	--	1	2	1	5	5	5	5	5
3												(b) (4)
	MEAN	--	--	--	106.7	105.0	--	110.0	108.0	102.0	94.0	101.2
	SD	--	--	--	15.3	7.1	--	10.0	7.6	11.0	16.7	13.3
	MIN	--	--	--	90	100	--	100	100	90	80	90
	MAX	--	--	--	120	110	--	120	120	120	120	120
	N	--	--	--	3	2	--	5	5	5	5	5
4												(b) (4)
	MEAN	--	100.0	95.0	140.0	110.0	--	112.0	110.0	95.6	120.0	116.0
	SD	--	NA	7.1	NA	NA	--	21.7	14.6	22.1	18.7	11.4
	MIN	--	100	90	140	110	--	100	95	64	100	100
	MAX	--	100	100	140	110	--	150	130	120	150	130
	N	--	1	2	1	1	--	5	5	5	5	5

APPENDIX NO. 9

(b) (4)

HEART RATE
HEART RATE (Beats/min)
PRE-TREATMENT AND GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 28	Day 35	Day 42	COMBINED DAYS (7 to 42)
1	(b) (4)				
	MEAN	108.0	104.8	97.0	105.6
	SD	13.0	21.6	8.9	10.3
	MIN	90	80	88	90
	MAX	120	130	108	119
	N	5	5	4	5
2	(b) (4)				
	MEAN	118.0	107.5	112.0	105.8
	SD	13.0	17.1	13.3	10.5
	MIN	110	90	92	96
	MAX	140	130	128	123
	N	5	4	5	5
3	(b) (4)				
	MEAN	110.0	106.0	107.2	103.4
	SD	15.8	15.2	20.9	12.4
	MIN	90	80	80	88
	MAX	130	120	128	120
	N	5	5	5	5
4	(b) (4)				
	MEAN	118.0	113.3	122.4	114.0
	SD	16.4	25.2	18.7	12.8
	MIN	100	90	96	98
	MAX	130	140	148	130
	N	5	3	5	5

(b) (4)

HEART RATE – LACTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation
MIN: Minimum
MAX: Maximum
N: Number of Animals
NA: Not Applicable
--: No data

APPENDIX NO. 10 (b) (4)

HEART RATE – LACTATION PERIOD
HEART RATE (Beats/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0	Day 2	Day 5	Day 28	Day 56
1	(b) (4)					
	MEAN	129.6	--	--	100.8	96.8
	SD	16.1	--	--	15.6	10.4
	MIN	112	--	--	88	84
	MAX	152	--	--	128	108
	N	5	--	--	5	5
2	(b) (4)					
	MEAN	124.0	96.0	--	106.0	107.0
	SD	19.8	NA	--	7.7	15.4
	MIN	92	96	--	100	92
	MAX	140	96	--	116	128
	N	5	1	--	4	4
3	(b) (4)					
	MEAN	109.6	--	136.0	99.0	85.0
	SD	33.1	--	NA	15.1	8.9
	MIN	60	--	136	84	76
	MAX	152	--	136	120	96
	N	5	--	1	4	4
4	(b) (4)					
	SD	25.0	--	--	9.8	12.4
	MIN	108	--	--	96	88
	MAX	160	--	--	120	116
	N	4	--	--	4	4

APPENDIX NO. 10

(b) (4)

HEART RATE – LACTATION PERIOD
HEART RATE (Beats/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS (0, 28 and 56)
1	(b) (4)	
	MEAN	109.1
	SD	9.8
	MIN	95
	MAX	119
	N	5
2	(b) (4)	
	MEAN	116.8
	SD	14.0
	MIN	104
	MAX	140
	N	5
3	(b) (4)	
	MEAN	99.5
	SD	12.9
	MIN	79
	MAX	111
4	(b) (4)	
	MEAN	113.3
	SD	7.9
	MIN	105
	MAX	124
	N	4

(b) (4)

RESPIRATORY RATE
PRE-TREATMENT AND GESTATION
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation
MIN: Minimum
MAX: Maximum
N: Number of Animals
NA: Not Applicable
--: No data
Resp: Respiration

NOTE:

Pre-Treatment Period = Day -8 to -1

Gestation Period = Day 0 to 42

APPENDIX NO. 11

(b) (4)

RESPIRATORY RATE
RESPIRATORY RATE (Resp/min)
PRE-TREATMENT AND GESTATION - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day -8	Day -7	Day -6	Day -5	Day -4	Day -1	Day 0	PRE-TREATMENT AVERAGE (Day -8 to 0)
1	(b) (4)								
	MEAN	28.0	26.0	28.0	--	28.0	24.0	25.6	26.1
	SD	NA	2.8	NA	--	NA	NA	4.6	1.4
	MIN	28	24	28	--	28	24	20	24
	MAX	28	28	28	--	28	24	32	28
	N	1	2	1	--	1	1	5	5
2	(b) (4)								
	MEAN	40.0	40.0	--	28.0	30.0	36.0	28.0	30.7
	SD	NA	NA	--	NA	2.8	NA	6.3	5.7
	MIN	40	40	--	28	28	36	20	24
	MAX	40	40	--	28	32	36	36	37
	N	1	1	--	1	2	1	5	5
3	(b) (4)								
	MEAN	--	--	--	30.7	30.0	--	26.4	28.4
	SD	--	--	--	4.6	8.5	--	6.1	5.4
	MIN	--	--	--	28	24	--	20	24
	MAX	--	--	--	36	36	--	36	36
	N	--	--	--	3	2	--	5	5
4	(b) (4)								
	MEAN	--	24.0	24.0	20.0	40.0	--	25.6	26.0
	SD	--	NA	0.0	NA	NA	--	4.6	5.3
	MIN	--	24	24	20	40	--	20	20
	MAX	--	24	24	20	40	--	32	34
	N	--	1	2	1	1	--	5	5

APPENDIX NO. 11

(b) (4)

RESPIRATORY RATE
RESPIRATORY RATE (Resp/min)
PRE-TREATMENT AND GESTATION - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	COMBINED DAYS (7 to 42)
1	(b) (4)							
	MEAN	24.0	25.6	22.4	25.6	27.2	22.0	24.7
	SD	4.9	4.6	3.6	4.6	5.2	2 3	2.4
	MIN	20	20	20	20	24	20	22
	MAX	32	32	28	32	36	24	28
2	(b) (4)							
	MEAN	24.8	28.8	28.0	24.0	30.0	24.0	26.6
	SD	4.4	7.7	7.5	4.9	5.2	2.8	2.8
	MIN	20	20	20	20	24	20	23
	MAX	28	40	36	32	36	28	30
3	(b) (4)							
	MEAN	28.8	25.6	27.2	26.4	29.6	27.2	27.5
	SD	8.7	8.3	5.9	6.1	8.8	5 2	6.3
	MIN	20	20	20	20	20	24	24
	MAX	40	40	36	36	44	36	39
	N	5	5	5	5	5	5	5
4	(b) (4)							
	MEAN	23.6	28.8	28.0	26.4	34.7	27.2	27.7
	SD	5.7	6.6	7.5	8.3	22.0	3 3	5.5
	MIN	16	20	20	20	20	24	23
	MAX	30	36	40	40	60	32	34
	N	5	5	5	5	3	5	5

APPENDIX NO. 12

RESPIRATORY RATE – LACTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation
MIN: Minimum
MAX: Maximum
N: Number of Animals
NA: Not Applicable
--: No data
Resp: Respiration

APPENDIX NO. 12

(b) (4)

RESPIRATORY RATE – LACTATION PE
RESPIRATORY RATE (Resp/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0	Day 2	Day 5	Day 28	Day 56
1	(b) (4)					
	SD	8.3	--	--	4.4	3.3
	MIN	32	--	--	28	24
	MAX	52	--	--	40	32
	N	5	--	--	5	5
2	(b) (4)					
	MEAN	37.6	44.0	--	37.0	29.0
	SD	12.2	NA	--	5.0	5.0
	MIN	24	44	--	32	24
	MAX	52	44	--	44	36
	N	5	1	--	4	4
3	(b) (4)					
	MEAN	32.0	--	60.0	40.0	29.0
	SD	6.3	--	NA	11.8	3.8
	MIN	24	--	60	28	24
	MAX	40	--	60	52	32
	N	5	--	1	4	4
4	(b) (4)					
	MEAN	29.0	--	--	32.0	29.0
	SD	5.0	--	--	10.8	6.0
	MIN	24	--	--	24	24
	MAX	36	--	--	48	36
	N	4	--	--	4	4

APPENDIX NO. 12 (b) (4)

RESPIRATORY RATE – LACTATION PERIOD
RESPIRATORY RATE (Resp/min)
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS (0, 28 and 56)
1	(b) (4)	
	MEAN	32.5
	SD	5.1
	MIN	28
	MAX	41
	N	5
2	(b) (4)	
	MEAN	36.5
	SD	8.8
	MIN	29
	MAX	48
	N	5
3	(b) (4)	
	MEAN	34.4
	SD	4.0
	MIN	29
	MAX	40
	N	5
4	(b) (4)	
	MEAN	30.0
	SD	4.9
	MIN	24
	MAX	36
	N	4

APPENDIX NO. 13

(b) (4)

BODY WEIGHT
PRE-TREATMENT AND GESTATION
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation
MIN: Minimum
MAX: Maximum
N: Number of Animals
NA: Not Applicable
--: No data

NOTE:

Pre-Treatment Period = Day -8 to -1

Gestation Period = Day 0 to 70

APPENDIX NO. 13

(b) (4)

BODY WEIGHT (kg)
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day -8	Day -7	Day -6	Day -5	Day -4	Day -1	Day 0	PRE-TREATMENT AVERAGE (Day -8 to 0)	Day 7	Day 14	Day 21
1	(b) (4)											
	MEAN	9.40	10.70	10.00	--	9.80	9.60	10.06	10.10	10.18	10.40	10.30
	SD	NA	1.56	NA	--	NA	NA	0.90	0.92	0.72	0.72	0.71
	MIN	9.4	9.6	10.0	--	9.8	9.6	9.4	9.5	9.6	9.8	9.6
	MAX	9.4	11.8	10.0	--	9.8	9.6	11.6	11.7	11.4	11.6	11.4
	N	1	2	1	--	1	1	5	5	5	5	5
2	(b) (4)											
	MEAN	11.20	9.90	--	9.50	10.75	11.00	10.22	10.32	10.22	10.58	10.30
	SD	NA	NA	--	NA	0.07	NA	0.69	0.69	0.83	0.88	0.81
	MIN	11.2	9.9	--	9.5	10.7	11.0	9.3	9.4	9.3	9.4	9.2
	MAX	11.2	9.9	--	9.5	10.8	11.0	10.9	11.0	11.2	11.6	11.3
	N	1	1	--	1	2	1	5	5	5	5	5
3	(b) (4)											
	MEAN				10.80	10.20		10.36	10.40	10.40	10.54	10.36
	SD	--	--	--	0.82	0.42	--	0.70	0.69	0.61	0.67	0.70
	MIN	--	--	--	9.9	9.9	--	9.8	9.9	9.8	10.0	9.5
	MAX	--	--	--	11.5	10.5	--	11.5	11.5	11.2	11.6	11.4
	N	--	--	--	3	2	--	5	5	5	5	5
4	(b) (4)											
	MEAN	--	10.00	10.65	10.00	11.30	--	10.46	10.49	10.46	11.06	10.82
	SD	--	NA	1.34	NA	NA	--	0.78	0.82	1.26	1.21	1.07
	MIN	--	10.0	9.7	10.0	11.3	--	9.7	9.7	9.0	9.8	9.6
	MAX	--	10.0	11.6	10.0	11.3	--	11.4	11.5	12.0	12.4	12.3
	N	--	1	2	1	1	--	5	5	5	5	5

APPENDIX NO. 13

(b) (4)

BODY WEIGHT (kg)
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 28	Day 35	Day 42	Day 49	Day 56	Day 63	Day 70	COMBINED DAYS (7 to 63)
1	(b) (4)								
	MEAN	10.00	9.74	10.30	11.34	12.00	12.65	12.00	10.72
	SD	0.66	0.55	0.93	0.91	0.94	1.05	NA	0.74
	MIN	9.3	9.0	8.7	10.0	10.6	11.6	12.0	9.8
	MAX	10.9	10.4	11.1	12.5	13.2	14.1	12.0	11.8
	N	5	5	5	5	5	4	1	5
2	(b) (4)								
	MEAN	9.92	10.12	11.14	12.12	12.68	13.18	--	11.12
	SD	0.76	0.97	1.16	1.29	1.10	1.36	--	0.89
	MIN	8.8	9.0	9.8	10.7	11.2	11.6	--	10.1
	MAX	10.8	11.6	12.8	13.7	13.9	14.5	--	12.1
	N	5	5	5	5	5	4	--	5
3	(b) (4)								
	MEAN	9.92	10.36	11.16	11.86	12.64	12.95	--	10.99
	SD	0.69	0.88	0.88	1.08	1.46	0.78	--	0.80
	MIN	8.9	9.2	10.2	11.0	11.5	12.4	--	10.1
	MAX	10.8	11.3	12.1	13.5	15.0	13.5	--	11.9
	N	5	5	5	5	5	2	--	5
4	(b) (4)								
	MEAN	10.52	10.58	11.62	12.96	13.28	13.90	--	11.52
	SD	0.96	0.72	0.98	1.08	0.80	1.13	--	0.87
	MIN	9.5	9.7	10.1	11.5	12.4	13.1	--	10.8
	MAX	11.8	11.4	12.7	14.1	14.4	14.7	--	12.7
	N	5	5	5	5	5	2	--	5

APPENDIX NO. 14

BODY WEIGHT
LACTATION PERIOD
F0 GENERATION

The following abbreviations and footnote have been used throughout the appendix and/or summary table

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

--: No data

APPENDIX NO. 14

(b) (4)

BODY WEIGHT (kg)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42	Day 49	Day 56
1	(b) (4)									
	MEAN	9.54	9.22	9.68	9.92	9.98	10.26	10.38	10.62	10.42
	SD	0.73	0.80	0.79	0.54	0.33	0.57	0.56	0.36	0.59
	MIN	8.8	8.3	8.6	9.3	9.5	9.4	9.7	10.1	9.8
	MAX	10.6	10.5	10.7	10.6	10.4	11.0	11.2	11.0	11.4
	N	5	5	5	5	5	5	5	5	5
2	(b) (4)									
	MEAN	9.82	9.38	9.65	9.98	10.05	10.35	10.30	10.43	9.85
	SD	0.58	0.71	0.82	0.86	0.95	1.11	0.90	1.13	0.90
	MIN	9.0	8.4	8.5	8.7	8.8	8.8	9.1	8.9	8.6
	MAX	10.5	10.0	10.4	10.6	11.0	11.2	11.2	11.5	10.6
	N	5	4	4	4	4	4	4	4	4
3	(b) (4)									
	SD	0.94	0.85	0.51	0.64	0.31	0.33	0.51	0.31	0.29
	MIN	8.6	8.4	8.9	9.0	9.6	9.9	9.7	9.9	9.7
	MAX	11.2	10.4	10.1	10.4	10.3	10.6	10.9	10.6	10.3
	N	5	4	4	4	4	4	4	4	4
4	(b) (4)									
	SD	1.06	1.22	1.21	1.35	1.15	1.08	1.36	1.41	1.45
	MIN	8.9	8.6	8.8	9.2	9.4	9.9	10.2	10.0	9.7
	MAX	11.4	11.4	11.5	12.2	12.0	12.3	13.2	13.2	13.0
	N	4	4	4	4	4	4	4	4	4

APPENDIX NO. 14

(b) (4)

BODY WEIGHT (kg)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS (0 to 56)
1	(b) (4)	
	MEAN	10.00
	SD	0.56
	MIN	9.3
	MAX	10.8
	N	5
2	(b) (4)	
	MEAN	10.01
	SD	0.75
	MIN	8.8
	MAX	10.6
	N	5
3	(b) (4)	
	SD	0.69
	MIN	9.3
	MAX	11.2
	N	5
4	(b) (4)	
	MEAN	10.44
	SD	1.24
	MIN	9.4
	MAX	12.2
	N	4

APPENDIX NO. 15

(b) (4)

BODY WEIGHT CHANGE
PRE-TREATMENT AND GESTATION
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

NA: Not Applicable

--: No data

NOTE:

Pre-Treatment Period = Day -8 to -1

Gestation Period = Day 0 to 70

APPENDIX NO. 15

(b) (4)

BODY WEIGHT CHANGE (kg)
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day -8 to -1	Day -7 to 0	Day -6 to 0	Day -5 to 0	Day -4 to 0	Day -1 to 0	Day 0 to 7	Day 7 to 14
1	(b) (4)								
	MEAN	0.20	-0.05	0.10	--	-0.30	-0.20	0.12	0.22
	SD	NA	0.21	NA	--	NA	NA	0.22	0.08
	MIN	0.2	-0.2	0.1	--	-0.3	-0.2	-0.2	0.1
	MAX	0.2	0.1	0.1	--	-0.3	-0.2	0.4	0.3
	N	1	2	1	--	1	1	5	5
2	(b) (4)								
	MEAN	-0.20	-0.20	--	-0.20	-0.15	-0.10	0.00	0.36
	SD	NA	NA	--	NA	0.07	NA	0.21	0.18
	MIN	-0.2	-0.2	--	-0.2	-0.2	-0.1	-0.3	0.1
	MAX	-0.2	-0.2	--	-0.2	-0.1	-0.1	0.3	0.6
	N	1	1	--	1	2	1	5	5
3	(b) (4)								
	MEAN	--	--	--	-0.20	-0.20	--	0.04	0.14
	SD	--	--	--	0.26	0.14	--	0.30	0.25
	MIN	--	--	--	-0.5	-0.3	--	-0.3	-0.1
	MAX	--	--	--	0.0	-0.1	--	0.4	0.4
	N	--	--	--	3	2	--	5	5
4	(b) (4)								
	MEAN	--	-0.10	-0.10	0.10	-0.10	--	0.00	0.60
	SD	--	NA	0.14	NA	NA	--	0.51	0.20
	MIN	--	-0.1	-0.2	0.1	-0.1	--	-0.7	0.4
	MAX	--	-0.1	0.0	0.1	-0.1	--	0.6	0.8
	N	--	1	2	1	1	--	5	5

APPENDIX NO. 15

(b) (4)

BODY WEIGHT CHANGE (kg)
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56	Day 56 to 63	Day 63 to 70
1	(b) (4)								
	MEAN	-0.10	-0.30	-0.26	0.56	1.04	0.66	0.65	0.40
	SD	0.14	0.23	0.23	0.52	0.32	0.17	0.37	NA
	MIN	-0.3	-0.5	-0.5	-0.3	0.6	0.4	0.2	0.4
	MAX	0.0	0.1	0.1	1.1	1.4	0.8	1.0	0.4
	N	5	5	5	5	5	5	4	1
2	(b) (4)								
	MEAN	-0.28	-0.38	0.20	1.02	0.98	0.56	0.80	--
	SD	0.15	0.13	0.35	0.48	0.43	0.43	0.39	--
	MIN	-0.5	-0.5	0.0	0.2	0.4	0.2	0.4	--
	MAX	-0.1	-0.2	0.8	1.4	1.6	1.2	1.3	--
	N	5	5	5	5	5	5	4	--
3	(b) (4)								
	MEAN	-0.18	-0.44	0.44	0.80	0.70	0.78	0.65	--
	SD	0.22	0.17	0.47	0.54	0.45	0.41	0.35	--
	MIN	-0.5	-0.6	-0.1	0.1	0.3	0.5	0.4	--
	MAX	0.1	-0.2	1.1	1.5	1.4	1.5	0.9	--
	N	5	5	5	5	5	5	2	--
4	(b) (4)								
	MEAN	-0.24	-0.30	0.06	1.04	1.34	0.32	0.50	--
	SD	0.44	0.16	0.68	0.44	0.47	0.86	0.28	--
	MIN	-1.0	-0.5	-0.6	0.4	0.9	-1.2	0.3	--
	MAX	0.1	-0.1	1.0	1.5	2.1	0.9	0.7	--
	N	5	5	5	5	5	5	2	--

APPENDIX NO. 15 (b) (4)

BODY WEIGHT CHANGE (kg)
PRE-TREATMENT AND GESTATION
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS (0 to 63)
1	(b) (4)	
	MEAN	0.28
	SD	0.04
	MIN	0.2
	MAX	0.3
	N	5
2	(b) (4)	
	MEAN	0.35
	SD	0.09
	MIN	0.2
	MAX	0.4
	N	5
3	(b) (4)	
	MEAN	0.31
	SD	0.14
	MIN	0.2
	MAX	0.6
	N	5
4	(b) (4)	
	MEAN	0.36
	SD	0.11
	MIN	0.2
	MAX	0.5
	N	5

APPENDIX NO. 16

(b) (4)

BODY WEIGHT CHANGE
LACTATION PERIOD
FEMALES
F0 GENERATION

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

APPENDIX NO. 16

(b) (4)

BODY WEIGHT CHANGE (kg)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0 to 7	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	(b) (4)								
	SD	0.32	0.36	0.40	0.30	0.25	0.19	0.27	0.38
	MIN	-0.7	0.2	-0.2	-0.2	-0.1	-0.2	-0.2	-0.6
	MAX	0.1	1.1	0.7	0.5	0.6	0.3	0.5	0.4
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	-0.35	0.28	0.33	0.08	0.30	-0.05	0.13	-0.58
	SD	0.37	0.35	0.19	0.34	0.32	0.29	0.24	0.25
	MIN	-0.6	-0.1	0.2	-0.4	0.0	-0.4	-0.2	-0.9
	MAX	0.2	0.7	0.6	0.4	0.7	0.3	0.3	-0.3
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	-0.13	0.10	0.30	-0.03	0.38	0.10	0.03	-0.43
	SD	0.43	0.34	0.16	0.46	0.30	0.36	0.24	0.33
	MIN	-0.7	-0.3	0.1	-0.5	0.1	-0.2	-0.3	-0.8
	MAX	0.2	0.5	0.5	0.6	0.8	0.5	0.2	-0.1
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	-0.30	0.10	0.48	0.13	0.55	0.33	-0.05	-0.23
	SD	0.22	0.14	0.17	0.25	0.31	0.45	0.19	0.25
	MIN	-0.5	-0.1	0.3	-0.2	0.3	-0.2	-0.2	-0.5
	MAX	0.0	0.2	0.7	0.4	1.0	0.9	0.2	0.1
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 16

[redacted]

BODY WEIGHT CHANGE (kg)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED DAYS (0 to 56)
1	[redacted]	
	MEAN	0.11
	SD	0.03
	MIN	0.1
	MAX	0.2
	N	5
2	[redacted]	
	MEAN	0.02
	SD	0.06
	MIN	-0.1
	MAX	0.1
	N	4
3	[redacted]	
	MEAN	0.04
	SD	0.07
	MIN	0.0
	MAX	0.1
	N	4
4	[redacted]	
	MEAN	0.13
	SD	0.06
	MIN	0.1
	MAX	0.2
	N	4

DAILY FOOD CONSUMPTION
PRE-TREATMENT AND GESTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

NA: Not Applicable

--: No data

NT: Not Taken

T: Technical Oversight

E: Excluded

S: Spillage

S1: Spillage, Slight Amount (1 to 100 g) Approximately

S3: Spillage, Severe Amount (201 to 300 g) Approximately

SC1: Spillage, Contaminated with liquid or solid material, Slight Amount (1 to 100 g) Approximately

NOTE:

Pre-Treatment Period = Day -8 to 0

Gestation Period = Day 0 to 72

APPENDIX NO. 17 (b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day -8 to -7	Day -7 to -6	Day -6 to -5	Day -5 to -4	Day -4 to -3	Day -3 to -2	Day -2 to -1	Day -1 to 0
1	(b) (4)								
	MEAN	156.0	206.0	148.5	177.3	159.6	163.2	150.4	165.5
	SD	NA	51.0	83.8	98.2	68.9	74.3	73.0	68.3
	MIN	156	148	86	110	92	76	90	100
	MAX	156	244	272	290	264	272	260	248
	N	1	3	4	3	5	5	5	4
2	(b) (4)								
	MEAN	108.0	150.0	169.0	131.3	207.0	175.2	167.2	166.4
	SD	NA	138.6	91.9	59.0	58.9	65.1	55.3	62.5
	MIN	108	52	104	86	126	128	106	106
	MAX	108	248	234	198	266	286	242	270
	N	1	2	2	3	4	5	5	5
3	(b) (4)								
	MEAN	--	--	--	126.7	197.3	190.8	161.6	106.5
	SD	--	--	--	3.1	126.3	56.9	39.3	39.4
	MIN	--	--	--	124	66	104	96	56
	MAX	--	--	--	130	318	250	198	150
	N	--	--	--	3	3	5	5	4
4	(b) (4)								
	MEAN	--	166.0	138.7	201.5	147.5	153.2	137.2	146.8
	SD	--	NA	95.9	39.5	62.2	73.4	30.0	40.0
	MIN	--	166	28	150	92	88	90	94
	MAX	--	166	196	238	224	278	172	188
	N	--	1	3	4	4	5	5	5

APPENDIX NO. 17

(b) (4)

MEAN DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0 to 1	Day 1 to 2	Day 2 to 3	Day 3 to 4	Day 4 to 5	Day 5 to 6	Day 6 to 7	Day 7 to 8
1	(b) (4)								
	MEAN	150.5	147.2	124.8	166.8	178.0	177.6	215.6	140.4
	SD	90.6	51.9	49.2	49.8	58.2	56.4	47.2	84.7
	MIN	62	84	72	94	78	124	146	0
	MAX	260	224	196	222	230	262	278	222
	N	4	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	184.4	178.4	219.6	250.8	249.6	201.6	210.4	221.2
	SD	73.4	61.1	25.3	54.6	38.6	68.0	42.6	54.3
	MIN	128	76	202	170	186	102	162	156
	MAX	292	234	262	302	284	264	274	296
	N	5	5	5	5	5	5	5	5
3	(b) (4)								
	MEAN	133.2	124.5	168.4	174.0	177.6	178.0	142.8	159.2
	SD	36.7	30.7	80.3	42.6	53.1	52.4	80.4	110.7
	MIN	92	106	70	118	104	96	12	0
	MAX	182	170	278	228	232	230	220	310
	N	5	4	5	5	5	5	5	5
4	(b) (4)								
	SD	45.4	103.3	99.4	115.4	19.8	52.4	140.4	97.6
	MIN	98	14	116	74	118	64	46	166
	MAX	222	248	360	374	172	180	392	424
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 17

(b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 8 to 9	Day 9 to 10	Day 10 to 11	Day 11 to 12	Day 12 to 13	Day 13 to 14	Day 14 to 15	Day 15 to 16
1	(b) (4)								
	MEAN	229.6	237.6	206.0	224.0	208.4	236.4	214.4	211.6
	SD	44.9	55.0	55.6	51.0	14.7	54.2	81.6	46.4
	MIN	154	168	132	174	190	176	152	144
	MAX	274	306	272	296	230	294	352	272
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	251.2	269.6	272.4	284.8	259.6	263.2	219.6	250.8
	SD	47.0	45.2	21.8	69.4	55.4	29.9	49.6	49.1
	MIN	206	226	244	166	206	218	156	198
	MAX	324	340	296	332	348	298	292	302
	N	5	5	5	5	5	5	5	5
3	(b) (4)								
	MEAN	186.4	222.0	278.8	214.4	249.6	260.8	151.6	150.4
	SD	70.8	107.5	99.1	104.8	66.3	129.9	113.3	71.2
	MIN	82	90	194	62	162	158	0	48
	MAX	256	344	420	322	348	482	258	240
	N	5	5	5	5	5	5	5	5
4	(b) (4)								
	MEAN	239.6	276.8	244.4	315.2	238.0	234.0	218.4	220.0
	SD	75.1	94.2	61.5	70.5	89.0	54.5	115.3	86.0
	MIN	166	152	146	216	96	180	136	116
	MAX	362	386	310	384	340	302	418	346
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 17

(b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 16 to 17	Day 17 to 18	Day 18 to 19	Day 19 to 20	Day 20 to 21	Day 21 to 22	Day 22 to 23	Day 23 to 24
1	(b) (4)								
	MEAN	223.6	157.2	195.2	216.8	170.8	130.0	150.4	140.4
	SD	84.6	64.4	25.3	76.6	46.1	60.0	38.8	48.7
	MIN	116	90	168	132	110	52	110	72
	MAX	338	230	222	314	216	212	208	196
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	206.8	199.6	179.6	123.6	182.8	117.2	143.6	142.0
	SD	34.3	39.6	81.1	44.4	50.4	35.2	42.4	56.5
	MIN	166	146	72	72	98	60	74	68
	MAX	248	242	274	172	222	146	180	206
	N	5	5	5	5	5	5	5	5
3	(b) (4)								
	MEAN	204.8	162.8	179.2	149.0	151.2	156.8	121.6	124.0
	SD	92.9	68.0	50.2	32.7	23.3	55.7	51.8	24.1
	MIN	98	60	120	120	120	98	64	102
	MAX	354	242	242	188	182	240	164	158
	N	5	5	5	4	5	5	5	4
4	(b) (4)								
	MEAN	180.0	158.4	205.6	139.2	146.8	118.0	137.6	136.8
	SD	76.0	118.9	51.8	59.6	85.2	51.9	35.1	55.1
	MIN	84	2	132	64	2	58	112	78
	MAX	280	266	266	220	210	184	194	196
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 17

(b) (4)

MEAN DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 24 to 25	Day 25 to 26	Day 26 to 27	Day 27 to 28	Day 28 to 29	Day 29 to 30	Day 30 to 31	Day 31 to 32
1									
	MEAN	111.6	137.6	127.2	101.6	85.2	75.2	68.8	85.6
	SD	42.9	59.5	48.9	79.8	47.0	47.8	44.3	25.7
	MIN	48	86	58	2	30	24	34	56
	MAX	164	214	192	220	154	130	142	122
	N	5	5	5	5	5	5	5	5
2									
	MEAN	182.0	93.6	77.6	86.0	91.6	66.4	93.2	108.8
	SD	96.7	52.7	31.0	43.3	75.4	27.7	40.5	33.2
	MIN	86	16	24	28	4	34	46	76
	MAX	344	158	98	136	194	100	126	154
	N	5	5	5	5	5	5	5	5
3									
	MEAN	98.0	113.6	77.6	129.0	96.8	114.8	109.2	106.4
	SD	55.5	27.8	59.2	55.3	42.2	91.9	50.1	67.5
	MIN	6	88	0	66	50	0	48	42
	MAX	156	158	152	192	138	222	172	220
	N	5	5	5	4	5	5	5	5
4									
	MEAN	87.2	116.5	103.6	87.2	47.6	108.0	69.2	107.2
	SD	26.6	26.3	24.4	37.3	31.0	85.0	47.6	78.4
	MIN	56	88	68	64	2	20	12	30
	MAX	116	146	128	152	82	222	130	232
	N	5	4	5	5	5	4	5	5

APPENDIX NO. 17

(b) (4)

MEAN DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 32 to 33	Day 33 to 34	Day 34 to 35	Day 35 to 36	Day 36 to 37	Day 37 to 38	Day 38 to 39	Day 39 to 40
1	(b) (4)								
	MEAN	84.6	121.8	77.8	101.5	120.0	132.0	111.6	180.6
	SD	35.9	58.8	48.8	75.9	82.9	93.5	73.6	108.7
	MIN	42	64	14	16	26	28	26	50
	MAX	120	190	150	181	234	244	198	314
	N	5	5	5	4	5	5	5	5
2	(b) (4)								
	MEAN	143.2	113.2	161.6	171.6	199.2	242.0	225.4	199.4
	SD	51.0	43.7	36.1	107.2	34.2	67.1	61.6	35.1
	MIN	90	56	104	66	146	140	129	145
	MAX	198	168	190	284	228	312	290	231
	N	5	5	5	5	5	5	5	5
3	(b) (4)								
	MEAN	135.2	195.6	191.8	162.8	161.4	233.6	228.8	209.6
	SD	75.4	56.9	119.7	43.2	91.1	96.7	109.3	63.9
	MIN	68	144	86	126	54	114	115	114
	MAX	254	280	356	232	260	358	374	278
	N	5	5	4	5	5	5	5	5
4	(b) (4)								
	MEAN	124.4	129.4	112.0	141.8	163.4	251.0	185.6	196.0
	SD	96.7	120.2	96.4	90.6	96.1	172.6	83.8	136.2
	MIN	38	32	16	20	32	30	53	1
	MAX	278	312	232	270	291	454	255	334
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 17

(b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 40 to 41	Day 41 to 42	Day 42 to 43	Day 43 to 44	Day 44 to 45	Day 45 to 46	Day 46 to 47	Day 47 to 48
1	(b) (4)								
	MEAN	210.4	200.8	243.2	270.0	270.0	256.0	223.4	220.6
	SD	102.8	64.4	95.9	76.6	86.1	18.9	94.4	64.4
	MIN	37	99	114	137	147	242	103	126
	MAX	288	267	379	331	349	288	344	296
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	192.0	263.2	233.8	234.8	171.2	233.4	220.2	282.0
	SD	94.5	42.1	46.9	56.7	79.4	82.5	73.5	57.5
	MIN	70	214	166	159	59	136	141	199
	MAX	308	330	277	312	265	340	306	332
	N	5	5	5	5	5	5	5	5
3	(b) (4)								
	MEAN	274.8	186.4	219.0	191.4	281.4	211.4	193.8	193.0
	SD	133.7	72.0	94.7	62.6	93.1	50.4	45.0	70.4
	MIN	117	90	118	107	184	153	130	71
	MAX	427	259	350	266	387	278	239	242
	N	5	5	5	5	5	5	5	5
4	(b) (4)								
	MEAN	247.8	210.4	287.8	231.2	282.2	235.4	240.6	270.6
	SD	119.0	54.0	70.7	100.2	110.0	86.7	81.7	113.1
	MIN	90	126	224	167	118	152	147	185
	MAX	422	248	367	409	417	362	331	428
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 17

(b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 48 to 49	Day 49 to 50	Day 50 to 51	Day 51 to 52	Day 52 to 53	Day 53 to 54	Day 54 to 55	Day 55 to 56
1	(b) (4)								
	MEAN	264.0	200.0	216.6	233.6	206.8	205.2	246.4	189.0
	SD	40.2	60.3	47.2	53.4	75.5	47.7	63.1	97.9
	MIN	204	138	180	170	86	163	144	74
	MAX	308	278	299	291	289	284	301	313
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	233.4	180.0	216.6	222.0	222.8	259.6	215.6	222.0
	SD	131.6	39.9	88.3	62.3	84.8	50.8	61.6	30.8
	MIN	105	130	96	140	120	195	125	185
	MAX	412	241	312	283	306	312	288	254
	N	5	5	5	5	5	5	5	5
3	(b) (4)								
	MEAN	191.8	222.8	260.6	189.6	211.8	177.2	188.6	216.0
	SD	49.2	46.2	23.6	84.3	83.6	86.8	31.3	90.2
	MIN	135	163	236	74	92	96	156	140
	MAX	260	280	295	273	317	312	224	369
	N	5	5	5	5	5	5	5	5
4	(b) (4)								
	SD	58.8	95.4	89.4	124.8	96.0	145.2	89.5	87.3
	MIN	189	178	2	66	3	3	2	41
	MAX	337	406	231	405	241	384	237	285
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 17 (b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 57	Day 57 to 58	Day 58 to 59	Day 58 to 60	Day 59 to 60	Day 60 to 61	Day 61 to 62	Day 61 to 63
1	(b) (4)								
	MEAN	219.0	268.6	209.0	--	198.6	162.6	196.3	--
	SD	79.1	73.4	69.6	--	85.7	73.9	48.2	--
	MIN	133	167	128	--	113	95	137	--
	MAX	316	347	304	--	303	276	237	--
	N	5	5	5	--	5	5	4	--
2	(b) (4)								
	MEAN	203.2	232.4	245.5	--	215.3	203.0	232.8	--
	SD	21.2	82.2	72.1	--	24.9	41.6	57.7	--
	MIN	179	158	166	--	180	161	171	--
	MAX	227	352	341	--	236	252	301	--
	N	5	5	4	--	4	4	4	--
3	(b) (4)								
	MEAN	206.2	263.6	159.4	--	185.4	149.0	164.4	--
	SD	29.7	136.4	50.0	--	62.3	66.1	118.5	--
	MIN	161	140	107	--	110	61	0	--
	MAX	240	481	229	--	250	204	288	--
	N	5	5	5	--	5	5	5	--
4	(b) (4)								
	MEAN	114.2	161.0	148.8	--	166.5	181.5	65.3	--
	SD	110.7	68.4	31.2	--	20.7	104.9	57.6	--
	MIN	0	88	115	--	148	102	2	--
	MAX	224	257	187	--	195	326	133	--
	N	5	5	4	--	4	4	4	--

APPENDIX NO. 17 (b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 62 to 63	Day 62 to 64	Day 63 to 64	Day 63 to 65	Day 64 to 65	Day 64 to 66	Day 65 to 66	Day 65 to 67
1	(b) (4)								
	MEAN	175.0	--	161.7	--	183.0	--	98.0	--
	SD	56.0	--	90.7	--	NA	--	NA	--
	MIN	131	--	95	--	183	--	98	--
	MAX	238	--	265	--	183	--	98	--
	N	3	--	3	--	1	--	1	--
2	(b) (4)								
	SD	116.2	--	36.4	--	16.3	--	--	--
	MIN	122	--	99	--	181	--	--	--
	MAX	361	--	171	--	204	--	--	--
	N	4		3		2			
3	(b) (4)								
	MEAN	184.5	--	154.0	--	144.0	--	--	--
	SD	218.5	--	56.6	--	NA	--	--	--
	MIN	30	--	114	--	144	--	--	--
	MAX	339	--	194	--	144	--	--	--
	N	2	--	2	--	1	--	--	--
4	(b) (4)								
	MEAN	60.7	--	--	--	--	--	--	--
	SD	53.7	--	--	--	--	--	--	--
	MIN	18	--	--	--	--	--	--	--
	MAX	121	--	--	--	--	--	--	--
	N	3	--	--	--	--	--	--	--

APPENDIX NO. 17

(b) (4)

DAILY FOOD CONSUMPTION (g)
PRE-TREATMENT AND GESTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 66 to 67	Day 66 to 68	Day 67 to 68	Day 68 to 69	Day 69 to 70	Day 70 to 72
1	(b) (4)						
	MEAN	2.0	--	294.0	115.0	195.0	--
	SD	NA	--	NA	NA	NA	--
	MIN	2	--	294	115	195	--
	MAX	2	--	294	115	195	--
	N	1	--	1	1	1	--
2	(b) (4)						
	MEAN	--	--	99.0	54.0	--	--
	SD	--	--	NA	NA	--	--
	MIN	--	--	99	54	--	--
	MAX	--	--	99	54	--	--
	N	--	--	1	1	--	--
3	(b) (4)						
	MEAN	100.0	--	--	--	--	--
	SD	NA	--	--	--	--	--
	MIN	100	--	--	--	--	--
	MAX	100	--	--	--	--	--
	N	1	--	--	--	--	--

(b) (4)

DAILY FOOD CONSUMPTION
LACTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

NA: Not Applicable

--: No data

E: Excluded

SC1: Spillage, Contaminated with liquid or solid material, Slight Amount (1 to 100 g) Approximately

SC2: Spillage, Contaminated with liquid or solid material, Moderate Amount (101 to 200 g) Approximately

APPENDIX NO. 18

(b) (4)

DAILY FOOD CONSUMPTION (g)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 0 to 1	Day 0 to 2	Day 1 to 2	Day 1 to 3	Day 2 to 3	Day 2 to 4	Day 3 to 4	Day 3 to 5
1	(b) (4)								
	MEAN	135.8	--	171.5	--	261.8	--	268.8	--
	SD	114.9	--	114.2	--	37.5	--	75.9	--
	MIN	1	--	85	--	217	--	147	--
	MAX	261	--	334	--	298	--	351	--
	N	4	--	4	--	5	--	5	--
2	(b) (4)								
	MEAN	184.3	--	222.8	--	279.5	--	434.5	--
	SD	158.4	--	212.0	--	101.6	--	23.4	--
	MIN	1	--	0	--	128	--	411	--
	MAX	324	--	473	--	339	--	467	--
	N	4	--	5	--	4	--	4	--
3	(b) (4)								
	MEAN	104.8	--	136.5	--	265.8	--	281.8	--
	SD	110.3	--	100.7	--	165.0	--	192.5	--
	MIN	1	--	61	--	104	--	21	--
	MAX	285	--	284	--	496	--	485	--
	N	5	--	4	--	4	--	4	--
4	(b) (4)								
	MEAN	222.7	--	144.7	--	344.0	--	269.3	--
	SD	292.5	--	94.6	--	152.3	--	23.6	--
	MIN	20	--	57	--	174	--	247	--
	MAX	558	--	245	--	468	--	294	--
	N	3	--	3	--	3	--	3	--

APPENDIX NO. 18

[redacted] (b) (4)

DAILY FOOD CONSUMPTION (g)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 4 to 5	Day 4 to 6	Day 5 to 6	Day 5 to 7	Day 6 to 7	Day 6 to 8	Day 7 to 8	Day 8 to 9
1	[redacted] (b) (4)								
	MEAN	206.4	--	256.8	--	286.4	--	315.2	411.6
	SD	85.7	--	72.3	--	58.0	--	80.2	74.1
	MIN	60	--	158	--	220	--	209	330
	MAX	280	--	336	--	377	--	429	481
	N	5	--	5	--	5	--	5	5
2	[redacted] (b) (4)								
	MEAN	388.8	--	334.3	--	374.0	--	393.0	478.0
	SD	113.7	--	139.4	--	41.5	--	64.3	93.6
	MIN	298	--	213	--	327	--	343	388
	MAX	555	--	494	--	418	--	486	568
	N	4	--	4	--	4	--	4	4
3	[redacted] (b) (4)								
	MEAN	298.3	--	371.7	--	403.0	--	368.5	332.5
	SD	212.0	--	145.6	--	198.1	--	69.1	112.8
	MIN	60	--	274	--	273	--	265	199
	MAX	505	--	539	--	631	--	409	450
	N	4	--	3	--	3	--	4	4
4	[redacted] (b) (4)								
	MEAN	277.5	--	291.0	--	321.0	--	304.7	321.0
	SD	159.1	--	200.8	--	79.0	--	143.2	141.9
	MIN	165	--	149	--	243	--	219	165
	MAX	390	--	433	--	401	--	470	463
	N	2	--	2	--	3	--	3	4

APPENDIX NO. 18

(b) (4)

DAILY FOOD CONSUMPTION (g)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 9 to 10	Day 10 to 11	Day 11 to 12	Day 12 to 13	Day 13 to 14	Day 14 to 15	Day 15 to 16	Day 16 to 17
1	(b) (4)								
	MEAN	335.0	372.8	387.2	356.6	497.4	334.6	413.0	485.2
	SD	61.3	138.7	99.2	138.3	180.2	114.6	63.6	121.1
	MIN	272	154	302	186	305	149	344	365
	MAX	420	502	529	538	686	444	514	624
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	423.0	348.0	465.0	447.3	509.3	421.0	418.3	526.5
	SD	130.0	32.6	32.1	69.6	54.6	132.0	113.1	74.7
	MIN	288	312	420	379	451	267	268	449
	MAX	567	379	495	529	582	532	524	591
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	341.8	387.0	451.0	385.0	509.0	570.8	406.8	525.5
	SD	147.6	119.7	115.0	130.9	87.2	90.0	203.4	172.2
	MIN	212	280	349	199	428	436	249	382
	MAX	547	547	612	487	624	624	702	766
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	352 3	421.8	378.3	397.0	451.5	494.0	345.0	471.3
	SD	165 9	101.7	82.1	121.6	197.2	77.5	188.9	128.1
	MIN	178	291	260	244	286	389	151	301
	MAX	556	532	450	530	718	567	574	592
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 18

(b) (4)

DAILY FOOD CONSUMPTION (g)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 17 to 18	Day 18 to 19	Day 19 to 20	Day 20 to 21	Day 21 to 22	Day 22 to 23	Day 23 to 24	Day 24 to 25
1	(b) (4)								
	MEAN	418.0	536.8	477.0	515.6	395.8	491.0	556.6	494.4
	SD	156.2	128.1	125.7	55.9	90.7	85.5	52.9	82.8
	MIN	174	413	329	439	299	401	474	386
	MAX	591	754	601	578	506	610	611	571
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	499.0	446.5	498.5	521.3	553.5	613.3	518.0	574.0
	SD	114.1	94.7	97.5	116.1	160.3	64.9	181.8	91.3
	MIN	341	380	369	359	363	537	294	455
	MAX	610	586	602	618	755	677	721	674
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	586.0	496.8	517.5	490.8	506.8	565.3	621.0	456.3
	SD	130.0	154.5	130.6	184.6	63.5	169.7	118.0	98.3
	MIN	430	279	392	258	417	400	497	389
	MAX	747	627	641	709	565	786	776	602
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	505.3	465.3	464.0	479.0	526.3	509.8	528.0	551.0
	SD	159.5	44.9	99.2	15.3	73.9	98.4	110.2	26.5
	MIN	330	421	356	464	419	402	420	516
	MAX	716	527	582	500	578	640	659	574
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 18

(b) (4)

DAILY FOOD CONSUMPTION (g)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 25 to 26	Day 26 to 27	Day 27 to 28	Day 28 to 29	Day 29 to 30	Day 30 to 31	Day 31 to 32	Day 32 to 33
1	(b) (4)								
	SD	117.1	121.4	82.8	104.8	117.7	132.1	81.6	93.9
	MIN	465	303	420	443	269	338	431	393
	MAX	725	592	623	723	564	664	639	589
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	461.0	621.8	511.3	528.8	550.5	504.0	559.0	626.8
	SD	115.8	98.5	137.5	139.6	90.7	85.5	72.0	145.3
	MIN	374	499	353	397	427	394	494	431
	MAX	625	718	656	662	645	597	646	776
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	601.8	559.0	551.0	641.8	518.5	687.3	446.3	673.0
	SD	75.3	158.0	62.6	146.4	131.9	75.9	132.8	120.3
	MIN	515	476	465	436	356	580	278	499
	MAX	694	796	615	767	679	758	578	755
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	593.3	600.5	500.8	591.5	589.0	555.3	556.8	546.5
	SD	121.1	105.8	165.9	177.4	31.1	42.9	119.4	69.8
	MIN	473	471	311	452	553	511	383	472
	MAX	700	711	685	844	628	614	652	631
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 18

(b) (4)

DAILY FOOD CONSUMPTION (g
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 34	Day 34 to 35	Day 35 to 36	Day 36 to 37	Day 37 to 38	Day 38 to 39	Day 39 to 40	Day 40 to 41
1	(b) (4)								
	MEAN	618.6	514.4	557.0	631.2	584.2	675.8	620.2	557.6
	SD	98.6	109.0	127.2	66.8	112.7	89.5	158.9	113.6
	MIN	482	400	360	535	425	567	341	390
	MAX	753	643	710	696	707	761	727	676
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	SD	69.4	92.0	119.3	83.2	150.8	194.9	91.7	91.6
	MIN	466	509	356	513	465	521	622	451
	MAX	615	716	631	709	778	877	821	665
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	678.3	566.5	543.3	603.5	672.8	594.3	636.3	699.5
	SD	202.6	148.5	100.4	156.3	128.3	153.9	141.4	55.7
	MIN	380	396	465	407	486	410	462	638
	MAX	806	746	680	786	766	772	767	773
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	616.5	565.0	653.0	665.3	571.8	663.5	680.0	739.0
	SD	118.4	52.0	66.7	184.7	69.6	130.0	103.8	107.2
	MIN	512	510	580	449	492	551	568	639
	MAX	723	634	741	900	652	848	798	891
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 18

(b) (4)

DAILY FOOD CONSUMPTION (g)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 41 to 42	Day 42 to 43	Day 43 to 44	Day 44 to 45	Day 45 to 46	Day 46 to 47	Day 47 to 48	Day 48 to 49
1	(b) (4)								
	MEAN	728.0	631.0	694.4	593.0	733.2	794.6	642.2	690.8
	SD	136.6	127.5	95.4	118.2	144.4	120.1	181.3	147.7
	MIN	541	494	592	449	590	585	324	526
	MAX	891	810	837	769	900	893	768	818
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	628.0	679.5	625.3	629.8	706.0	775.8	576.5	752.0
	SD	127.1	68.4	132.5	101.9	111.9	148.6	257.6	156.3
	MIN	511	606	431	553	585	604	274	527
	MAX	770	770	728	780	856	900	846	873
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	721.3	609.3	712.0	657.8	690.5	716.0	704.5	750.0
	SD	94.3	151.2	35.9	91.4	187.8	224.7	173.2	119.0
	MIN	612	480	662	534	525	407	539	623
	MAX	841	812	741	734	900	900	858	900
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	721.0	644.8	683.5	670.3	844.3	720.8	777.3	680.5
	SD	10.9	71.9	121.2	118.1	65.1	131.3	125.0	111.4
	MIN	712	553	540	514	752	565	601	555
	MAX	736	702	833	780	900	885	890	823
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 18

(b) (4)

DAILY FOOD CONSUMPTION (g)
LACTATION PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 49 to 50	Day 50 to 51	Day 51 to 52	Day 52 to 53	Day 53 to 54	Day 54 to 55
1	(b) (4)						
	MEAN	622.2	749.2	629.6	783.0	706.6	739.6
	SD	132.1	139.5	120.9	127.3	159.6	153.6
	MIN	448	591	450	607	487	490
	MAX	757	900	751	900	893	900
	N	5	5	5	5	5	5
2	(b) (4)						
	MEAN	628.8	750.3	797.8	726.3	696.8	651.3
	SD	52.5	85.2	53.3	112.0	63.7	157.8
	MIN	560	654	734	617	621	495
	MAX	688	858	847	879	768	845
	N	4	4	4	4	4	4
3	(b) (4)						
	MEAN	653.8	727.5	726.8	755.0	626.8	633.8
	SD	168.6	109.9	163.0	157.7	54.1	37.4
	MIN	517	568	512	545	573	607
	MAX	897	816	900	887	700	689
	N	4	4	4	4	4	4
4	(b) (4)						
	MEAN	762.0	662.3	698.0	747.8	638.3	722.3
	SD	107.7	190.1	64.7	115.5	61.2	104.5
	MIN	613	422	644	609	582	618
	MAX	850	846	790	886	713	853
	N	4	4	4	4	4	4

APPENDIX NO. 18

(b) (4)

FOOD CONSUMPTION (g)
F0 GENERATION – LACTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
1	(b) (4)								
	MEAN	233.3	382.3	454.3	495.2	533.3	622.0	682.7	705.0
	SD	60.5	56.3	79.5	64.3	39.8	71.9	93.8	114.0
	MIN	154	340	349	412	498	499	553	556
	MAX	284	446	554	575	600	688	785	833
	N	5	5	5	5	5	5	5	5
2	(b) (4)								
	MEAN	269.8	437.6	475.9	550.4	558.5	615.3	677.8	708.5
	SD	158.6	31.6	65.3	58.6	58.1	57.4	53.4	34.9
	MIN	1	401	411	503	494	559	645	665
	MAX	388	470	553	631	632	694	758	748
	N	5	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	247.4	396.4	513.4	551.6	601.6	638.7	691.4	687.3
	SD	146.6	78.4	113.4	73.1	69.0	50.0	55.5	36.5
	MIN	85	349	454	509	514	589	643	648
	MAX	477	513	683	661	657	687	771	727
	N	5	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	269.2	376.5	460.5	544.2	574.4	670.5	717.3	705.1
	SD	127.3	100.8	73.3	46.0	22.2	25.3	52.4	69.5
	MIN	155	297	404	507	547	638	653	645
	MAX	397	524	568	606	597	697	772	783
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 18

(b) (4)

FOOD CONSUMPTION (g)
F0 GENERATION – LACTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED WEEKS (1 to 8)
1	(b) (4)	
	MEAN	513.5
	SD	64.1
	MIN	423
	MAX	582
	N	5
2	(b) (4)	
	MEAN	436.2
	SD	245.8
	MIN	1
	MAX	579
	N	5
3	(b) (4)	
	MEAN	453.8
	SD	213.6
	MIN	85
	MAX	635
	N	5
4	(b) (4)	
	MEAN	539.7
	SD	46.7
	MIN	506
	MAX	609
	N	4

(b) (4)

APPENDIX NO. 19
CLINICAL PATHOLOGY ABBREVIATIONS, METHODS AND UNITS

CLINICAL PATHOLOGY ABBREVIATIONS, METHODS AND UNITS

PARAMETER	ABBREVIATIONS	METHOD	UNITS	ALLOWABLE RESULTS	DECIMAL PLACES
HEMATOLOGY					
ADVIA 120 Analyzer [1]					
White Blood Cell Count	WBC	Light Scatter	$x10^9/L$	Numeric	2
Red Blood Cell Count	RBC	Light Scatter	$x10^{12}/L$	Numeric	2
Hemoglobin	HGB	Cyanmethemoglobin	g/L	Numeric	0
Hematocrit	HCT	Calculated	L/L	Numeric	2
Mean Corpuscular Volume	MCV	Light Scatter	fL	Numeric	1
Mean Corpuscular Hemoglobin	MCH	Calculated	pg	Numeric	1
Mean Corpuscular Hemoglobin Concentration	MCHC	Calculated	g/L	Numeric	0
Red Cell Distribution Width	RDW	Calculated	%	Numeric	1
Hemoglobin Distribution Width	HDW	Calculated	g/L	Numeric	1
Platelet Count	PLT	Light Scatter	$x10^9/L$	Numeric	0
Mean Platelet Volume	MPV	Light Scatter	fL	Numeric	1
Platelet Distribution Width	PDW	Calculated	%	Numeric	1
Plateletcrit/Thrombocrit	PCT	Calculated	L/L	Numeric	3
Neutrophils (relative)	NEUT	Peroxidase Channel	%	Numeric	1
Lymphocytes (relative)	LYMPH	Peroxidase Channel	%	Numeric	1
Monocytes (relative)	MONO	Peroxidase Channel	%	Numeric	1
Eosinophils (relative)	EOS	Peroxidase Channel	%	Numeric	1
Basophils (relative)	BASO	Basophil/Lobularity	%	Numeric	1
Large Unstained Cells (relative)	LUC	Peroxidase Channel	%	Numeric	1
Neutrophils (absolute)	NEUT	Calculated	$x10^9/L$	Numeric	2
Lymphocytes (absolute)	LYMPH	Calculated	$x10^9/L$	Numeric	2
Monocytes (absolute)	MONO	Calculated	$x10^9/L$	Numeric	2
Eosinophils (absolute)	EOS	Calculated	$x10^9/L$	Numeric	2
Basophils (absolute)	BASO	Calculated	$x10^9/L$	Numeric	2
Large Unstained Cells (absolute)	LUC	Calculated	$x10^9/L$	Numeric	2
Reticulocytes (relative)	RETIC	Light Scatter	%	Numeric	1
Reticulocytes (absolute)	RETIC	Calculated	$x10^9/L$	Numeric	1

Note 1: Due to system limitation, units '$x10^9$/ L' and '$x10^{12}$/ L' appear in (b) (4) eports and printouts as 'x10^9/ L' and 'x10^12/ L' respectively

CLINICAL PATHOLOGY ABBREVIATIONS, METHODS AND UNITS

PARAMETER	METHOD	UNITS	ALLOWABLE RESULTS	DECIMAL PLACES
HEMATOLOGY MORPHOLOGY				
Note For reporting of manual evaluation of morphology by microscopic examination, a 'plus' system of reporting is used N = Normal 1+ = Minimal 2+ = Mild 3+ = Moderate 4+ = Marked				
Normal Morphology		N/ A	N	N/ A
Hypochromia		N/ A	1+, 2+, 3+, 4+	N/ A
Anisocytosis		N/ A	1+, 2+, 3+, 4+	N/ A
Polychromasia		N/ A	1+, 2+, 3+, 4+	N/ A
Nucleated Red Blood Cells		/ 100 WBC	# of NRBC	N/ A
Large Platelets		N/ A	1+, 2+, 3+, 4+	N/ A
Platelet Clumps		N/ A	1+, 2+, 3+, 4+	N/ A
Howell-Jolly Bodies		N/ A	1+, 2+, 3+, 4+	N/ A
Red Blood Cell Parasite		N/ A	negative, positive	N/ A
Spherocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Eccentrocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Heinz Bodies		N/ A	1+, 2+, 3+, 4+	N/ A
Elliptocytosis		N/ A	1+, 2+, 3+, 4+	N/ A
Rouleaux		N/ A	1+, 2+, 3+, 4+	N/ A
Poikilocytosis		N/ A	1+, 2+, 3+, 4+	N/ A
Acanthocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Basophilic Stippling		N/ A	1+, 2+, 3+, 4+	N/ A
Elliptocytosis		N/ A	1+, 2+, 3+, 4+	N/ A
Ovalocytosis		N/ A	1+, 2+, 3+, 4+	N/ A
Schistocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Keratocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Echinocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Codocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Stomatocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Teardrop Cells		N/ A	1+, 2+, 3+, 4+	N/ A
Pappenheimer Bodies		N/ A	1+, 2+, 3+, 4+	N/ A
Band Neutrophils		N/ A	1+, 2+, 3+, 4+	N/ A
Immature Neutrophils		N/ A	1+, 2+, 3+, 4+	N/ A
Toxic Granules		N/ A	1+, 2+, 3+, 4+	N/ A
Vacuoles		N/ A	1+, 2+, 3+, 4+	N/ A
Cytoplasmic Basophilia		N/ A	1+, 2+, 3+, 4+	N/ A
Döhle Bodies		N/ A	1+, 2+, 3+, 4+	N/ A
Atypical Lymphocytes		N/ A	1+, 2+, 3+, 4+	N/ A
Smudge Cells		N/ A	1+, 2+, 3+, 4+	N/ A

APPENDIX NO. 19

[redacted] (b) (4)

CLINICAL PATHOLOGY ABBREVIATIONS, METHODS AND UNITS

PARAMETER	ABBREVIATIONS	METHOD	UNITS	ALLOWABLE RESULTS	DECIMAL PLACES
COAGULATION					
STA Compact					
Appearance (Plasma)[1]	APPP	Visual	N/ A	HE1, HE2, HE3 (Hemolysis)	
			N/ A	L1, L2, L3 (Lipemia)	
			N/ A	OP1,OP2,OP3 (Opalescence)	
			N/ A	I1, I2, I3 (Icterus)	
Prothrombin Time	PT	Mechanical	sec	Numeric	1
Activated Partial Thromboplastin Time	APTT	Mechanical	sec	Numeric	1
Fibrinogen	FIB	Mechanical	g/L	Numeric	1
D-Dimer	DDI	Immuno-Turbidimetric	µg/ mL	Numeric	2
Factor VIII	FVIII	Mechanical	%	Numeric	0

Note 1: H1, H2 and H3 (Hemolysis) previously accepted for plasma appearance

APPENDIX NO. 19 (b) (4)

CLINICAL PATHOLOGY ABBREVIATIONS, METHODS AND UNITS

PARAMETER	ABBREVIATIONS	METHOD	UNITS	ALLOWABLE RESULTS	DECIMAL PLACES
CLINICAL CHEMISTRY (SERUM)					
Cobas 6000 c501					
Appearance (Serum)[1]	APPS	Visual	N/ A	HE1, HE2, HE3 (Hemolysis)	
			N/ A	L1, L2, L3 (Lipemia)	
			N/ A	OP1,OP2,OP3 (Opalescence)	
			N/ A	I1, I2, I3 (Icterus)	
Albumin [2]	ALB	BCG	g/L	Numeric	1
Alkaline Phosphatase	ALP	p-NPP	U/L	Numeric	0
Amylase	AMYL	G7PNP	U/L	Numeric	0
Aspartate Aminotransferase	AST	ά-ketoglutarate	U/L	Numeric	0
Alanine Aminotransferase	ALT	ά-ketoglutarate	U/L	Numeric	0
Albumin/Globulin Ratio	A/G	Calculated	-	Numeric	2
Bicarbonate	HCO3	Enzymatic (PEPC)	mmol/L	Numeric	0
Bilirubin (Total)	BIL-T	Diazo	µmol/L	Numeric	1
Bilirubin (Total)	BILT3	Diazo Gen 3	µmol/L	Numeric	1
Bilirubin (Direct)	BILD	Diazo Gen.2	µmol/L	Numeric	1
Bilirubin (Indirect)	IBILI	Calculated	µmol/L	Numeric	1
Calcium (Total)	CA	5-Nitro-5'-methyl-BAPTA	mmol/L	Numeric	2
Chloride	Cl	Indirect Potentiometry	mmol/L	Numeric	0
Cholesterol (Total)	CHOL	Cholesterol Esterase	mmol/L	Numeric	2
Cholesterol (HDL)	HDL	Homogeneous enzymatic	mmol/L	Numeric	2
Cholesterol (LDL)	LDL	Homogeneous enzymatic	mmol/L	Numeric	2
Cholinesterase	CHE	Butyrylthiocholine	U/L	Numeric	0
Creatinine	CREA	Picric Acid	µmol/L	Numeric	0
Creatinine (enzymatic)	CREAT	Creatininase	µmol/L	Numeric	0
Creatine Kinase	CK	Creatine Phosphate	U/L	Numeric	0
Gamma Glutamyltransferase	GGT	GPNA	U/L	Numeric	0
Glutamate Dehydrogenase	GLDH3	Colorimetric Enzymatic	U/L	Numeric	1
Glucose	GLUC	Hexokinase	mmol/L	Numeric	1
Globulin	GLOB	Calculated	g/L	Numeric	1
Iron	IRON	Ferrozine	µmol/L	Numeric	1
Lactate Dehydrogenase	LDH	Pyruvate-NADH	U/L	Numeric	0
Lactate Dehydrogenase	LDHI2	L-Lactate-NAD+	U/L	Numeric	0
Lactate	LACT2	Pyruvate	mmol/L	Numeric	2
Lipase	LIPC	Colorimetric Enzymatic	U/L	Numeric	1
Magnesium	MG	Xylidyl Blue	mmol/L	Numeric	2
Non-Esterified Fatty Acids	NEFA	Enzymatic	mEq/L	Numeric	2
Potassium	K	Indirect Potentiometry	mmol/L	Numeric	2
Phosphorus (Inorganic)	PHOS	Molybdate Ammonium	mmol/L	Numeric	2
Phospholipids	PPL	Enzymatic	mg/dL	Numeric	0
Sodium	Na	Indirect Potentiometry	mmol/L	Numeric	0
Sorbitol Dehydrogenase	SDH	Fructose-NADH	U/ L	Numeric	1
Total Bile Acids	TBA	Cyclic Enzymatic	µmol/L	Numeric	1
Total Ketones	TKB	Cyclic Enzymatic	µmol/L	Numeric	2
Total Protein	TP	Biuret	g/L	Numeric	1
Triglycerides	TRIG	Lipoprotein Lipase	mmol/L	Numeric	2
Urea	UREA	Urease	mmol/L	Numeric	1
Urea Nitrogen	BUN	Calculated (UREA mmol/L X 2.8)	mg/dL	Numeric	1
Uric Acid	UA	Uricase	µmol/L	Numeric	0
Osmolality					
Advanced Micro Osmometer Model 3300	OSMO	Freezing Point Depression	mOsm/kg	Numeric	0

Note 1: H1, H2 and H3 (Hemolysis) previously accepted for serum appearance
Note 2: For rabbit studies method is BCP

(b) (4)

CLINICAL PATHOLOGY ABBREVIATIONS, METHODS AND UNITS

PARAMETER	ABBREVIATIONS	METHOD	UNITS	ALLOWABLE RESULTS	DECIMAL PLACES
URINALYSIS					
Appearance and Semi- Quantitative Chemical Analysis *Clinitek 500 (English SI Reporting)*					
Tr-Intact = Trace Intact Tr-Lysed = Trace Lysed					
Color *User selects from listed options or adds other colours as comment*	COL	Visual	N/ A	Yellow Orange Red Green Blue Brown	N/ A N/ A N/ A N/ A N/ A N/ A
Clarity *User selects from listed options or adds other appearance as comment*	CLA	Visual	N/ A	Clear Cloudy Turbid	N/ A N/ A N/ A
pH	pH	Spectrophotometry	N/ A	5 0 5 5 6 0 6 5 7 0 7 5 8 0 8 5 ≥ 9 0	1 1 1 1 1 1 1 1 1
Glucose	GLU	Spectrophotometry	mmol/ L	Negative 5 5 14 28 ≥ 55	N/ A 1 0 0 0
Bilirubin	BIL	Spectrophotometry	N/ A	Negative Small Moderate Large	N/ A N/ A N/ A N/ A
Ketone	KET	Spectrophotometry	mmol/ L	Negative Trace 1 5 3 9 ≥ 7 8	N/ A N/ A 1 1 1
Blood	BLD	Spectrophotometry	Ery/ µL	Negative Tr-Lysed Tr-Intact Approx 25 Approx 80 Approx 200	N/ A N/ A N/ A 0 0 0
Protein	PRO	Spectrophotometry	g/ L	Negative Trace 0 3 1 0 ≥ 3 0	N/ A N/ A 1 1 1
Urobilinogen	UBG	Spectrophotometry	µmol/L	3 2 16 33 66 ≥ 131	1 0 0 0 0
Nitrite	NIT	Spectrophotometry	N/ A	Negative Positive	N/ A N/ A
Leukocytes	LEU	Spectrophotometry	Leu/ µL	Negative Approx 15 Approx 70 Approx 125 Approx 500	N/ A 0 0 0 0
Ca = Circa					

APPENDIX NO. 19 (b) (4)

CLINICAL PATHOLOGY ABBREVIATIONS, METHODS AND UNITS

PARAMETER	ABBREVIATIONS	METHOD	UNITS	ALLOWABLE RESULTS	DECIMAL PLACES
URINALYSIS					
Miscellaneous Analysis					
Volume	VOL	-	mL	Numeric	1
Specific Gravity *Reichert AR200 Refractometer*	SG	Refractometry	N/A	Numeric	3
Osmolality *Advanced Micro Osmometer Model 3300*	OSMO	Freezing Point Depression	mOsm/kg	Numeric	0
Sediment Microscopy					
Microscopic Examination					
Casts					
Note: Allowable results alongside casts section apply to all cast types, and to urinary red and white blood cells (below)					
Granular	GC	-	/LPF	None	N/A
Hyaline	HC	-		<1	N/A
White Blood Cell	WBCC	-		1-5	N/A
Red Blood Cell	RBCC	-		6-10	N/A
		-		11-25	N/A
				>25	N/A
Blood Cells					
White Blood Cells	WBC	-	/HPF	See casts	N/A
Red Blood Cells	RBC	-		(above)	N/A
Crystals and Other Elements					
Note: For reporting of crystals and other elements, a 'plus' system of reporting is used:					
PR (Present) = <2/ hpf 1+ = 2-10 /hpf 2+ = 11-20 /hpf 3+ = >20 /hpf					
Amorphous Phosphate Crystals	AP	-	/HPF	1+, 2+, 3+	N/A
Amorphous Urate Crystals	AU	-		1+, 2+, 3+	N/A
Calcium Oxalate Crystals	CO	-		1+, 2+, 3+	N/A
Triple Phosphate Crystals	TP	-		1+, 2+, 3+	N/A
Calcium Carbonate Crystals	CC	-		1+, 2+, 3+	N/A
Uric Acid Crystals	UA	-		1+, 2+, 3+	N/A
Unidentified Crystals	UC	-		1+, 2+, 3+	N/A
Bilirubin Crystals	BILI	-		PR, 1+, 2+, 3+	N/A
Trichomonas	TC	-		PR, 1+, 2+, 3+	N/A
Ephithelial Cells	EPITH	-		1+, 2+, 3+	N/A
Bacteria	BACT	-		1+, 2+, 3+	N/A
Mucus	-	-		1+, 2+, 3+	N/A
Spermatozoa	SP	-		1+, 2+, 3+	N/A
Yeast	-	-		PR, 1+, 2+, 3+	N/A
Unidentified Substances	US	-		1+, 2+, 3+	N/A

APPENDIX NO. 20

(b) (4)

HEMATOLOGY
PRE-TREATMENT AND GESTATION PERIOD
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix and/or summary table

SD: Standard Deviation
MIN: Minimum
MAX: Maximum
N: Number of Animals
NT: Not Taken
NC: Not Calculable
U: Unscheduled

APPENDIX NO. 20

[redacted] (b) (4)

HEMATOLOGY
PRE-TREATMENT PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	[redacted] (b) (4)								
	MEAN	7.132	169.6	0.542	75.94	23.78	313.6	12.40	252.6
	SD	0.310	9.7	0.033	2 34	0.67	12.9	0.55	21.7
	MIN	6.72	158	0.51	72.8	23.0	302	11.9	227
	MAX	7.54	181	0.59	78.6	24.8	330	13.3	284
	N	5	5	5	5	5	5	5	5
2	[redacted] (b) (4)								
	MEAN	7.128	164.4	0.542	76.06	23.08	303.6	12.86	251.4
	SD	0.426	9.0	0.040	1.84	0.23	9.3	0.54	38.2
	MIN	6.68	155	0.49	72.8	22.8	298	12.4	206
	MAX	7.83	179	0.60	77.2	23.3	320	13.5	287
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 20

[redacted] (b) (4)

HEMATOLOGY
PRE-TREATMENT PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
3	[redacted] (b) (4)								
	MEAN	7.562	171.8	0.552	73.12	22.74	311.6	13.06	232.2
	SD	0.485	10.1	0.038	4.76	1.11	11.9	1.02	18.7
	MIN	7.01	164	0.51	65.0	21.1	300	12.2	215
	MAX	8.27	186	0.61	77.4	24.0	325	14.6	258
	N	5	5	5	5	5	5	5	5
4	[redacted] (b) (4)								
	MEAN	6.990	161.6	0.513	73.50	23.14	315.0	12.66	301.0
	SD	0.348	8.2	0.023	2.58	0.46	11.7	0.75	45.7
	MIN	6.65	153	0.48	71.4	22.6	300	11.8	256
	MAX	7.37	173	0.53	77.7	23.6	326	13.6	370
	N	5	5	5	5	5	5	5	5

APPENDIX NO. 20

[redacted] (b) (4)

HEMATOLOGY
PRE-TREATMENT PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	[redacted] (b) (4)							
	MEAN	9.144	5.968	2.412	0.458	0.246	0.032	0.026
	SD	1.744	1.506	0.339	0.036	0.092	0.013	0.018
	MIN	7.63	4.22	2.04	0.42	0.16	0.02	0.01
	MAX	11.87	8.16	2.75	0.50	0.40	0.05	0.05
	N	5	5	5	5	5	5	5
2	[redacted] (b) (4)							
	MEAN	8.916	6.202	2.024	0.392	0.260	0.024	0.018
	SD	0.343	0.297	0.370	0.084	0.119	0.011	0.004
	MIN	8 52	5.92	1.68	0.34	0.13	0.01	0.01
	MAX	9 28	6.68	2.50	0.54	0.44	0.04	0.02
	N	5	5	5	5	5	5	5

APPENDIX NO. 20

[redacted] (b) (4)

HEMATOLOGY
PRE-TREATMENT PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
3	[redacted] (b) (4)							
	MEAN	11.218	8.132	2.246	0.522	0.252	0.040	0.026
	SD	2.181	1.676	0.284	0.180	0.156	0.012	0.013
	MIN	9.08	6.34	1.92	0.25	0.09	0.02	0.01
	MAX	13.82	10.29	2.64	0.72	0.43	0.05	0.04
	N	5	5	5	5	5	5	5
4	[redacted] (b) (4)							
	MEAN	10.366	6.946	2.726	0.450	0.188	0.030	0.026
	SD	2.206	2.120	0.293	0.070	0.076	0.012	0.009
	MIN	6.65	3.60	2.44	0.33	0.09	0.01	0.02
	MAX	12.32	8.93	3.21	0.50	0.27	0.04	0.04
	N	5	5	5	5	5	5	5

APPENDIX NO. 20

[redacted] (b) (4)

HEMATOLOGY
PRE-TREATMENT PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	[redacted] (b) (4)								
	MEAN	64.70	26.84	5.12	2.66	0.38	0.32	NA	NA
	SD	5.54	4.95	0.67	0.56	0.20	0.22	NA	NA
	MIN	55.3	22.6	4.2	2.1	0.2	0.1	NA	NA
	MAX	68.8	35.0	5.9	3.4	0.7	0.6	NA	NA
	N	5	5	5	5	5	5	0	0
2	[redacted] (b) (4)								
	MEAN	69.58	22.64	4.40	2.96	0.28	0.18	NA	NA
	SD	2.36	3.48	1.09	1.43	0.13	0.04	NA	NA
	MIN	67.0	19.5	3.6	1.4	0.1	0.1	NA	NA
	MAX	72.8	27.0	6.3	5.1	0.4	0.2	NA	NA
	N	5	5	5	5	5	5	0	0

APPENDIX NO. 20

[redacted] (b) (4)

HEMATOLOGY
PRE-TREATMENT PERIOD
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
3	[redacted] (b) (4)								
	SD	2.55	1.75	1.32	1.02	0.11	0.11	NA	NA
	MIN	69.8	17.5	2.4	1.0	0.2	0.1	NA	NA
	MAX	75.7	22.2	5.8	3.2	0.5	0.4	NA	NA
	N	5	5	5	5	5	5	0	0
4	[redacted] (b) (4)								
	MEAN	65.74	27.48	4.42	1.80	0.34	0.26	NA	NA
	SD	8.06	7.50	0.55	0.63	0.15	0.09	NA	NA
	MIN	54.1	21.5	3.8	1.1	0.1	0.2	NA	NA
	MAX	72.5	38.8	5.0	2.7	0.5	0.4	NA	NA
	N	5	5	5	5	5	5	0	0

APPENDIX NO. 20

[redacted]

HEMATOLOGY
DAY 60 (UNSCHEDULED)
GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	MCV (fL)	MCH (pg)	RDW (%)	PLT (x10^9/L)
2	[redacted]					

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
2	[redacted]							

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
2	[redacted]								

APPENDIX NO. 21

(b) (4)

HEMATOLOGY
LACTATION PERIOD
F0 GENERATION

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

APPENDIX NO. 21

[redacted] (b) (4)

HEMATOLOGY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	[redacted] (b) (4)								
	MEAN	7.200	171.2	0.506	70.36	23.82	338.4	12.36	324.0
	SD	0.610	11.4	0.040	1 27	0.53	2.6	0.95	60.2
	MIN	6.62	158	0.46	68.8	23.0	334	11.4	223
	MAX	8.23	189	0.57	72.1	24.4	341	13.7	376
	N	5	5	5	5	5	5	5	5
2	[redacted] (b) (4)								
	MEAN	7.503	174.0	0.525	69.65	23.20	333.5	12.38	302.0
	SD	0.856	20.2	0.064	0.64	0.36	3.7	0.51	74.3
	MIN	6.77	156	0.47	69.0	22.9	329	11.8	214
	MAX	8.43	193	0.59	70.5	23.7	337	13.0	393
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 21

[redacted] (b) (4)

HEMATOLOGY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
3	[redacted] (b) (4)								
	MEAN	7.013	158.5	0.473	67.65	22.63	334.3	13.20	305.5
	SD	0.498	12.1	0.039	2.45	0.91	2.2	1.36	36.7
	MIN	6.40	148	0.44	65.0	21.7	332	12.0	276
	MAX	7.48	173	0.52	70.2	23.5	337	14.7	356
	N	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)								
	MEAN	7.093	162.8	0.483	68.40	22.95	335.8	13.18	332.0
	SD	0.304	12.6	0.034	3.81	1.39	2.4	1.61	56.4
	MIN	6.78	152	0.45	62.9	21.0	334	11.8	267
	MAX	7.45	181	0.53	71.7	24.3	339	15.5	384
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 21

[redacted] (b) (4)

HEMATOLOGY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	[redacted] (b) (4)							
	MEAN	7.518	4.014	2.294	0.402	0.746	0.034	0.032
	SD	1.718	0.934	0.682	0.082	0.523	0.011	0.015
	MIN	5.08	3.09	1.24	0.27	0.34	0.02	0.01
	MAX	9.46	5.16	2.97	0.48	1.56	0.05	0.05
	N	5	5	5	5	5	5	5
2	[redacted] (b) (4)							
	MEAN	7.698	5.000	1.868	0.308	0.463	0.038	0.020
	SD	0.393	0.337	0.632	0.045	0.254	0.013	0.000
	MIN	7 22	4.58	1.25	0.25	0.29	0.02	0.02
	MAX	8.03	5.37	2.73	0.36	0.84	0.05	0.02
	N	4	4	4	4	4	4	4

APPENDIX NO. 21

[redacted] (b) (4)

HEMATOLOGY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
3	[redacted] (b) (4)							
	MEAN	9.925	6.425	2.063	0.528	0.835	0.035	0.035
	SD	1.336	0.676	0.464	0.135	0.588	0.006	0.006
	MIN	8.62	5.51	1.60	0.34	0.27	0.03	0.03
	MAX	11.79	7.13	2.60	0.63	1.65	0.04	0.04
	N	4	4	4	4	4	4	4
4	[redacted] (b) (4)							
	MEAN	8.085	4.998	2.228	0.440	0.378	0.025	0.020
	SD	1.435	1.272	0.452	0.133	0.105	0.006	0.008
	MIN	6 23	3.12	1.74	0.32	0.30	0.02	0.01
	MAX	9 53	5.82	2.78	0.63	0.53	0.03	0.03
	N	4	4	4	4	4	4	4

APPENDIX NO. 21

[redacted] (b) (4)

HEMATOLOGY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	[redacted] (b) (4)								
	MEAN	53.78	30.10	5.48	9.74	0.42	0.44	29.40	0.42
	SD	6.53	3.79	1.45	6.49	0.16	0.22	5.91	0.11
	MIN	43.0	24.5	3.9	5.3	0.3	0.3	20.8	0.3
	MAX	60.8	33.9	7.5	20.8	0.7	0.8	33.8	0.5
	N	5	5	5	5	5	5	5	5
2	[redacted] (b) (4)								
	MEAN	65.28	24.03	3.98	5.93	0.48	0.28	30.35	0.38
	SD	7.67	7.08	0.51	3.08	0.13	0.05	18.50	0.21
	MIN	57.1	17.3	3.5	4.0	0.3	0.2	14.0	0.2
	MAX	74.5	33.9	4.7	10.5	0.6	0.3	50.8	0.6
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 21

[redacted] (b) (4)

HEMATOLOGY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
3	[redacted] (b) (4)								
	MEAN	64.98	20.78	5.38	8.18	0.35	0.35	32.20	0.48
	SD	3.69	3.97	1.51	4.77	0.06	0.06	3.72	0.05
	MIN	60.5	18.4	3.5	2.8	0.3	0.3	28.6	0.4
	MAX	69.2	26.7	7.2	14.0	0.4	0.4	36.6	0.5
	N	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)								
	MEAN	61.15	28.18	5.40	4.73	0.33	0.28	26.48	0.38
	SD	8.13	7.36	1.19	1.06	0.10	0.05	18.25	0.22
	MIN	50.1	22.5	4.1	3.4	0.2	0.2	14.8	0.2
	MAX	68.4	38.2	6.6	6.0	0.4	0.3	53.7	0.7
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 21

(b) (4)

HEMATOLOGY - MORPHOLOGY
DAY 56
LACTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
3	(b) (4)	Morphology N
4		Anisocytosis 1+

APPENDIX NO. 22

CLINICAL CHEMISTRY
PRE-TREATMENT AND GESTATION PERIOD
F0 GENERATION

The following abbreviations and footnote have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

U : Unscheduled

APPENDIX NO. 22

[redacted] (b) (4)

CLINICAL CHEMISTRY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	[redacted] (b) (4)									
	MEAN	26.6	32.6	50.6	5.81	4.714	0.479	4.14	3.57	44.2
	SD	5.9	7.9	23.7	0.94	0.478	0.068	0.31	0.44	6.3
	MIN	21	23	32	5.1	4.17	0.41	3.7	3.2	35
	MAX	35	44	83	6.8	5.26	0.58	4.4	4.3	53
	N	5	5	5	5	5	5	5	5	5
2	[redacted] (b) (4)									
	MEAN	27.0	28.8	38.4	4.79	5.714	0.475	3.56	3.71	47.7
	SD	3.4	3.1	6.8	0.76	0.164	0.083	0.47	0.54	7.9
	MIN	23	25	29	3.4	5.49	0.41	2.9	3.2	35
	MAX	31	32	46	5.1	5.91	0.61	4.3	4.3	53
	N	5	5	5	5	5	5	5	5	5

APPENDIX NO. 22

[redacted] (b) (4)

CLINICAL CHEMISTRY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
3	[redacted] (b) (4)									
	MEAN	23.8	28.2	42.8	5.47	6.123	0.538	3.62	3.43	51.5
	SD	2.5	7.1	7.3	0.76	1.296	0.114	0.27	0.96	7.1
	MIN	20	21	34	5.1	4.71	0.40	3.4	2.5	44
	MAX	26	37	53	6.8	8.00	0.66	3.9	5.0	62
	N	5	5	5	5	5	5	5	5	5
4	[redacted] (b) (4)									
	MEAN	27.6	33.0	40.8	5.81	5.475	0.509	4.10	3.79	44.2
	SD	3.3	4.2	7.4	0.94	0.843	0.092	0.67	1.17	0.0
	MIN	23	27	31	5.1	4.01	0 37	3.2	1.8	44
	MAX	32	38	48	6.8	6.09	0.60	4.9	4.6	44
	N	5	5	5	5	5	5	5	5	5

APPENDIX NO. 22

[redacted] (b) (4)

CLINICAL CHEMISTRY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	[redacted] (b) (4)									
	MEAN	61.60	32.60	29.00	1 140	2.640	1.247	146.2	4 360	112.4
	SD	5.50	2.07	4.30	0 152	0.095	0.106	0.4	0 241	1.1
	MIN	54.0	29.0	25.0	0.90	2.50	1.13	146	4 10	111
	MAX	69.0	34.0	36.0	1.30	2.75	1.36	147	4.70	114
	N	5	5	5	5	5	5	5	5	5
2	[redacted] (b) (4)									
	MEAN	59.80	33.20	26.60	1 260	2.685	1.214	145.8	4 520	113.0
	SD	1.10	1.10	1.82	0 114	0.052	0.109	1.3	0 148	1.2
	MIN	58.0	32.0	25.0	1.10	2.60	1.10	144	4 30	112
	MAX	61.0	35.0	29.0	1.40	2.73	1.39	147	4.70	115
	N	5	5	5	5	5	5	5	5	5

APPENDIX NO. 22

[redacted] (b) (4)

CLINICAL CHEMISTRY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
3	[redacted] (b) (4)									
	MEAN	62.80	34.80	28.00	1 260	2.700	1.266	147.0	4 240	112.6
	SD	3.11	1.48	1.87	0.055	0.047	0.090	1.6	0 182	0.9
	MIN	60.0	33.0	26.0	1.20	2.63	1.16	145	4.00	112
	MAX	68.0	37.0	31.0	1.30	2.75	1.36	149	4 50	114
	N	5	5	5	5	5	5	5	5	5
4	[redacted] (b) (4)									
	MEAN	61.60	32.60	29.20	1 120	2.650	1.298	146.4	4 520	113.6
	SD	1.34	0.89	1.10	0.084	0.047	0.126	0.5	0 377	2.3
	MIN	60.0	32.0	28.0	1.00	2.60	1.16	146	4 10	111
	MAX	63.0	34.0	31.0	1.20	2.73	1.49	147	5 10	117
	N	5	5	5	5	5	5	5	5	5

APPENDIX NO. 22

[redacted]

CLINICAL CHEMISTRY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	GGT (U/L)	AMYL (U/L)	MG (mmol/L)
1	[redacted]					
	MEAN	92.6	138.2	7.2	517.2	0.855
	SD	48.8	57.3	1.6	65.0	0.034
	MIN	46	69	5	454	0.82
	MAX	165	216	9	614	0.90
	N	5	5	5	5	5
2	[redacted]					
	SD	19.5	36.3	1.1	49.6	0.034
	MIN	83	123	5	505	0.82
	MAX	127	211	7	642	0.90
	N	5	5	5	5	5

APPENDIX NO. 22

[redacted]

CLINICAL CHEMISTRY
PRE-TREATMENT
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	GGT (U/L)	AMYL (U/L)	MG (mmol/L)
3	[redacted]					
	MEAN	92.0	120.2	6.6	610.6	0.855
	SD	32.3	52.1	0.9	129.1	0.018
	MIN	66	68	6	467	0.82
	MAX	147	185	8	803	0.86
	N	5	5	5	5	5
4	[redacted]					
	MEAN	111.0	165.0	6.8	665.2	0.847
	SD	36.7	63.8	1.5	228.8	0.037
	MIN	52	89	5	400	0.82
	MAX	142	257	9	1010	0.90
	N	5	5	5	5	5

APPENDIX NO. 22

[redacted]

CLINICAL CHEMISTRY
DAY 60 (UNSCHEDULED)
GESTATION PERIOD - FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	AST (U/L)	ALT (U/L)	ALP (U/L)
2	[redacted]			

GROUP NO.	ANIMAL NO.	A/G	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
2	[redacted]				

APPENDIX NO. 23

CLINICAL CHEMISTRY
LACTATION PERIOD
F0 GENERATION

The following abbreviations and footnote have been used throughout the appendix and/or summary table

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

NA: Not Applicable

<: Below the lower limit of quantification or Calculated using a measurement below the lower limit of quantification

APPENDIX NO. 23

[redacted] (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	APPS	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	[redacted] (b) (4)										
	MEAN		26.6	32.4	97.6	NA	6 940	0.512	5.44	5.54	46.0
	SD		3.2	10.6	53.4	NA	0.845	0.064	0.18	0.92	4.2
	MIN		23	26	49	NA	5.67	0.42	5.2	4.3	42
	MAX		31	51	187	NA	7.65	0.59	5.6	6.7	53
	N		5	5	5	0	5	5	5	5	5
2	[redacted] (b) (4)										
	MEAN		27.3	42.8	99.3	NA	6.823	0.405	4.73	5.45	47.8
	SD		4.6	22.9	22.9	NA	0.644	0.068	0.15	1.39	10.6
	MIN		22	30	77	NA	6 24	0.35	4.6	3.9	34
	MAX		32	77	120	NA	7.74	0.49	4.9	6.9	57
	N		4	4	4	0	4	4	4	4	4

APPENDIX NO. 23

[redacted]

CLINICAL CHEMISTRY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	APPS	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
[redacted]											
	MEAN		24.3	31.0	91.5	NA	6 995	0.385	5.75	6.25	48.8
	SD		1.7	5.5	30.6	NA	2 190	0.039	0.40	2.01	16.1
	MIN		22	27	60	NA	5.03	0.33	5.2	4.5	36
	MAX		26	39	131	NA	10.08	0.42	6.1	8.9	71
	N		4	4	4	0	4	4	4	4	4
4	[redacted]										
	SD		6.1	3.3	9.9	NA	0.866	0.111	0.61	1.13	3.1
	MIN		26	32	68	NA	4 91	0.29	4.9	4.0	35
	MAX		38	40	92	NA	6 91	0.56	6.3	6.4	42
	N		4	4	4	0	4	4	4	4	4

APPENDIX NO. 23

[redacted] (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	[redacted] (b) (4)									
	MEAN	61.30	34.36	26.94	1 278	2.548	1.102	146.2	4.602	106.6
	SD	2.94	1.77	1.64	0.075	0.041	0.141	1.1	0 176	2.0
	MIN	56.3	31.5	24.8	1.17	2.50	0.90	145	4 34	104
	MAX	63.8	35.9	28.9	1.38	2.61	1.23	148	4.81	109
	N	5	5	5	5	5	5	5	5	5
2	[redacted] (b) (4)									
	MEAN	60.03	35.55	24.48	1.458	2.550	1.240	147.3	4.713	108.1
	SD	1.54	1.30	1.60	0 128	0.170	0.324	1.5	0.473	0.8
	MIN	58.1	34.1	22.9	1.30	2.43	0.94	146	4 30	107
	MAX	61.5	36.7	26.7	1.60	2.80	1.69	149	5 36	109
	N	4	4	4	4	4	4	4	4	4

APPENDIX NO. 23

[redacted] (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
3	[redacted] (b) (4)									
	MEAN	61.58	35.60	25.98	1 370	2.538	1.103	147.5	4.640	107.1
	SD	1.58	1.70	0.46	0.076	0.084	0.112	1.9	0.428	2.6
	MIN	60.0	33.8	25.5	1.29	2.46	0.97	146	4 23	104
	MAX	63.6	37.9	26.5	1.47	2.62	1.23	150	5 24	110
	N	4	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)									
	SD	2.63	1.56	1.64	0.086	0.013	0.125	0.5	0 115	1.1
	MIN	58.7	32.4	24.4	1.23	2.49	0.91	146	4.63	106
	MAX	64.5	36.1	28.4	1.43	2.52	1.19	147	4.87	108
	N	4	4	4	4	4	4	4	4	4

APPENDIX NO. 23

[redacted] (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	GGT (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	[redacted] (b) (4)						
	SD	38.7	32.6	NA	0.28	27.5	0.050
	MIN	55	102	NA	1.5	352	0.80
	MAX	161	185	NA	1.9	418	0.92
	N	5	5	0	2	5	5
2	[redacted] (b) (4)						
	MEAN	94.5	155.8	NA	1.15	389.5	0.860
	SD	52.4	51.4	NA	0.21	43.8	0.042
	MIN	42	115	NA	1.0	330	0.81
	MAX	152	231	NA	1.3	435	0.90
	N	4	4	0	2	4	4

APPENDIX NO. 23

[redacted] (b) (4)

CLINICAL CHEMISTRY - LACTATION PERIOD
DAY 56
FEMALES
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	LDHI2 (U/L)	CK (U/L)	GGT (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
3	[redacted] (b) (4)						
	MEAN	59.0	112.3	NA	4.00	475.3	0.830
	SD	21.1	15.8	NA	4.24	97.7	0.022
	MIN	37	93	NA	1.0	380	0.81
	MAX	79	131	NA	7.0	585	0.86
	N	4	4	0	2	4	4
4	[redacted] (b) (4)						
	MEAN	112.0	170.3	NA	1.80	780.8	0.835
	SD	58.0	42.9	NA	NA	426.7	0.029
	MIN	31	113	NA	1.8	430	0.81
	MAX	164	216	NA	1.8	1389	0.86
	N	4	4	0	1	4	4

APPENDIX NO. 24 (b) (4)

MATERNAL PERFORMANCE
F0 GENERATION

The following abbreviations and footnotes have been used throughout the appendix

SD : Standard Deviation
N : Number of animals
MIN: Minimum
MAX: Maximun
NO : Start not observed
IPM: In progress in the morning
--: No data

APPENDIX NO. 24

[redacted]

MATERNAL PERFORMANCE
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DURATION OF PARTURATION (h)	NO. OF PUPS LIVE	NO. OF PUPS DEAD	NO. OF PUPS MALFORMED	OBSERVATIONS AT PARTURITION
1	[redacted]	9.13	5	2	0	3 pups with umbilical cord attached
		8.23	9	0	0	--
		7.22	7	0	0	--
		6.03	7	0	0	2 pups with umbilical cord attached
		12.38	6	2	0	3 pups with umbilical cord attached
	MEAN	8.600	6.8	0.8	0.0	
	SD	2.410	1.5	1.1	0.0	
	MIN	6.03	5.00	0.00	0.00	
	MAX	12.38	9.00	2.00	0.00	
	N	5	5	5	5	
2	[redacted]	NO	9	1	0	--
		10.27	11	1	0	--
		8.45	8	0	0	3 pups with umbilical cord attached
		6.68	4	0	0	--
		IPM	8	1	0	--
	MEAN	8.467	8.0	0.6	0.0	
	SD	1.792	2.5	0.5	0.0	
	MIN	6.68	4.00	0.00	0.00	
	MAX	10.27	11.00	1.00	0.00	
	N	3	5	5	5	

APPENDIX NO. 24

[redacted] (b) (4)

MATERNAL PERFORMANCE
F0 GENERATION

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DURATION OF PARTURATION (h)	NO. OF PUPS LIVE	NO. OF PUPS DEAD	NO. OF PUPS MALFORMED	OBSERVATIONS AT PARTURITION
3	[redacted] (b) (4)	5.37	6	0	0	2 pups with umbilical cord attached
		8.47	6	0	0	--
		18.55	9	2	0	--
		6.72	7	0	0	--
		NO	6	0	0	--
	MEAN	9.775	6.8	0.4	0.0	
	SD	5.986	1.3	0.9	0.0	
	MIN	5.37	6.00	0.00	0.00	
	MAX	18.55	9.00	2.00	0.00	
	N	4	5	5	5	
4	[redacted] (b) (4)	10.92	10	0	0	--
		7.12	9	0	0	--
		6.22	10	0	0	1 pup with umbilical cord attached
		6.90	9	0	0	1 pup with umbilical cord attached
	MEAN	7.788	9.5	0.0	0.0	
	SD	2.121	0.6	0.0	0.0	
	MIN	6.22	9.00	0.00	0.00	
	MAX	10.92	10.00	0.00	0.00	
	N	4	4	4	4	

(b) (4)

APPENDICES
F1 PUPPIES PRE-WEANING

LITTER SIZE - F1 GENERATION

The following abbreviations and footnote have been used throughout the appendix

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

--: No data

*: Calculation based on Day 1 live versus Day 0 Total

**: Calculation based on Day 2 live versus Day 2 total

***: Calculation based on Day 3 live versus Day 2 total

&: Calculation based on Day 4 live versus Day 2 total

&&: Calculation based on Day 5 live versus Day 5 total

$: Calculation based on Day 6 to 56 live versus Day 5 total

APPENDIX NO. 25

[redacted] (b) (4)

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

		PRE-CULLING											
GROUP NO.	ANIMAL NO.	DAY 0 Male	DAY 0 Female	DAY 0 Total	DAY 0 Live	DAY 0 Dead	DAY 0 % Live	DAY 1 Male	DAY 1 Female	DAY 1 Total	DAY 1 Live	DAY 1 Died	DAY 1 % Live*
1	[redacted] (b) (4)	4	3	7	5	2	71.43	2	3	5	5	0	71.43
		7	2	9	9	0	100.00	7	2	9	6	3	66.67
		2	5	7	7	0	100.00	2	5	7	7	0	100.00
		3	4	7	7	0	100.00	3	4	7	7	0	100.00
		7	1	8	6	2	75.00	5	1	6	6	0	75.00
	MEAN	4.600	3.000	7.600	6.800	0.800	89.286	3.800	3.000	6.800	6.200	0.600	82.62
	SD	2.302	1.581	0.894	1.483	1.095	14.725	2.168	1.581	1.483	0.837	1.342	16.14
	MIN	2.00	1.00	7.00	5.00	0.00	71.43	2.00	1.00	5.00	5.00	0.00	66.67
	MAX	7.00	5.00	9.00	9.00	2.00	100.00	7.00	5.00	9.00	7.00	3.00	100.00
	N	5	5	5	5	5	5	5	5	5	5	5	5
2	[redacted] (b) (4)	5	4	9	9	0	100.00	5	4	9	9	0	100.00
		6	6	12	11	1	91.67	5	6	11	11	0	91.67
		2	6	8	8	0	100.00	2	6	8	8	0	100.00
		1	3	4	4	0	100.00	1	3	4	4	0	100.00
		5	4	9	8	1	88.89	4	4	8	3	5	33.33
	MEAN	3.800	4.600	8.400	8.000	0.400	96.111	3.400	4.600	8.000	7.000	1.000	85.00
	SD	2.168	1.342	2.881	2.550	0.548	5.415	1.817	1.342	2.550	3.391	2.236	29.11
	MIN	1.00	3.00	4.00	4.00	0.00	88.89	1.00	3.00	4.00	3.00	0.00	33.33
	MAX	6.00	6.00	12.00	11.00	1.00	100.00	5.00	6.00	11.00	11.00	5.00	100.00
	N	5	5	5	5	5	5	5	5	5	5	5	5

APPENDIX NO. 25

(b) (4)

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

		PRE-CULLING											
GROUP NO.	ANIMAL NO.	DAY 0 Male	DAY 0 Female	DAY 0 Total	DAY 0 Live	DAY 0 Dead	DAY 0 % Live	DAY 1 Male	DAY 1 Female	DAY 1 Total	DAY 1 Live	DAY 1 Died	DAY 1 % Live*
3	(b) (4)	4	2	6	6	0	100.00	4	2	6	5	1	83.33
		3	3	6	6	0	100.00	3	3	6	5	1	83.33
		7	4	11	9	2	81.82	6	3	9	5	4	45.45
		2	5	7	7	0	100.00	2	5	7	7	0	100.00
		2	4	6	6	0	100.00	2	4	6	6	0	100.00
	MEAN	3.600	3.600	7.200	6.800	0.400	96.364	3.400	3.400	6.800	5.600	1.200	82.42
	SD	2.074	1.140	2.168	1.304	0.894	8.131	1.673	1.140	1.304	0.894	1.643	22.28
	MIN	2.00	2.00	6.00	6.00	0.00	81.82	2.00	2.00	6.00	5.00	0.00	45.45
	MAX	7.00	5.00	11.00	9.00	2.00	100.00	6.00	5.00	9.00	7.00	4.00	100.00
	N	5	5	5	5	5	5	5	5	5	5	5	5
4	(b) (4)	7	3	10	10	0	100.00	7	3	10	10	0	100.00
		4	5	9	9	0	100.00	4	5	9	9	0	100.00
		4	6	10	10	0	100.00	4	6	10	10	0	100.00
		6	3	9	9	0	100.00	6	3	9	9	0	100.00
	MEAN	5.250	4.250	9.500	9.500	0.000	100.000	5.250	4.250	9.500	9.500	0.000	100.00
	SD	1.500	1.500	0.577	0.577	0.000	0.000	1.500	1.500	0.577	0.577	0.000	0.00
	MIN	4.00	3.00	9.00	9.00	0.00	100.00	4.00	3.00	9.00	9.00	0.00	100.00
	MAX	7.00	6.00	10.00	10.00	0.00	100.00	7.00	6.00	10.00	10.00	0.00	100.00
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 25

[redacted]

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

CULLING - ADJUSTED UP TO 6 PUPPIES													
GROUP NO.	ANIMAL NO.	DAY 2 Male	DAY 2 Female	DAY 2 Total	DAY 2 Live	DAY 2 Died	DAY 2 % Live**	DAY 3 Male	DAY 3 Female	DAY 3 Total	DAY 3 Live	DAY 3 Died	DAY 3 % Live***
1	[redacted]	2	3	5	4	1	80.00	2	2	4	4	0	80.00
		4	2	6	5	1	83.33	3	2	5	5	0	83.33
		2	4	6	6	0	100.00	2	4	6	6	0	100.00
		3	3	6	6	0	100.00	3	3	6	6	0	100.00
		5	1	6	4	2	66.67	4	0	4	3	1	50.00
	MEAN	3.200	2.600	5.800	5.000	0.800	86.000	2.800	2.200	5.000	4.800	0.200	82.67
	SD	1.304	1.140	0.447	1.000	0.837	14.220	0.837	1.483	1.000	1.304	0.447	20.47
	MIN	2.00	1.00	5.00	4.00	0.00	66.67	2.00	0.00	4.00	3.00	0.00	50.00
	MAX	5.00	4.00	6.00	6.00	2.00	100.00	4.00	4.00	6.00	6.00	1.00	100.00
	N	5	5	5	5	5	5	5	5	5	5	5	5
2	[redacted]	3	3	6	6	0	100.00	3	3	6	6	0	100.00
		3	3	6	6	0	100.00	3	3	6	6	0	100.00
		2	4	6	6	0	100.00	2	4	6	6	0	100.00
		1	3	4	4	0	100.00	1	3	4	4	0	100.00
		2	1	3	0	3	0.00	--	--	--	--	--	--
	MEAN	2.200	2.800	5.000	4.400	0.600	80.000	2.250	3.250	5.500	5.500	0.000	100.00
	SD	0.837	1.095	1.414	2.608	1.342	44.721	0.957	0.500	1.000	1.000	0.000	0.00
	MIN	1.00	1.00	3.00	0.00	0.00	0.00	1.00	3.00	4.00	4.00	0.00	100.00
	MAX	3.00	4.00	6.00	6.00	3.00	100.00	3.00	4.00	6.00	6.00	0.00	100.00
	N	5	5	5	5	5	5	4	4	4	4	4	4

APPENDIX NO. 25

[redacted]

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

		CULLING - ADJUSTED UP TO 6 PUPPIES											
GROUP NO.	ANIMAL NO.	DAY 2 Male	DAY 2 Female	DAY 2 Total	DAY 2 Live	DAY 2 Died	DAY 2 % Live**	DAY 3 Male	DAY 3 Female	DAY 3 Total	DAY 3 Live	DAY 3 Died	DAY 3 % Live***
3	[redacted]	3	2	5	5	0	100.00	3	2	5	5	0	100.00
		3	2	5	2	3	40.00	1	1	2	1	1	20.00
		4	1	5	5	0	100.00	4	1	5	5	0	100.00
		2	4	6	6	0	100.00	2	4	6	6	0	100.00
		2	4	6	6	0	100.00	2	4	6	6	0	100.00
	MEAN	2.800	2.600	5.400	4.800	0.600	88.000	2.400	2.400	4.800	4.600	0.200	84.00
	SD	0.837	1.342	0.548	1.643	1.342	26.833	1.140	1.517	1.643	2.074	0.447	35.78
	MIN	2.00	1.00	5.00	2.00	0.00	40.00	1.00	1.00	2.00	1.00	0.00	20.00
	MAX	4.00	4.00	6.00	6.00	3.00	100.00	4.00	4.00	6.00	6.00	1.00	100.00
		5	5	5	5	5	5	5	5	5	5	5	5
4	[redacted]	3	3	6	6	0	100.00	3	3	6	6	0	100.00
		3	3	6	6	0	100.00	3	3	6	5	1	83.33
		3	3	6	6	0	100.00	3	3	6	6	0	100.00
		3	3	6	6	0	100.00	3	3	6	6	0	100.00
	MEAN	3.000	3.000	6.000	6.000	0.000	100.000	3.000	3.000	6.000	5.750	0.250	95.83
	SD	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.500	0.500	8.33
	MIN	3.00	3.00	6.00	6.00	0.00	100.00	3.00	3.00	6.00	5.00	0.00	83.33
	MAX	3.00	3.00	6.00	6.00	0.00	100.00	3.00	3.00	6.00	6.00	1.00	100.00
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 25

(b) (4)

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

								CULLING - ADJUSTED UP TO 4 PUPPIES					
GROUP NO.	ANIMAL NO.	DAY 4 Male	DAY 4 Female	DAY 4 Total	DAY 4 Live	DAY 4 Died	DAY 4 % Live&	DAY 5 Male	DAY 5 Female	DAY 5 Total	DAY 5 Live	DAY 5 Died	DAY 5 % Live&&
1	(b) (4)	2	2	4	4	0	80.00	2	2	4	4	0	100.00
		3	2	5	5	0	83.33	2	2	4	4	0	100.00
		2	4	6	6	0	100.00	2	2	4	4	0	100.00
		3	3	6	6	0	100.00	2	2	4	4	0	100.00
		3	0	3	3	0	50.00	3	0	3	3	0	100.00
	MEAN	2.600	2.200	4.800	4.800	0.000	82.67	2.200	1.600	3.800	3.800	0.000	100.00
	SD	0.548	1.483	1.304	1.304	0.000	20.47	0.447	0.894	0.447	0.447	0.000	0.00
	MIN	2.00	0.00	3.00	3.00	0.00	50.00	2.00	0.00	3.00	3.00	0.00	100.00
	MAX	3.00	4.00	6.00	6.00	0.00	100.00	3.00	2.00	4.00	4.00	0.00	100.00
	N	5	5	5	5	5	5	5	5	5	5	5	5
2	(b) (4)	3	3	6	6	0	100.00	2	2	4	4	0	100.00
		3	3	6	6	0	100.00	2	2	4	4	0	100.00
		2	4	6	6	0	100.00	2	2	4	4	0	100.00
		1	3	4	4	0	100.00	1	3	4	4	0	100.00
	MEAN	2.250	3.250	5.500	5.500	0.000	100.000	1.750	2.250	4.000	4.000	0.000	100.00
	SD	0.957	0.500	1.000	1.000	0.000	0.000	0.500	0.500	0.000	0.000	0.000	0.00
	MIN	1.00	3.00	4.00	4.00	0.00	100.00	1.00	2.00	4.00	4.00	0.00	100.00
	MAX	3.00	4.00	6.00	6.00	0.00	100.00	2.00	3.00	4.00	4.00	0.00	100.00
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 25

[redacted] (b) (4)

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

								CULLING - ADJUSTED UP TO 4 PUPPIES					
GROUP NO.	ANIMAL NO.	DAY 4 Male	DAY 4 Female	DAY 4 Total	DAY 4 Live	DAY 4 Died	DAY 4 % Live&	DAY 5 Male	DAY 5 Female	DAY 5 Total	DAY 5 Live	DAY 5 Died	DAY 5 % Live&&
3	[redacted] (b) (4)	3	2	5	5	0	100.00	2	2	4	4	0	100.00
		0	1	1	1	0	20.00	0	1	1	0	1	0.00
		4	1	5	5	0	100.00	3	1	4	4	0	100.00
		2	4	6	6	0	100.00	2	2	4	4	0	100.00
		2	4	6	6	0	100.00	2	2	4	4	0	100.00
	MEAN	2.200	2.400	4.600	4.600	0.000	84.00	1.800	1.600	3.400	3.200	0.200	80.00
	SD	1.483	1.517	2.074	2.074	0.000	35.78	1.095	0.548	1.342	1.789	0.447	44.72
	MIN	0.00	1.00	1.00	1.00	0.00	20.00	0.00	1.00	1.00	0.00	0.00	0.00
	MAX	4.00	4.00	6.00	6.00	0.00	100.00	3.00	2.00	4.00	4.00	1.00	100.00
	N	5	5	5	5	5	5	5	5	5	5	5	5
4	[redacted] (b) (4)	3	3	6	6	0	100.00	2	2	4	4	0	100.00
		3	2	5	4	1	66.67	3	1	4	4	0	100.00
		3	3	6	6	0	100.00	2	2	4	4	0	100.00
		3	3	6	6	0	100.00	2	2	4	4	0	100.00
	MEAN	3.000	2.750	5.750	5.500	0 250	91.67	2.250	1.750	4.000	4.000	0.000	100.00
	SD	0.000	0.500	0.500	1.000	0 500	16.67	0.500	0.500	0.000	0.000	0.000	0.00
	MIN	3.00	2.00	5.00	4.00	0.00	66.67	2.00	1.00	4.00	4.00	0.00	100.00
	MAX	3.00	3.00	6.00	6.00	1.00	100.00	3.00	2.00	4.00	4.00	0.00	100.00
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 25

[redacted]

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

		POST CULLING					
GROUP NO.	ANIMAL NO.	DAY 6 to 56 Male	DAY 6 to 56 Female	DAY 6 to 56 Total	DAY 6 to 56 Live	DAY 6 to 56 Died	DAY 6 to 56 % Live$
1	[redacted]	2	2	4	4	0	100.00
		2	2	4	4	0	100.00
		2	2	4	4	0	100.00
		2	2	4	4	0	100.00
		3	0	3	3	0	100.00
	MEAN	2.200	1.600	3.800	3.800	0.000	100.000
	SD	0.447	0.894	0.447	0.447	0.000	0.000
	MIN	2.00	0.00	3.00	3.00	0.00	100.00
	MAX	3.00	2.00	4.00	4.00	0.00	100.00
	N	5	5	5	5	5	5
2	[redacted]	2	2	4	4	0	100.00
		2	2	4	4	0	100.00
		2	2	4	4	0	100.00
		1	3	4	4	0	100.00
	MEAN	1.750	2.250	4.000	4.000	0.000	100.000
	SD	0.500	0.500	0.000	0.000	0.000	0.000
	MIN	1.00	2.00	4.00	4.00	0.00	100.00
	MAX	2.00	3.00	4.00	4.00	0.00	100.00
	N	4	4	4	4	4	4

APPENDIX NO. 25

[redacted] (b) (4)

LITTER SIZE - F1 GENERATION
PUP COUNT
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	POST CULLING DAY 6 to 56 Male	DAY 6 to 56 Female	DAY 6 to 56 Total	DAY 6 to 56 Live	DAY 6 to 56 Dead	DAY 6 to 56 % Live$
3	[redacted] (b) (4)	2	2	4	4	0	100.00
		3	1	4	4	0	100.00
		2	2	4	4	0	100.00
		2	2	4	4	0	100.00
	MEAN	2.250	1.750	4.000	4.000	0.000	100.000
	SD	0.500	0.500	0.000	0.000	0.000	0.000
	MIN	2.00	1.00	4.00	4.00	0.00	100.00
	MAX	3.00	2.00	4.00	4.00	0.00	100.00
	N	4	4	4	4	4	4
4	[redacted] (b) (4)	2	2	4	4	0	100.00
		3	1	4	4	0	100.00
		2	2	4	4	0	100.00
		2	2	4	4	0	100.00
	MEAN	2.250	1.750	4.000	4.000	0.000	100.000
	SD	0.500	0.500	0.000	0.000	0.000	0.000
	MIN	2.00	1.00	4.00	4.00	0.00	100.00
	MAX	3.00	2.00	4.00	4.00	0.00	100.00
	N	4	4	4	4	4	4

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATIONS
F1 GENERATION PUPPIES

The following abbreviations and footnote have been used throughout the appendix:

F : Female
M : Male
#: Severity not recorded
Ab: Aberrant data

APPENDIX NO. 26

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
1		(b) (4)	M	2, 3	Skin Scab - Cervical Dorsal
				25 to 28	Swelling Soft - Flank Left - Slight
				29 to 33	Swelling Firm - Flank Left - Slight
				4, 34	Puppy Normal
			M	2 to 8	Skin Scab - Cervical Dorsal
				25 to 28, 32	Swelling Soft - Flank Left - Slight
				29 to 31	Swelling Firm - Flank Left - Slight
				41	Skin Red - Urogenital
				41	Skin Red - Penis
				9, 33, 42	Puppy Normal
			F	25 to 33	Swelling Soft - Flank Left - Slight
				41	Skin Red - Abdominal
				34, 42	Puppy Normal
			F	2 to 4	Skin Scab - Cervical Dorsal
				25 to 28, 31 to 33	Swelling Soft - Flank Left - Slight
				29, 30	Thin - Slight
				29, 30	Swelling Firm - Flank Left - Slight
				5, 34	Puppy Normal
		(b) (4)	M	26 to 33	Swelling Firm - Flank Right - Slight
				34	Puppy Normal
				52 to 56	Skin Red - Penis
				56	Puppy Weaned
			M	0	Skin Turgor Slow - Slight
				1	Skin Turgor Slow - Moderate
				1	Thin - Slight
				1	Cold To Touch
				1	Respiratory Rate - Decreased
				1	Activity Decreased - Slight
				2	Puppy Found Dead
			M	0, 5 to 7, 15	Skin Turgor Slow - Slight
				1, 2 to 13	Thin - Slight
				1 to 4	Skin Turgor Slow - Moderate
				25 to 37	Swelling Firm - Flank Right - Slight
				40, 41	Skin Red - Abdominal
				14, 16, 38, 42	Puppy Normal
			M	1	Cold To Touch
				1	Lying on Cage Floor

APPENDIX NO. 26

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
1		(b) (4)	M	1	Activity Decreased - Severe
				1	Skin Turgor Slow - Severe
				1	Thin #
				1	Respiratory Rate - Decreased
				1	Weak - Severe
				1	Puppy Found Dead
			M	0	Skin Turgor Slow - Slight
				1	Puppy Found Dead
			F	0, 4	Skin Turgor Slow - Slight
				26 to 34	Swelling Firm - Flank Right - Slight
				1, 5, 35	Puppy Normal
			F	2 to 4	Skin Turgor Slow - Slight
				26 to 38	Swelling Firm - Flank Right - Slight
				5, 39	Puppy Normal
			M	26 to 29	Swelling Firm - Flank Left - Slight
				30, 31	Swelling Soft - Flank Left - Slight
				32	Puppy Normal
			M	26 to 29	Swelling Firm - Flank Left - Slight
				30 to 32	Swelling Soft - Flank Left - Slight
				52 to 54	Skin Scab - Penis
				33, 55	Puppy Normal
			F	1	Skin Turgor Slow - Slight
				1	Puppy Culled
			F	25 to 30	Swelling Firm - Flank Left - Slight
				31 to 35	Swelling Soft - Flank Left - Slight
				36	Puppy Normal
		(b) (4)	F	2, 3	Skin Turgor Slow - Slight
				4	Puppy Normal
				4	Puppy Culled
			F	2 to 4	Skin Turgor Slow - Slight
				2 to 4	Thin - Slight
				4	Puppy Culled
			F	29 to 29, 32 to 40	Swelling Firm - Flank Left - Slight
				30, 31	Swelling Firm - Flank Left - Moderate

(b) (4)

APPENDIX NO. 26

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
1	(b) (4)		F	52	Material Vomitus Beige - During Rx - Slight
				41, 53	Puppy Normal
				55	Skin Red - Abdominal
				56	Skin Red - Cervical Ventral
				56	Puppy Weaned
			M	1	Skin Turgor Slow - Slight
				2, 3	Skin Scab - Cervical Dorsal
				25, 26, 32	Swelling Soft - Flank Left - Slight
				27 to 31	Swelling Firm - Flank Left - Slight
				48 to 52	Skin Dry - Hindpaw Left
				48 to 52	Skin Dry - Hindpaw Right
				54, 55	Skin Red - Urogenital
				4, 33, 53, 56	Puppy Normal
			M	25, 26	Swelling Soft - Flank Left - Slight
				27 to 29, 33, 34	Swelling Firm - Flank Left - Slight
				30 to 32	Swelling Firm - Flank Left - Moderate
				49 to 52	Skin Dry - Hindpaw Left
				49 to 52	Skin Dry - Hindpaw Right
				35, 53	Puppy Normal
			F	25, 26	Swelling Soft - Flank Left - Slight
				27 to 33	Swelling Firm - Flank Left - Slight
				39	Skin Red - Abdominal
				48 to 52	Skin Dry - Hindpaw Left
				48 to 52	Skin Dry - Hindpaw Right
				34, 40, 53	Puppy Normal
			F	25, 26	Swelling Soft - Flank Left - Slight
				27 to 34	Swelling Firm - Flank Left - Slight
				50 to 52	Skin Dry - Hindpaw Left
				50 to 52	Skin Dry - Hindpaw Right
				35, 53	Puppy Normal
			M	2	Thin - Slight
				2	Cold To Touch
				3	Puppy Found Dead
			M	1 to 26, 28 to 32	Thin - Slight
				2 to 11	Skin Turgor Slow - Slight
				27	Swelling Firm - Flank Right - Slight
				33	Puppy Normal
				36 to 56	Fur Dull - Forelimb Left

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
1	(b) (4)		M	36 to 56	Fur Dull - Forelimb Right
				36 to 53, 55, 56	Fur Dull - Hindlimb Left
				36 to 53, 55, 56	Fur Dull - Hindlimb Right
				54	Skin Wound with Discharge - Penis - Slight
				54	Fur Dull - Forepaw Left
				54	Fur Dull - Forepaw Right
				55, 56	Skin Scab - Penis
				56	Puppy Weaned
			M	8 to 17	Skin Scab - Thoracic Dorsal
				8	Skin Wound - Thoracic Dorsal - Slight
				27 to 31	Swelling Firm - Flank Right - Slight
				18, 32	Puppy Normal
				36 to 56	Fur Dull - Forelimb Left
				36 to 56	Fur Dull - Forelimb Right
				36 to 56	Fur Dull - Hindlimb Left
				36 to 56	Fur Dull - Hindlimb Right
				56	Puppy Weaned
			M	0, 1	Thin - Slight
				0, 1	Cold To Touch
				2	Puppy Found Dead
			M	27 to 30	Swelling Firm - Flank Right - Slight
				31	Puppy Normal
				36 to 56	Fur Dull - Forelimb Left
				36 to 56	Fur Dull - Forelimb Right
				36 to 56	Fur Dull - Hindlimb Left
				36 to 56	Fur Dull - Hindlimb Right
				56	Puppy Weaned
			F	0, 1	Thin - Slight
				1	Cold To Touch
				2	Puppy Found Dead
2	(b) (4)		M	26, 27	Swelling Firm - Flank Right - Slight
				28	Swelling Soft - Flank Right - Slight
				29	Puppy Normal
				45 to 56	Skin Red - Abdominal
				54 to 56	Skin Red - Penis
				56	Puppy Weaned
			M	23	Skin Red - Urogenital
				26	Discharge Red - Mouth - Slight

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATIO
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
2	(b) (4)		M	28	Skin Lump - Flank Right
				24, 27, 29	Puppy Normal
				44 to 56	Skin Red - Abdominal
				54 to 56	Skin Red - Penis
				56	Puppy Weaned
			F	0, 1, 4	Thin #
				0, 1, 3	Skin Turgor Slow - Slight
				2, 3	Thin - Slight
				4	Puppy Culled
			F	5	Skin Scab - Abdominal
				31, 32	Skin Lump - Abdominal
				45, 46	Skin Red - Abdominal
				6, 33, 47	Puppy Normal
			F	2	Skin Wound - Abdominal
				3 to 5	Skin Scab - Abdominal
				26	Swelling Firm - Flank Right - Slight
				28	Skin Lump - Flank Right
				52 to 54	Skin Scab - Vulva
				52 to 54	Skin Red - Vulva
				6, 27, 29, 55	Puppy Normal
			M	27 to 37	Swelling Firm - Flank Right - Slight
				52 to 55	Skin Red - Abdominal
				52 to 54	Skin Red - Penis
				38, 56	Puppy Normal
			M	27 to 31	Swelling Firm - Flank Right - Slight
				49	Skin Scab - Penis
				49 to 54	Skin Red - Penis
				51	Skin Red - Forepaw Right
	(b) (4)			54, 55	Skin Red - Abdominal
				32, 56	Puppy Normal
			F	0 to 3	Thin - Slight
				27 to 31	Swelling Firm - Flank Right - Slight
				4, 32	Puppy Normal
			F	1	Thin - Slight
				1	Puppy Culled

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATIO
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
2		(b) (4)	F	27 to 30	Swelling Firm - Flank Right - Slight
				31	Puppy Normal
				56	Fur Stained Red - Cervical Ventral
				56	Puppy Weaned
			M	27	Swelling Soft - Flank Right - Slight
				32	Ab
				28, 33	Puppy Normal
				56	Skin Scab - Cervical Ventral
				56	Puppy Weaned
			M	27	Swelling Soft - Flank Right - Slight
				28, 29	Swelling Firm - Flank Right - Slight
				30	Puppy Normal
			F	26	Discharge Red - Mouth - Slight
				27	Swelling Soft - Flank Right - Slight
				28, 29	Swelling Firm - Flank Right - Slight
				31 to 34	Skin Scab - Pinna Right
				30, 35	Puppy Normal
			F	0 to 3	Thin - Slight
				1, 2	Skin Turgor Slow - Slight
				27	Swelling Soft - Flank Right - Slight
				28 to 30	Swelling Firm - Flank Right - Slight
				4, 31	Puppy Normal
			M	25 to 28	Swelling Firm - Flank Left - Slight
				29	Swelling Soft - Flank Left - Slight
				30	Puppy Normal
				48 to 56	Skin Dry - Hindpaw Left
				50 to 56	Skin Dry - Hindpaw Right
				55	Skin Red - Penis
				56	Puppy Weaned
			F	25, 26, 29 to 32	Swelling Firm - Flank Left - Slight
				27, 28	Swelling Soft - Flank Left - Slight
				46 to 50, 54 to 56	Skin Dry - Forepaw Left
				46 to 49, 54 to 56	Skin Dry - Forepaw Right
				47 to 50, 54 to 56	Skin Dry - Hindpaw Left
				47 to 49, 54 to 56	Skin Dry - Hindpaw Right
				33, 51	Puppy Normal
				56	Puppy Released

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
2	(b) (4)		F	25 to 36	Swelling Firm - Flank Left - Slight
				37	Puppy Normal
				46 to 49	Skin Dry - Forepaw Left
				46 to 49	Skin Dry - Forepaw Right
				50 to 56	Skin Dry - Hindpaw Left
				50 to 56	Skin Dry - Hindpaw Right
				56	Puppy Released
			F	1, 2	Skin Turgor Slow
				3 to 5	Skin Scab - Cervical Dorsal
				25 to 29, 31 to 36	Swelling Firm - Flank Left - Slight
				25 to 27, 29, 32, 41 to 43	Skin Red - Abdominal
				30	Swelling Firm - Flank Left - Moderate
				37 to 42	Swelling Soft - Flank Left - Slight
				6, 44	Puppy Normal
				46 to 56	Skin Dry - Hindpaw Left
				46 to 56	Skin Dry - Hindpaw Right
				48, 49	Skin Dry - Forepaw Left
				56	Puppy Weaned
			M	0	Weak - Slight
				0	Cold To Touch
				1	Puppy Found Dead
			M	1	Weak - Slight
				1	Cold To Touch
				2	Puppy Found Dead
			M	1	Weak - Slight
				1	Cold To Touch
				2	Puppy Found Dead or Missing
			F	0	Weak - Slight
				0	Cold To Touch
				1	Puppy Found Dead
			F	0, 1	Weak - Slight
				1	Cold To Touch
				2	Puppy Found Dead or Missing
			F	0	Skin Wound - Cervical Dorsal - Moderate
				0	Weak - Slight
				0	Cold To Touch
				1	Puppy Found Dead

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
3		(b) (4)	M	27, 28	Swelling Firm - Flank Right - Slight
				29	Puppy Normal
			M	27, 28	Swelling Firm - Flank Right - Slight
				29	Puppy Normal
			M	0	Thin - Slight
				0	Skin Wound - Abdominal - Moderate
				0	Cold To Touch
				1	Puppy Found Dead
			F	26 to 29	Swelling Firm - Flank Right - Slight
				30	Puppy Normal
				56	Skin Scab - Cervical Ventral
				56	Puppy Weaned
			F	0 to 4	Thin - Slight
				27 to 36	Swelling Firm - Flank Right - Slight
				5, 37	Puppy Normal
			M	2	Skin Turgor Slow - Slight
				2	Thin - Slight
				3	Puppy Found Dead
			M	0	Thin - Slight
				0, 1	Cold To Touch
				0	Skin Turgor Slow - Slight
				1	Skin Turgor Slow - Severe
				1	Thin #
				1	Activity Decreased - Slight
				2	Puppy Found Dead
			F	0, 1	Cold To Touch
				1	Skin Turgor Slow - Slight
				2	Puppy Found Dead
			F	0	Skin Wound - Abdominal - Moderate
				0	Respiration Labored - Moderate
				0	Cold To Touch
				0	Fur Wet - Abdominal
				0	Fur Stained Yellow - Abdominal
				0	Fur Wet - Urogenital
				0	Fur Stained Yellow - Urogenital
				0	Fur Wet - Hindpaw Left

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
3	(b) (4)		F	0	Fur Wet - Hindpaw Right
				1	Puppy Found Dead
			M	3	Skin Turgor Slow - Slight
				4	Skin Turgor Slow - Moderate
				4	Thin - Slight
				4	Activity Decreased - Slight
				4	Puppy Culled
			M	27	Swelling Soft - Flank Right - Slight
				28 to 32	Swelling Firm - Flank Right - Slight
				49 to 51	Skin Scab - Penis
			M	49, 51, 52	Skin Red - Penis
				33, 53	Puppy Normal
			M	2, 3	Skin Turgor Slow - Slight
				27	Swelling Soft - Flank Right - Slight
				28 to 32	Swelling Firm - Flank Right - Slight
				52, 56	Skin Red - Abdominal
				4, 33, 53	Puppy Normal
				56	Skin Scab - Cervical Ventral
				56	Puppy Weaned
			M	0	Cold To Touch
				0	Skin Turgor Slow - Slight
				1	Puppy Found Dead
			M	1	Skin Wound - Abdominal
				2 to 6	Thin - Slight
				2, 3	Skin Scab - Abdominal
				7	Puppy Normal
				12 to 27 to 56	Skin Blue - Penis
				27	Swelling Firm - Flank Right - Slight
				56	Puppy Weaned
			F	1 to 6	Thin - Slight
				3, 5, 6	Skin Turgor Slow - Slight
				27	Swelling Soft - Flank Right - Slight
				28 to 31	Swelling Firm - Flank Right - Slight
				32 to 49, 53 to 56	Skin Red - Abdominal
				32 to 34, 41 to 47	Skin Scab - Abdominal
				7, 50	Puppy Normal

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
		(b) (4)			
3			F	52	Skin Red - Hindlimb Left
				56	Puppy Weaned
			M	27, 28	Swelling Soft - Flank Right - Slight
				29	Puppy Normal
			M	27 to 30	Swelling Soft - Flank Right - Slight
				31	Puppy Normal
			F	27 to 33	Swelling Soft - Flank Right - Slight
				34	Puppy Normal
			F	5	Skin Turgor Slow - Slight
				34, 35	Thin - Slight
				41 to 46	Skin Red - Abdominal
				6, 36, 47	Puppy Normal
			M	35 to 39	Skin Red - Abdominal
				40	Puppy Normal
			M	26, 36 to 40	Skin Red - Abdominal
				27, 41	Puppy Normal
				56	Skin Red - Cervical Ventral
				56	Puppy Weaned
			F	30	Swelling Soft - Flank Right - Slight
				35 to 41	Skin Red - Abdominal
			F	35 to 37	Fur Stained Brown - Abdominal
				31, 42	Puppy Normal
			F	28 to 31	Swelling Firm - Flank Right - Slight
				31, 32, 34 to 40	Skin Red - Abdominal
				35, 36	Fur Stained Brown - Abdominal
				33, 41	Puppy Normal
4			M	2, 3	Skin Scab - Cervical Dorsal
				4	Puppy Normal
			M	27	Skin Lump - Flank Right
				28 to 34	Swelling Soft - Flank Right - Slight
				35	Puppy Normal
			F	27	Skin Lump - Flank Right
				28 to 30	Swelling Soft - Flank Right - Slight

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
4		(b) (4)	F	42	Skin Red - Abdominal
				31, 43	Puppy Normal
			F	27	Skin Lump - Flank Right
				28 to 34	Swelling Soft - Flank Right - Slight
				35	Puppy Normal
			M	26 to 32	Swelling Soft - Flank Left - Slight
				30 to 56	Tail Kinked
				55, 56	Skin Scab - Abdominal
				56	Skin Red - Abdominal
				56	Puppy Weaned
			M	4	Backbone Prominent
				4	Skin Turgor Slow - Slight
				4 to 8	Thin - Slight
				26 to 32	Swelling Soft - Flank Left - Slight
				33 to 35	Swelling Firm - Flank Left - Slight
				38	Tremors - Slight
				9, 36, 39	Puppy Normal
			M	2 to 9	Skin Scab - Cervical Dorsal
				26 to 32, 34, 35	Swelling Soft - Flank Left - Slight
				33	Swelling Firm - Flank Left - Slight
				10, 36	Puppy Normal
			F	26 to 35	Swelling Soft - Flank Left - Slight
				36	Puppy Normal
			F	3	Thin - Slight
				3	Backbone Prominent
				3	Skin Turgor Slow - Moderate
				4	Puppy Found Dead
			M	0, 2, 3	Skin Turgor Slow - Slight
				3	Thin - Slight
				25, 26	Swelling Soft - Flank Left - Slight
				27 to 34	Swelling Firm - Flank Left - Slight
				43	Skin Red - Inguinal Left
				1, 4, 35, 44	Puppy Normal
			M	26	Swelling Soft - Flank Left - Slight
				27 to 33	Swelling Firm - Flank Left - Slight
				27, 28, 32 to 36	Skin Blue - Penis

APPENDIX NO. 26

(b) (4)

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
		(b) (4)			
4			M	37	Puppy Normal
				55, 56	Skin Red - Abdominal
				56	Skin Scab - Abdominal
				56	Puppy Weaned
			M	1, 2	Skin Turgor Slow - Slight
				3	Puppy Normal
			F	1	Skin Turgor Slow - Slight
				1	Puppy Culled
			F	26, 29 to 31	Swelling Soft - Flank Left - Slight
				27, 28	Swelling Firm - Flank Left - Slight
				38, 39	Skin Red - Abdominal
				32, 40	Puppy Normal
			F	1	Skin Turgor Slow - Slight
				1	Puppy Culled
			F	1	Skin Turgor Slow - Slight
				25, 26, 29, 30	Swelling Soft - Flank Left - Slight
				27, 28	Swelling Firm - Flank Left - Slight
				33, 50 to 53	Skin Red - Abdominal
				50	Skin Scab - Abdominal
				2, 31, 34, 53	Puppy Normal
			F	1 to 3	Skin Turgor Slow - Slight
				3, 4	Thin - Slight
				4	Swelling Firm - Cervical Dorsal - Slight
				4	Puppy Culled
			M	2 to 9	Skin Scab - Cervical Dorsal
				25 to 32	Swelling Soft - Flank Left - Slight
				10, 33	Puppy Normal
				56	Discharge Red - Mouth - Slight
				56	Respiration Labored
				56	Respiratory Rate - Increased
				56	Cold To Touch
				56	Retching
				56	Puppy Weaned
			M	2	Skin Turgor Slow - Slight
				25 to 28, 31, 32	Swelling Soft - Flank Left - Slight
				29, 30	Swelling Firm - Flank Left - Slight

(b) (4)

APPENDIX NO. 26

CLINICAL OBSERVATION
F1 GENERATION PUPPIES
DAY 0 TO 56 POST-PARTUM

See Appendix No. 3 Experimental Design for group definition

GROUP	LITTER NO.	PUP NO.	SEX	DAY POST PARTUM	OBSERVATION
4		(b) (4)	M	3, 33	Puppy Normal
			M	2 to 4	Skin Scab - Cervical Dorsal
				4	Puppy Culled
			F	25 to 28	Swelling Soft - Flank Left - Slight
				29	Puppy Normal
			F	25 to 28, 38, 39	Swelling Soft - Flank Left - Slight
				29, 30, 36, 37	Swelling Firm - Flank Left - Slight
				31 to 34	Swelling Firm - Flank Left - Moderate
				40	Puppy Normal
			F	2 to 4	Skin Scab - Cervical Dorsal
				4	Puppy Culled

BODY WEIGHTS BY LITTER - PUPPIES

The following footnotes have been used throughout the appendix

--: No data

*: Excluded from repeated measures analysis.

Ab: Aberrant value

E: Excluded

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 0 FEMALES	Day 0 MALES	Day 4 FEMALES	Day 4 MALES	Day 7 FEMALES	Day 7 MALES	Day 10 FEMALES	Day 10 MALES	Day 14 FEMALES	Day 14 MALES	Day 17 FEMALES	Day 17 MALES
1	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)													

APPENDIX NO. 27

(b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2														

(b) (4)

APPENDIX NO. 27

(b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3														

(b) (4)

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)													

APPENDIX NO. 27

(b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3														

(b) (4)

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
			FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)													

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)													

APPENDIX NO. 27

(b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3														

(b) (4)

APPENDIX NO. 27

[redacted] (b) (4)

BODY WEIGHTS
BODY WEIGHTS BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
			FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)													

LITTER MEAN BODY WEIGHTS - PUPPIES

The following abbreviations and footnotes have been used throughout the appendix and/or summary table

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

--: No data

NF: No Female

*: Calculated on all puppies.

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 0*		Day 0		Day 4*		Day 4		Day 7		Day 10		Day 14		Day 17	
Group No.		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)																
	MEAN	208.43	227.30	219.25	228.97	312.98	328.97	311.75	320.00	431.00	443.40	568.38	587.60	748.50	784.27	884.50	925.93
	SD	34.83	35.21	30.55	31.47	42.03	60.56	40.10	62.18	53.62	90.32	66.11	113.14	115.39	134.46	139.64	157.94
	MIN	166.0	177.3	178.5	187.5	260.5	251.0	260.5	251.0	380.0	347.0	499.5	460.0	630.0	650.3	722.0	746.7
	MAX	241 3	263.5	251.0	263.5	355.7	386.5	347.5	386 5	484.5	563.0	640.5	734.0	880.5	961.5	1033.0	1132.5
	N	5	5	4	5	4	5	4	5	4	5	4	5	4	5	4	5

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 0		Day 0*		Day 4		Day 4*		Day 7		Day 10		Day 14		Day 17	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)																
	MEAN	225.45	247.10	235.46	258.88	369.58	410.25	370.71	406.38	528.63	598.00	682.67	766.75	874.17	963.25	1002.63	1109.00
	SD	42.94	36.40	21.17	19.33	18.71	47.51	17.51	51.59	19.35	80.92	34.19	69.43	41.73	62.31	52.49	76.23
	MIN	158 3	192.5	211.5	237.0	351.0	380.0	351.0	362 5	511.0	534.5	649.5	716.0	830.5	905.5	935.5	1035.5
	MAX	259 3	284.0	259.3	284.0	393.3	481.0	393.3	481.0	551.0	714.0	730.5	865.0	931.0	1028.0	1060.0	1196.0
	N	5	5	4	4	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 0		Day 0*		Day 4		Day 4*		Day 7		Day 10		Day 14		Day 17	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)																
	MEAN	250.08	270.30	264.13	284.58	329.75	405.65	360.50	415.63	519 25	580.33	680.38	735.88	904.25	944.75	1035.50	1105.33
	SD	34.83	20.43	48.02	17.69	104.22	63.79	116.01	51.94	167 27	81.84	187.46	78.64	236.14	101.37	290.17	128.06
	MIN	222.7	253.8	225.0	263.3	216.0	322.3	288.0	352.0	394.0	508.3	522.0	654.0	684.0	857.0	799.0	999.3
	MAX	307.0	303.0	328.5	303.0	500.3	477.0	533.0	477.0	764.5	688.5	952.0	839.0	1239.0	1091.0	1458.5	1291.5
	N	5	5	4	4	5	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 0		Day 0*		Day 4		Day 4*		Day 7		Day 10		Day 14		Day 17	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)																
	MEAN	213.85	235.27	227.75	230.46	275.29	337.67	308.13	322.71	419.00	450.38	543.75	590.92	700.38	790.54	854.25	938.54
	SD	10.82	15.29	19.87	17.03	36.15	32.14	21.24	18.79	49.28	59.22	64.01	72.30	65.49	103.92	75.39	143.02
	MIN	204.7	222.6	210.5	216.5	236.5	313.3	279.5	305 5	373.5	397.5	491.0	533.5	657.5	696.0	776.0	809.0
	MAX	225.7	256.0	256.0	253.3	312.3	384.0	325.0	343.0	486.0	532.0	627.0	696.5	798.0	922.0	953.0	1112.5
	N	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)												
	MEAN	1099.63	1127.90	1227.00	1260.60	1329.63	1368.20	1433 13	1487.77	1519.00	1605.17	1671.50	1756.73
	SD	184.40	164.88	212.90	152.67	204.60	156.36	197.12	139.16	163.57	121.63	153.32	113.59
	MIN	870.5	951.0	971.0	1088.0	1072.0	1167.0	1195.5	1312.3	1304.0	1444.3	1462.5	1588.7
	MAX	1303.5	1354.5	1481.5	1468.5	1563.5	1562.5	1674.5	1675.5	1688.5	1760.0	1823.5	1895.0
	N	4	5	4	5	4	5	4	5	4	5	4	5

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)												
	MEAN	1181.21	1318.13	1325.08	1452.63	1450.13	1582.75	1554 25	1702.63	1659.21	1833.50	1802.79	1988.75
	SD	51.62	91.07	69.57	67.95	108.56	81.31	103.29	88.48	120.08	103.53	134.33	88.66
	MIN	1104.0	1226.5	1226.0	1397.0	1294.0	1487.5	1400.0	1598.0	1481.5	1701.5	1606.0	1860.5
	MAX	1212.3	1443.0	1388.3	1546.0	1541.0	1682.0	1619.0	1809.0	1745.0	1951.0	1907.0	2064.5
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)												
	MEAN	1230.88	1337.25	1386.13	1465.58	1506.63	1604.13	1651 13	1738.58	1764.13	1886.13	1897.63	2071.17
	SD	325.68	111.86	373.50	159.97	365.28	148.28	407.71	161.05	410.20	137.39	426.77	143.66
	MIN	935.5	1273.0	1061.0	1331.3	1203.0	1496.0	1315.5	1611.3	1447.0	1786.5	1632.5	1949.5
	MAX	1695.0	1504.5	1924.0	1697.5	2036.5	1821.0	2242.0	1969.5	2365.0	2088.0	2531.5	2266.0
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 21		Day 24		Day 27		Day 30		Day 33		Day 37	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)												
	MEAN	1028.13	1124.33	1154.00	1249.42	1283.50	1382.50	1402.63	1505.17	1478.50	1623.71	1627.75	1786.29
	SD	79.70	139.65	103.87	157.40	131.55	180.36	145.20	188.54	128.57	179.54	139.36	195.20
	MIN	926.5	967.5	1043.5	1059.5	1109.5	1168.5	1190.0	1277.5	1302.0	1394.5	1449.0	1532.0
	MAX	1118.5	1253.0	1277.0	1398.5	1391.0	1553.5	1496.5	1694.0	1597.5	1783.5	1789.5	1956.0
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)												
	MEAN	1801.38	1894.73	1969.88	2046.97	2192.13	2273.20	2360.75	2481.90	2538.25	2673.53	2679.00	2747.53
	SD	143.13	126.49	138.01	135.26	176.68	171.19	170.01	195.16	230.14	226.47	131.30	255.04
	MIN	1600.0	1699.7	1764.0	1825.3	1930.0	1998.0	2111.0	2160.0	2207.0	2333.7	2510.0	2411.7
	MAX	1928.0	2014.0	2052.0	2179.0	2313.0	2429.0	2490.5	2666.5	2723.5	2849.5	2830.5	3042.0
	N	4	5	4	5	4	5	4	5	4	5	4	5

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)												
	MEAN	1930.13	2151.75	2046.71	2307.00	2215.58	2525.38	2371 25	2712.50	2553.38	2908.13	2549.92	2964.63
	SD	138.19	87.51	147.16	126.69	166.02	162.79	163.46	117.87	154.80	139.70	149.20	167.67
	MIN	1754.5	2058.0	1853.5	2188.5	2035.0	2393.5	2201.0	2602.0	2396.5	2814.0	2365.0	2854.5
	MAX	2085.0	2257.0	2203.5	2482.0	2400.5	2739.5	2586.5	2869.5	2761.0	3114.5	2721.0	3214.5
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)												
	MEAN	2025.00	2216.50	2163.00	2374.21	2329.13	2553.04	2457 25	2733.33	2582.63	2862.71	2639.13	2945.29
	SD	443.88	134.36	470.01	131.63	474.65	85.26	504.15	37.18	519.76	91.20	555.94	28.94
	MIN	1730.5	2064.0	1855.5	2221.5	1980.0	2442.0	2115.5	2688.5	2265.0	2741.5	2283.0	2918.0
	MAX	2684.0	2379.5	2862.0	2522.0	3030.5	2630.5	3206.5	2773.0	3359.5	2962.5	3468.5	2972.5
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 28

[redacted] (b) (4)

BODY WEIGHTS
LITTER MEAN BODY WEIGHTS - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 40		Day 43		Day 47		Day 50		Day 53		Day 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)												
	MEAN	1773.00	1952.17	1896.63	2103.75	2105.50	2347.46	2240 13	2511.88	2395.38	2695.83	2432.38	2728.33
	SD	123.41	151.19	162.51	150.71	231.90	137.83	268.22	159.88	312.31	144.42	292.02	134.13
	MIN	1625.5	1783.0	1730.5	1914.5	1913.0	2203.0	1978.0	2379.0	2107.5	2556.0	2188.5	2612.0
	MAX	1925.0	2111.0	2089.0	2278.5	2389.0	2528.0	2567.5	2741.5	2780.0	2845.5	2806.5	2907.5
	N	4	4	4	4	4	4	4	4	4	4	4	4

BODY WEIGHT CHANGES BY LITTER - PUPPIES

The following footnotes have been used throughout the appendix

--: No data

NC: Not Calculable

APPENDIX NO. 29

[redacted]

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted]													

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)													

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)													

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)													

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted]													

(b) (4)

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)													

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 17 to 24		Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted]															

(b) (4)

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)													

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)											

APPENDIX NO. 29

(b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2												

(b) (4)

APPENDIX NO. 29

[redacted] (b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)											

APPENDIX NO. 29

(b) (4)

BODY WEIGHT CHANGES
BODY WEIGHT CHANGES BY LITTER - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4												

(b) (4)

APPENDIX NO. 30 (b) (4)

LITTER MEAN BODY WEIGHT CHANGES - PUPPIES

The following abbreviations and footnotes have been used throughout the appendix and/or summary table

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

NF: No Female

--: No data

NA: Not Applicable

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)												
	MEAN	92.50	91.03	119.25	123.40	137.38	144.20	180.13	196.67	136.00	141.67	215.13	201.97
	SD	16.60	42.39	22.34	31.67	20.14	23.51	49.50	24.77	29.73	28.84	50.73	12.02
	MIN	82.0	38.7	90.5	96.0	109.5	113.0	130.5	165.0	92.0	96.3	148.5	193.5
	MAX	117.0	139.0	145.0	176.5	156.0	171.0	240.0	227.5	155.5	171.0	270.5	222.0
	N	4	5	4	5	4	5	4	5	4	5	4	5

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)												
	MEAN	135.25	147.50	157.92	191.63	154.04	168.75	191.50	196.50	128.46	145.75	178.58	209.13
	SD	13.70	37.68	13.93	33.51	29.42	14.61	25.82	31.29	20.72	16.01	29.76	37.58
	MIN	125.5	107.0	139.0	158.0	126.7	151.0	157.5	163.0	105.0	130.0	143.0	165.5
	MAX	155.0	197.0	172.0	233.0	192.0	185.0	219.0	238.5	155.3	168.0	212.5	247.0
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)												
	MEAN	96.38	131.04	158.75	164.71	161.13	155.54	223.88	208.88	131.25	160.58	195.38	216.50
	SD	79.96	49.44	52.90	37.19	26.63	14.13	51.04	36.12	59.67	28.11	43.26	13.10
	MIN	15.0	88.7	106.0	121.5	128.0	145.7	162.0	164.5	91.0	139.5	136.5	205.5
	MAX	204.5	199.5	231.5	211.5	187.5	176.5	287.0	252.0	219.5	200.5	236.5	235.5
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 0 to 4		Day 4 to 7		Day 7 to 10		Day 10 to 14		Day 14 to 17		Day 17 to 21	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)												
	MEAN	80.38	92.25	110.88	127.67	124.75	140.54	156.63	199.63	153.88	148.00	173.88	185.79
	SD	17.02	23.40	34.71	42.87	17.50	25.50	30.91	46.15	30.59	39.88	19.99	43.39
	MIN	69.0	74.5	88.0	89.5	103.5	106.7	112.0	159.0	118.5	113.0	150.5	140.5
	MAX	105.0	126.5	162.5	189.0	141.0	164.5	182.0	251.5	193.0	190.5	196.0	232.5
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)												
	MEAN	127.38	132.70	102.63	107.60	103.50	119.57	85.88	117.40	152.50	151.57	129.88	138.00
	SD	35.17	14.55	16.13	27.38	21.06	21.97	49.67	22.39	16.19	20.31	16.93	29.57
	MIN	100.5	114.0	82.0	79.0	74.0	87.5	14.0	84.5	135.0	132.0	104.5	111.0
	MAX	178.0	154.0	121.0	141.0	123.5	145.3	126.5	143.0	172.0	173.5	139.0	180.5
	N	4	5	4	5	4	5	4	5	4	5	4	5

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)												
	MEAN	143.88	134.50	125.04	130.13	104.13	119.88	104.96	130.88	143.58	155.25	127.33	163.00
	SD	23.09	29.57	39.69	27.17	35.05	7.43	18.49	18.67	15.76	65.85	46.80	47.26
	MIN	122.0	103.0	68.0	90.5	55.0	110.5	81.5	103.5	124.5	61.0	69.3	95.0
	MAX	176.0	170.5	152.7	151.5	136.5	127.0	126.0	143.5	162.0	203.5	178.0	197.5
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

			Day 17 to 24		Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
Group No.	Litter No.		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)															
	MEAN	--	324.00	155.25	144.75	120.50	138.54	144.50	134.46	113.00	147.54	133.50	185.04	127.38	145 33	
	SD	--	NA	49.45	32.36	16.03	22.23	43.75	17.21	18.12	38.91	51.81	35.75	24.95	37.22	
	MIN	--	324.0	125.5	124.0	105.0	117.0	112.5	115.3	90.5	118.5	73.0	161.7	98.0	113.5	
	MAX	--	324.0	229.0	193.0	142.0	164.7	205.5	149.5	131.5	204.7	185.5	237.5	152.5	187.3	
	N	--	1	4	4	4	4	4	4	4	4	4	4	4	4	

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 21 to 24		Day 24 to 27		Day 27 to 30		Day 30 to 33		Day 33 to 37		Day 37 to 40	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)												
	MEAN	125.88	125.08	129.50	133.08	119.13	122.67	75.88	118.54	149.25	162.58	145.25	165.88
	SD	35.29	23.38	50.76	23.31	40.20	14.65	35.75	21.46	42.98	33.03	25.74	58.38
	MIN	80.0	92.0	66.0	109.0	80.5	109.0	42.0	89.5	91.0	137.5	116.0	121.5
	MAX	158.5	145.5	182.0	155.0	175.0	140.5	112.0	139.7	192.0	207.5	176.5	251.0
	N	4	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)										
	MEAN	168.500	152.233	222.25	226.23	168.63	208.70	177.50	191.63	140.75	74.00
	SD	49.469	30.457	45.55	57.33	24.21	64.44	81.55	67.01	245.61	76.33
	MIN	124.00	116.50	166.0	172.7	132 5	128.0	96.0	95.0	-55.5	-11.5
	MAX	238.50	190.00	261.0	314.0	183 5	292.0	290.5	271.0	475.5	192 5
	N	4	5	4	5	4	5	4	5	4	5

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)										
	MEAN	116.583	155.250	168.88	218.38	155.67	187.13	182.13	195.63	-3.46	56.50
	SD	12.082	46.997	50.73	48.10	44.59	48.64	10.32	83.84	37.49	51.40
	MIN	99.00	124.50	94.0	156.0	90.0	130.0	173.5	81.5	-40.0	-17.5
	MAX	125.50	225.00	203.0	257.5	186.0	242.0	195.5	270.0	31.0	100.0
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)										
	MEAN	138.000	157.708	166.13	178.83	128.13	180.29	125.38	129.38	56.50	82.58
	SD	26.920	14.631	40.80	51.34	40.35	51.86	30.71	57.16	38.02	113 95
	MIN	120.00	142.50	124.5	108.5	78.0	122.0	91.0	53.0	18.0	-44.5
	MAX	178.00	177.50	221.0	220.5	176.0	246.5	153.0	189.5	109.0	231.0
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 30

[redacted] (b) (4)

BODY WEIGHT CHANGES
LITTER MEAN BODY WEIGHT CHANGES - PUPPIES (g)

See Appendix No. 3 Experimental Design for group definition

		Day 40 to 43		Day 43 to 47		Day 47 to 50		Day 50 to 53		Day 53 to 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)										
	MEAN	123.625	151.583	208.88	243.71	134.63	164.42	155.25	183.96	37.00	32.50
	SD	59.075	48.606	76.33	63.97	48.75	38.99	80.40	90.56	46.18	54.12
	MIN	48.50	97.00	120.0	151.5	65.0	124.7	37.5	104.0	6.0	-39.0
	MAX	177.00	210.33	300.0	288.5	178 5	213.5	212.5	300.3	105.0	84.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 31

(b) (4)

BODY WEIGHTS - PUPPIES

The following abbreviations and footnote have been used throughout the appendix and/or summary table

SD: Standard Deviation

N: Number of animals

MIN: Minimum value

MAX: Maximum value

--: No data

Ab: Aberrant value

E: Excluded

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
1	[redacted] (b) (4)										
	MEAN	211.5	323.6	434.6	576.0	772.1	909.6	1111.8	1244.9	1349.9	1471.8
	SD	41.7	75.5	105 5	139.3	159.0	187.1	203.2	201.2	206.2	192.2
	MIN	148	170	241	315	471	537	683	805	865	1040
	MAX	265	423	569	743	979	1180	1393	1494	1590	1707
	N	19	13	11	11	11	11	11	11	11	11

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
2	[redacted] (b) (4)										
	MEAN	239.5	396.3	581.4	752.7	954.0	1096.6	1300.3	1439.3	1568.6	1687.4
	SD	35.0	38.0	65.4	61.1	70.1	87.1	101.8	92.3	109.9	109.7
	MIN	178	345	517	684	863	971	1175	1283	1420	1544
	MAX	294	481	714	865	1044	1196	1443	1546	1699	1810
	N	17	9	7	7	7	7	7	7	7	7

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
3	[redacted] (b) (4)										
	MEAN	264.3	391.6	572.3	726.8	935.0	1093.6	1337.3	1450.7	1592.1	1724.4
	SD	39.5	79.2	95.7	96.0	127 9	143.2	135.4	185.5	195.1	197.5
	MIN	183	233	416	569	698	876	1170	1200	1352	1472
	MAX	317	508	737	880	1139	1332	1547	1781	1977	2071
	N	17	11	9	9	9	9	8	9	9	9

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
4	[redacted] (b) (4)										
	MEAN	233.7	337.7	450.8	587.6	782.7	927.0	1115.7	1242.0	1373.3	1496.7
	SD	26.6	69.2	91.1	117.6	146.1	162.5	170.7	179.4	206.5	210.0
	MIN	175	216	308	380	500	647	821	941	1032	1158
	MAX	272	466	586	772	994	1161	1309	1429	1587	1704
	N	21	12	9	9	9	9	9	9	9	9

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
1	[redacted] (b) (4)								
	MEAN	1590.5	1741.5	1877.0	2026.8	2248.2	2452.6	2642.6	2717.0
	SD	180.8	193.3	198.8	230.6	263.2	308.7	345.3	363.7
	MIN	1177	1309	1435	1514	1677	1804	1922	2014
	MAX	1789	1979	2128	2344	2626	2909	3227	3308
	N	11	11	11	11	11	11	11	11

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
2	[redacted] (b) (4)								
	MEAN	1816.7	1985.4	2158.1	2315.4	2542.7	2722.0	2919.0	2974.3
	SD	123.4	131.0	141.0	173.5	202.7	195.6	208.8	252.7
	MIN	1679	1847	2002	2127	2319	2493	2630	2638
	MAX	1962	2174	2368	2593	2839	2979	3245	3359
	N	7	7	7	7	7	7	7	7

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
3	[redacted] (b) (4)								
	MEAN	1878.3	2060.8	2210.8	2368.0	2550.7	2731.8	2863.2	2942.8
	SD	187.6	204.1	216.7	228.0	226.9	244.3	262.7	287.2
	MIN	1669	1794	1924	2053	2253	2393	2543	2471
	MAX	2210	2360	2492	2659	2894	3093	3326	3365
	N	9	9	9	9	9	9	9	9

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
4	[redacted] (b) (4)								
	MEAN	1617.6	1780.7	1943.2	2101.3	2349.7	2509.7	2706.6	2731.1
	SD	213.6	231.7	229.2	231.9	238.9	250.9	280.8	257.6
	MIN	1264	1402	1499	1700	1959	2067	2265	2283
	MAX	1810	2025	2198	2366	2676	2889	3078	3080
	N	9	9	9	9	9	9	9	9

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
1	[redacted] (b) (4)										
	MEAN	222.5	321.1	431.0	568.4	748.5	884.5	1099.6	1227.0	1329.6	1433.1
	SD	32.8	41.8	58.4	69.0	113.3	137.5	178.2	207.1	198.5	194.2
	MIN	166	258	375	485	601	679	800	891	987	1098
	MAX	265	391	520	661	901	1053	1333	1520	1611	1730
	N	15	11	8	8	8	8	8	8	8	8

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
2	[redacted] (b) (4)										
	MEAN	228.4	368.8	531.1	682.1	873 3	1004.8	1184.7	1332.1	1460.2	1558.9
	SD	45.3	49.7	54.3	74.8	80.2	82.2	98.6	118.9	141.2	148.8
	MIN	135	300	434	569	734	844	1004	1140	1191	1280
	MAX	323	444	609	790	978	1120	1298	1459	1615	1718
	N	23	13	9	9	9	9	9	9	9	9

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
3	[redacted] (b) (4)										
	MEAN	255.9	367.3	530.9	689.7	913.7	1050.7	1246.6	1404.3	1527.0	1676.0
	SD	46.2	113.0	171.8	195.8	247.8	297.7	333.9	379.2	372.4	411.3
	MIN	178	216	320	434	574	675	832	946	1083	1215
	MAX	335	543	770	961	1250	1484	1706	1931	2049	2250
	N	17	12	7	7	7	7	7	7	7	7

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 0	DAY 4	DAY 7	DAY 10	DAY 14	DAY 17	DAY 21	DAY 24	DAY 27	DAY 30
4	[redacted] (b) (4)										
	MEAN	213.0	278.8	418 3	541.3	704.3	858.9	1029.6	1162.0	1287.7	1398.9
	SD	24.6	64.8	81.5	90.4	103.5	124.7	117.3	130.4	155.9	161.7
	MIN	169	148	332	445	580	681	852	970	1033	1123
	MAX	256	385	580	726	912	1098	1244	1397	1514	1600
	N	17	11	7	7	7	7	7	7	7	7

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
1	[redacted] (b) (4)								
	MEAN	1519.0	1671.5	1801.4	1969.9	2192.1	2360.8	2538.3	2679.0
	SD	172.1	176.9	166.4	168.5	214.0	218.8	271.6	275.3
	MIN	1199	1317	1479	1640	1786	1950	2073	2294
	MAX	1767	1927	2028	2170	2464	2680	2844	3069
	N	8	8	8	8	8	8	8	8

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
2	[redacted] (b) (4)								
	MEAN	1663.6	1806.7	1927.6	2044.9	2205.4	2363.9	2546.3	2546.2
	SD	160.5	179.6	181.4	201.2	236.8	258.7	248.8	263.8
	MIN	1352	1501	1618	1753	1813	1959	2154	2172
	MAX	1834	2009	2168	2310	2520	2740	2859	2884
	N	9	9	9	9	9	9	9	9

APPENDIX NO. 31

[redacted] (b) (4)

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
3	[redacted] (b) (4)								
	MEAN	1789.9	1932.0	2057.1	2196.4	2354.7	2490.0	2617.9	2675.3
	SD	414.6	428.7	452.5	482.0	496.2	529.8	545.6	581.9
	MIN	1320	1478	1551	1672	1795	1890	2054	2036
	MAX	2395	2558	2743	2981	3189	3383	3565	3676
	N	7	7	7	7	7	7	7	7

APPENDIX NO. 31

[redacted]

BODY WEIGHTS - PUPPIES (g)

FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 33	DAY 37	DAY 40	DAY 43	DAY 47	DAY 50	DAY 53	DAY 56
4	[redacted]								
	MEAN	1479.6	1626.3	1770.4	1886.4	2091.9	2225.1	2378.1	2419.6
	SD	146.4	177.6	177.9	214.8	273.5	313.0	361.3	334.2
	MIN	1236	1283	1417	1485	1652	1688	1853	1901
	MAX	1640	1847	1940	2111	2401	2568	2803	2833
	N	7	7	7	7	7	7	7	7

BODY WEIGHT CHANGES - PUPPIES

The following abbreviations and footnote have been used throughout the appendix and/or summary table

SD: Standard Deviation

N: Number of animals

MIN: Minimum value

MAX: Maximum value

--: No data

NC: Not calculable

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
1	[redacted] (b) (4)										
	MEAN	95.8	120.9	141.4	196.1	137.5	202.2	133.1	105.0	121.9	118.7
	SD	52.0	33.4	37.7	31.8	40.4	28.9	18.8	37.5	40.3	23.1
	MIN	2	71	74	139	66	146	101	39	75	82
	MAX	186	179	186	236	201	252	169	158	186	150
	N	13	11	11	11	11	11	11	11	11	11

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
2	[redacted] (b) (4)										
	MEAN	141.4	185.7	171.3	201.3	142.6	203.7	139.0	129.3	118.9	129.3
	SD	29.3	28.6	22.2	34.0	23.0	37.7	29.2	41.2	18.2	22.4
	MIN	95	154	141	163	108	164	103	39	82	82
	MAX	197	233	203	268	174	262	189	166	139	152
	N	9	7	7	7	7	7	7	7	7	7

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 17 to 24	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
3	[redacted] (b) (4)											
	MEAN	111.2	163.8	154.4	208.2	158.6	216.5	324.0	144.8	141.4	132.3	153.9
	SD	70.1	38.3	17.9	49.0	39.8	30.5	NA	43.0	48.1	32.4	41.1
	MIN	-54	117	125	129	96	161	324	98	51	94	98
	MAX	210	229	191	259	208	263	324	234	210	203	212
	N	11	9	9	9	9	8	1	8	9	9	9

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
4	[redacted] (b) (4)										
	MEAN	102.7	126.8	136.8	195.1	144.3	188.7	126.3	131.3	123.3	120.9
	SD	63.4	40.9	36.0	45.9	41.4	44.9	41.1	34.6	21.8	38.6
	MIN	-47	66	72	120	84	131	70	70	95	73
	MAX	205	190	186	252	214	248	183	165	164	211
	N	12	9	9	9	9	9	9	9	9	9

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
I	[redacted] (b) (4)							
	SD	37.5	33.1	49.9	61.1	80.2	69.0	72.8
	MIN	101	93	79	153	109	81	-55
	MAX	218	195	230	334	388	318	224
	N	11	11	11	11	11	11	11

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
2	[redacted] (b) (4)							
	MEAN	168.7	172.7	157.3	227.3	179.3	197.0	55.3
	SD	77.4	45.5	61.3	43.2	51.5	92.5	66.0
	MIN	61	95	109	156	120	38	-19
	MAX	299	232	291	279	243	318	149
	N	7	7	7	7	7	7	7

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
3	[redacted] (b) (4)							
	MEAN	182.4	150.0	157.2	182.7	181.1	131.4	79.6
	SD	46.3	47.9	26.7	60.5	55.3	110.6	141.4
	MIN	125	95	119	64	98	-138	-128
	MAX	286	229	200	235	269	244	397
	N	9	9	9	9	9	9	9

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
4	[redacted] (b) (4)							
	MEAN	163.1	162.6	158.1	248.3	160.0	196.9	24.6
	SD	38.3	67.4	47.2	67.0	40.3	99.7	59.5
	MIN	135	97	88	147	108	93	-84
	MAX	223	302	221	323	214	372	99
	N	9	9	9	9	9	9	9

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
I	[redacted] (b) (4)										
	MEAN	96.1	119.3	137.4	180.1	136.0	215.1	127.4	102.6	103.5	85.9
	SD	19.0	23.6	19.6	49.2	33.9	50.5	50.4	21.1	27.7	58.0
	MIN	74	81	109	116	78	121	87	73	51	-9
	MAX	133	161	158	240	179	280	246	132	136	178
	N	11	8	8	8	8	8	8	8	8	8

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
2	[redacted] (b) (4)										
	MEAN	126.5	157.9	151.0	191.2	131.4	179.9	147.4	128.1	98.7	104.7
	SD	29.4	15.1	34.3	27.7	27.7	42.2	40.4	38.3	43.2	24.2
	MIN	74	134	102	150	99	108	82	51	5	72
	MAX	186	174	208	229	176	239	204	163	138	137
	N	13	9	9	9	9	9	9	9	9	9

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
3	[redacted] (b) (4)										
	MEAN	91.2	161.3	158.9	224.0	137.0	195.9	157.7	122.7	149.0	113.9
	SD	94.0	53.8	28.9	53.9	59.8	53.8	50.3	21.5	43.8	28.1
	MIN	-76	97	114	140	76	116	112	93	93	76
	MAX	221	247	202	289	234	266	233	147	210	158
	N	12	7	7	7	7	7	7	7	7	7

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 1 to 4	Day 4 to 7	Day 7 to 10	Day 10 to 14	Day 14 to 17	Day 17 to 21	Day 21 to 24	Day 24 to 27	Day 27 to 30	Day 30 to 33
4	[redacted] (b) (4)										
	MEAN	66.3	112.6	123.0	163.0	154.6	170.7	132.4	125.7	111.1	80.7
	SD	51.2	40.9	18.6	32.6	37.5	26.2	29.5	49.5	35.1	39.0
	MIN	-53	70	94	112	101	130	80	63	71	36
	MAX	143	195	146	205	206	202	164	184	175	136
	N	11	7	7	7	7	7	7	7	7	7

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
1	[redacted] (b) (4)							
	MEAN	152.5	129.9	168.5	222.3	168.6	177.5	140.8
	SD	29.7	28.8	47.7	51.3	32.7	87.4	332.9
	MIN	110	101	106	146	121	69	-74
	MAX	199	172	255	294	216	328	927
	N	8	8	8	8	8	8	8

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
2	[redacted] (b) (4)							
	MEAN	143.1	120.9	117.3	160.6	158.4	182.4	-0.1
	SD	31.7	54.0	39.3	62.4	50.4	31.4	56.1
	MIN	95	12	63	17	54	119	-105
	MAX	182	186	180	210	220	230	81
	N	9	9	9	9	9	9	9

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
3	[redacted] (b) (4)							
	MEAN	142.1	125.1	139.3	158.3	135.3	127.9	57.4
	SD	47.4	34.5	43.9	40.9	43.9	35.5	46.6
	MIN	73	73	115	123	78	82	-18
	MAX	213	185	238	221	194	182	111
	N	7	7	7	7	7	7	7

APPENDIX NO. 32

[redacted] (b) (4)

BODY WEIGHT CHANGES - PUPPIES (g)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 33 to 37	Day 37 to 40	Day 40 to 43	Day 43 to 47	Day 47 to 50	Day 50 to 53	Day 53 to 56
4	[redacted] (b) (4)							
	MEAN	146.7	144.1	116.0	205.4	133.3	153.0	41.4
	SD	72.8	43.1	62.8	80.1	52.1	84.3	49.7
	MIN	47	93	9	78	36	19	-27
	MAX	247	219	177	310	190	235	117
	N	7	7	7	7	7	7	7

APPENDIX NO. 33 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS BY LITTER - PUPPIES

The following footnotes have been used throughout the appendix

--: No data

Ab: Aberrant value

E: Excluded

APPENDIX NO. 33

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1												

(b) (4)

APPENDIX NO. 33

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)											

APPENDIX NO. 33

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES

(b) (4)

APPENDIX NO. 33

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No	Pup No	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4												

(b) (4)

APPENDIX NO. 33

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 42		Day 49		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1								

(b) (4)

APPENDIX NO. 33

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 42 FEMALES	Day 42 MALES	Day 49 FEMALES	Day 49 MALES	Day 56 FEMALES	Day 56 MALES
2	[redacted]							

APPENDIX NO. 33

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 42 FEMALES	Day 42 MALES	Day 49 FEMALES	Day 49 MALES	Day 56 FEMALES	Day 56 MALES
3								

(b) (4)

APPENDIX NO. 33

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
HEAD CIRCUMFERENCE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 42 FEMALES	Day 42 MALES	Day 49 FEMALES	Day 49 MALES	Day 56 FEMALES	Day 56 MALES
4	[redacted] (b) (4)							

APPENDIX NO. 34 (b) (4)

LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

NF: No Female

NC: Not Calculable

APPENDIX NO. 34

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)										
	MEAN	15.688	15.700	18.188	18.617	20.583	21.100	21.625	21.767	22.500	23.267
	SD	1.028	1.022	1.048	0.600	0.804	0.945	1.601	0.824	1.837	1.006
	MIN	14.50	14.00	16.75	17.83	20.00	19.50	20.50	20.83	21.50	22.00
	MAX	17.00	16.75	19.25	19.50	21.50	21.75	24.00	23.00	25.25	24.33
	N	4	5	4	5	3	5	4	5	4	5

APPENDIX NO. 34

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)										
	MEAN	17.083	17.625	19.250	20.250	20.583	21.563	22.333	23.438	24.750	25.063
	SD	0.204	0.250	0.456	0.354	1.041	0.427	1.568	1.612	1 208	1 231
	MIN	16.83	17.50	18.75	19.75	19.50	21.00	20.75	21.50	23.00	23.25
	MAX	17.25	18.00	19.75	20.50	21.83	22.00	24.33	25.00	25.75	26.00
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 34

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)										
	MEAN	16.875	17.167	20.063	20.354	21.313	21.833	21.167	22.361	23.375	23.979
	SD	1.436	0.850	2.401	1.621	1 599	1.296	0.764	1.248	0.777	0 267
	MIN	15.00	16.00	18.00	19.17	20.00	20.33	20.50	21.33	22.25	23.75
	MAX	18.50	18.00	23.50	22.75	23.50	23.50	22.00	23.75	24.00	24.25
	N	4	4	4	4	4	4	3	3	4	4

APPENDIX NO. 34

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)										
	MEAN	15.250	15.604	17.625	17.938	20.188	20.896	22.188	22.375	22.688	23.229
	SD	0.842	0.657	0.777	0.427	0.688	0.515	1.919	1.797	1 546	1.420
	MIN	14.25	15.00	16.75	17.50	19.50	20.25	20.75	21.00	21.75	21.75
	MAX	16.25	16.50	18.50	18.50	21.00	21.50	25.00	25.00	25.00	25.17
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 34

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 42		Day 49		Day 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)						
	MEAN	23.438	24.583	24.625	25.417	25.500	26.150
	SD	1.477	0.328	0.750	0.493	0.913	0 576
	MIN	22.00	24.25	24.00	24.83	24.50	25.50
	MAX	25.50	25.00	25.50	26.00	26.50	27.00
	N	4	5	4	5	4	5

APPENDIX NO. 34

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 42		Day 49		Day 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted]						
	MEAN	25.229	25.750	25.417	25.938	25.917	27.188
	SD	0.826	1.258	0.612	0.921	0.842	0 944
	MIN	24.00	24.00	24.50	24.75	24.75	26.50
	MAX	25.75	27.00	25.75	27.00	26.75	28.50
	N	4	4	4	4	4	4

APPENDIX NO. 34

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 42		Day 49		Day 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)						
	MEAN	24.188	25.021	24.938	25.583	25.438	26.583
	SD	0.851	0.172	1.281	0.612	1.087	0 289
	MIN	23.00	24.83	23.75	25.25	24.50	26.33
	MAX	25.00	25.25	26.75	26.50	27.00	27.00
	N	4	4	4	4	4	4

APPENDIX NO. 34

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS
LITTER MEAN HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 42		Day 49		Day 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted]						
	MEAN	23.875	23.896	24.500	25.313	25.125	25.917
	SD	1.548	1.487	1.061	0.826	0.629	0 553
	MIN	22.50	22.50	23.75	24.75	24.50	25.50
	MAX	26.00	25.83	26.00	26.50	26.00	26.67
	N	4	4	4	4	4	4

APPENDIX NO. 35 (b) (4)

HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES

The following abbreviation and footnote have been used throughout the appendix

--: No data

NC: Not Calculable

APPENDIX NO. 35

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 14 to 28		Day 21 to 28	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)									

APPENDIX NO. 35

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 21 to 28	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2								

(b) (4)

APPENDIX NO. 35

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 21 to 28	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)							

APPENDIX NO. 35

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 21 to 28	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4								

(b) (4)

APPENDIX NO. 35

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 28 to 35		Day 35 to 42		Day 42 to 49	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted]							

(b) (4)

APPENDIX NO. 35

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 28 to 35		Day 35 to 42		Day 42 to 49	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2								

(b) (4)

APPENDIX NO. 35

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 21 to 35		Day 28 to 35		Day 35 to 42		Day 42 to 49	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)									

APPENDIX NO. 35

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 28 to 35		Day 35 to 42		Day 42 to 49	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)							

APPENDIX NO. 35

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 49 to 56 FEMALES	Day 49 to 56 MALES
1	[redacted]			

APPENDIX NO. 35

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 49 to 56 FEMALES	Day 49 to 56 MALES
2	[redacted]			

APPENDIX NO. 35

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 49 to 56 FEMALES	Day 49 to 56 MALES
3	[redacted]			

APPENDIX NO. 35

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
HEAD CIRCUMFERENCE CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 49 to 56 FEMALES	Day 49 to 56 MALES
4	[redacted]			

APPENDIX NO. 36 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

The following abbreviations and footnotes have been used throughout the appendix

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

NF: No Female

--: No data

NC: Not Calculable

NA: Not Applicable

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 14 to 28		Day 21 to 28	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)								
	SD	0.289	0.825	0.866	0.747	NA	NA	1.090	0.591
	MIN	2.25	1.75	1.75	1.67	1.75	1.50	0.50	0.00
	MAX	2.75	3.83	3.25	3.50	1.75	1.50	2.50	1.33
	N	4	5	3	5	1	1	3	5

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 21 to 28	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)						
	MEAN	2.167	2.625	1.333	1.313	1.750	1.875
	SD	0.471	0.595	1.047	0.625	1.339	1 199
	MIN	1.50	1.75	0.50	0.50	0.50	0.50
	MAX	2.50	3.00	2.83	2.00	3.25	3.00
	N	4	4	4	4	4	4

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 21 to 28	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)						
	MEAN	3.188	3.188	1.250	1.479	0.750	1.083
	SD	1.281	1.638	0.979	0.625	0.901	0.878
	MIN	2.00	1.75	0.00	0.75	0.00	0.25
	MAX	5.00	5.25	2.25	2.00	1.75	2.00
	N	4	4	4	4	3	3

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 21 to 28	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)						
	MEAN	2.375	2.333	2.563	2.958	2.000	1.479
	SD	1.233	0.882	0.427	0.344	1.860	1.796
	MIN	1.00	1.50	2.00	2.50	0.25	0.50
	MAX	3.75	3.50	3.00	3.33	4.50	4.17
	N	4	4	4	4	4	4

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 28 to 35		Day 35 to 42		Day 42 to 49	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)						
	MEAN	0.875	1.500	0.938	1.317	1.188	0.833
	SD	0.433	1.146	0.800	0.771	0.987	0.738
	MIN	0.50	0.75	0.25	0.33	0.00	0.00
	MAX	1.25	3.50	1.75	2.25	2.00	1.75
	N	4	5	4	5	4	5

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 28 to 35		Day 35 to 42		Day 42 to 49	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)						
	MEAN	2.417	1.625	0.479	0.688	0.188	0 188
	SD	1.467	0.924	0.443	0.239	0.239	0 375
	MIN	0.67	0.50	0.00	0.50	0.00	0.00
	MAX	4.25	2.75	1.00	1.00	0.50	0.75
	N	4	4	4	4	4	4

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 21 to 35		Day 28 to 35		Day 35 to 42		Day 42 to 49	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)								
	MEAN	1.250	0.250	1.917	1.694	0.813	1.042	0.750	0.563
	SD	1.061	NA	1.465	1.496	0.239	0.276	0.736	0.657
	MIN	0.50	0.25	0.25	0.00	0.50	0.67	0.00	0.00
	MAX	2.00	0.25	3.00	2.83	1.00	1.25	1.75	1.50
	N	2	1	3	3	4	4	4	4

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 28 to 35		Day 35 to 42		Day 42 to 49	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)						
	MEAN	0.500	0.854	1.188	0.667	0.625	1.417
	SD	0.456	0.554	0.625	0.514	0.520	0 965
	MIN	0.00	0.17	0.50	0.00	0.00	0.50
	MAX	1.00	1.50	2.00	1.25	1.25	2.25
	N	4	4	4	4	4	4

APPENDIX NO. 36

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 49 to 56 FEMALES	MALES
1	(b) (4)		
	MEAN	0.875	0.733
	SD	0.479	0.356
	MIN	0.50	0.25
	MAX	1.50	1.25
	N	4	5

APPENDIX NO. 36

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 49 to 56 FEMALES	Day 49 to 56 MALES
2	[redacted]		
	MEAN	0.500	1.250
	SD	0.354	0.540
	MIN	0.25	0.50
	MAX	1.00	1.75
	N	4	4

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Pup No.	Day 49 to 56 FEMALES	Day 49 to 56 MALES
3	[redacted] (b) (4)			
	MEAN		0.500	1.000
	SD		0.204	0.736
	MIN		0.25	0.00
	MAX		0.75	1.75
	N		4	4

APPENDIX NO. 36

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS CHANGE
LITTER MEAN HEAD CIRCUMFERENCE CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 49 to 56	
Group No.	Litter No.	FEMALES	MALES
4	[redacted] (b) (4)		
	MEAN	0.938	0.604
	SD	1.087	0.292
	MIN	0.00	0.17
	MAX	2.50	0.75
	N	4	4

APPENDIX NO. 37 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

Max: Maximum value

MIN: Minimum value

E: Excluded

Ab: Aberrant value

APPENDIX NO. 37

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	(b) (4)								
	MEAN	15.55	18.55	20.90	21.68	23.36	24.59	25.36	26.09
	SD	1 27	0.93	1.17	1.17	1.14	0.77	0.67	0.77
	MIN	13.0	16.5	18.5	19.0	21.5	23.0	24.0	24.5
	MAX	18.0	19.5	22.5	23.0	25.0	25.5	26.5	27.0
	N	11	11	10	11	11	11	11	11
2	(b) (4)								
	MEAN	17.64	20.21	21.50	23.21	25.00	25.71	25.93	27.29
	SD	0.48	0.49	0.50	1.50	1.29	1.25	0.93	0.99
	MIN	17.0	19.5	20.5	21.0	23.0	24.0	24.5	26.0
	MAX	18.0	21.0	22.0	25.0	26.5	27.0	27.0	29.0
	N	7	7	7	7	7	7	7	7

APPENDIX NO. 37

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
3	[redacted] (b) (4)								
	MEAN	17.17	20.22	21.67	22.21	24.00	25.00	25.56	26.56
	SD	0 90	1.56	1.35	1.22	0.35	0.25	0.68	0.73
	MIN	16.0	18.5	19.5	20.5	23.5	24.5	25.0	26.0
	MAX	18.5	23.5	23.5	24.0	24.5	25.5	27.0	28.0
	N	9	9	9	7	9	9	9	9
4	[redacted] (b) (4)								
	MEAN	15.61	17.89	20.89	22.67	23.44	24.11	25.44	26.00
	SD	0 93	0.82	0.99	1.94	1.61	1.52	1.07	0.71
	MIN	14.5	16.0	19.0	20.5	21.0	22.0	23.5	25.0
	MAX	17.5	18.5	21.5	26.0	26.0	26.5	27.0	27.0
	N	9	9	9	9	9	9	9	9

APPENDIX NO. 37

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	[redacted] (b) (4)								
	MEAN	15.69	18.19	20.58	21.63	22.50	23.44	24.63	25.50
	SD	1.07	1.03	1.11	1.55	1.75	1.45	0.74	0.96
	MIN	14.0	16.5	19.0	20.0	21.0	21.5	23.5	24.0
	MAX	17.0	19.5	22.0	24.0	25.5	25.5	25.5	27.0
	N	8	8	6	8	8	8	8	8
2	[redacted] (b) (4)								
	MEAN	17.06	19.22	20.72	22.56	24.78	25.28	25.44	25.94
	SD	0.68	0.71	1.06	1.78	1.28	1.00	0.85	0.92
	MIN	16.0	18.5	19.5	20.0	22.0	23.5	24.5	24.5
	MAX	18.0	20.5	22.0	25.5	26.0	27.0	27.0	27.0
	N	9	9	9	9	9	9	9	9

APPENDIX NO. 37

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS - PUPPIES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
3	[redacted] (b) (4)								
	MEAN	16.86	20.21	21.50	21.38	23.36	24.14	25.00	25.50
	SD	1.60	2.45	1.55	1.11	0.90	1.03	1.29	1.22
	MIN	14.5	17.0	20.0	20.5	21.5	22.0	23.5	23.5
	MAX	19.0	24.0	24.0	23.0	24.0	25.0	27.0	27.0
	N	7	7	7	4	7	7	7	7
4	[redacted] (b) (4)								
	MEAN	15.21	17.50	20.14	21.79	22.36	23.57	24.29	25.00
	SD	0 99	0.87	0.80	1.55	1.21	1.24	1.15	0.63
	MIN	14.0	16.5	19.0	20.0	21.5	22.5	22.5	24.0
	MAX	17.0	18.5	21.5	25.0	25.0	26.0	26.0	26.0
	N	7	7	7	7	7	7	7	6

APPENDIX NO. 38 (b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - PUPPIES

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

Max: Maximum value

MIN: Minimum value

NA: Not Applicable

NC: Not Calculable

--: No data

APPENDIX NO. 38

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - PUPPIES
HEAD CIRCUMFERENCE CHANGE (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 14 to 28	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	[redacted] (b) (4)								
	MEAN	3.000	2.450	1.500	0.850	1.682	1 227	0.773	0.727
	SD	1.000	0.762	NA	0.669	1.383	0.876	0.876	0.410
	MIN	1.00	1.50	1.50	0.00	0.50	0.00	0.00	0.00
	MAX	4.00	3.50	1.50	2.00	5.00	2.50	2.50	1.50
	N	11	10	1	10	11	11	11	11
2	[redacted] (b) (4)								
	MEAN	2.571	1.286	--	1.714	1.786	0.714	0.214	1.357
	SD	0.932	0.699	--	1.113	1.035	0.488	0.393	0.556
	MIN	1.50	0.50	--	0.50	0.50	0.00	0.00	0.50
	MAX	4.00	2.50	--	3.00	3.50	1.50	1.00	2.00
	N	7	7	--	7	7	7	7	7

APPENDIX NO. 38

[redacted]

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - PUPPIES
HEAD CIRCUMFERENCE CHANGE (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 21 to 35	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
3	[redacted]								
	MEAN	3.056	1.444	1.071	0.250	1.857	1.000	0.556	1.000
	SD	1.530	0.726	0.838	0.354	1.345	0.433	0.682	0.750
	MIN	1.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00
	MAX	5.50	2.50	2.50	0.50	3.50	1.50	2.00	2.50
	N	9	9	7	2	7	9	9	9
4	[redacted]								
	MEAN	2.278	3.000	1.778	--	0.778	0.667	1.333	0.556
	SD	0.833	0.829	1.839	--	0.618	0.612	0.968	0.527
	MIN	1.00	1.00	0.00	--	0.00	0.00	0.50	0.00
	MAX	3.50	4.00	4.50	--	2.00	1.50	3.00	1.50
	N	9	9	9	--	9	9	9	9

APPENDIX NO. 38

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - PUPPIES
HEAD CIRCUMFERENCE CHANGE (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 14 to 28	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	[redacted] (b) (4)								
	MEAN	2.500	2.750	1.750	1.250	0.875	0 938	1.188	0.875
	SD	0.535	0.935	1.061	1.173	0.443	1.050	0.961	0.582
	MIN	1.50	1.00	1.00	0.00	0.50	0.00	0.00	0.50
	MAX	3.00	3.50	2.50	3.00	1.50	3.00	2.50	2.00
	N	8	6	2	6	8	8	8	8
2	[redacted] (b) (4)								
	MEAN	2.167	1.500	--	1.833	2.222	0 500	0.167	0.500
	SD	0.750	1.146	--	1.436	1.543	0 500	0.354	0.500
	MIN	1.50	0.00	--	0.50	0.00	0.00	0.00	0.00
	MAX	3.50	3.00	--	4.50	4.50	1.50	1.00	1.50
	N	9	9	--	9	9	9	9	9

APPENDIX NO. 38

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - PUPPIES
HEAD CIRCUMFERENCE CHANGE (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 21 to 35	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
3	[redacted] (b) (4)								
	MEAN	3.357	1.286	1.000	1.000	1.500	0.786	0.857	0.500
	SD	1.406	1.075	1.080	1.000	1.472	0 267	0.852	0.577
	MIN	2.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00
	MAX	6.00	3.00	2.50	2.00	3.00	1.00	2.00	1.50
	N	7	7	4	3	4	7	7	7
4	[redacted] (b) (4)								
	MEAN	2.286	2.643	1.643	--	0.571	1 214	0.714	0.833
	SD	1.286	0.476	1.547	--	0.535	0.699	0.906	1.033
	MIN	1.00	2.00	0.00	--	0.00	0.00	0.00	0.00
	MAX	4.50	3.00	4.50	--	1.50	2.00	2.50	2.50
	N	7	7	7	--	7	7	7	6

APPENDIX NO. 39 (b) (4)

HEIGHT MEASUREMENTS BY LITTER - PUPPIES

The following footnotes have been used throughout the appendix

--: No data

Ab: Aberrant value

E: Excluded

APPENDIX NO. 39

(b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1												

(b) (4)

APPENDIX NO. 39

(b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2												

(b) (4)

APPENDIX NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)											

APPENDIX NO. 39

(b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4												

(b) (4)

APPENDIX NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 42		Day 49		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)							

APPENDIX NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 42		Day 49		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)							

APPENDIX NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 42		Day 49		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)							

APPENDIX NO. 39

[redacted] (b) (4)

HEIGHT MEASUREMENTS
HEIGHT MEASUREMENTS BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 42		Day 49		Day 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)							

APPENDIX NO. 40

LITTER MEAN HEIGHT CIRCUMFERENCE MEASUREMENTS - PUPPIES

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

NF: No Female

NC: Not Calculable

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)										
	MEAN	12.750	12.200	14.938	15.167	17.188	17.100	20.063	20.067	21.313	21.433
	SD	0.612	1.217	1.772	1.535	1.886	1.557	0.473	1.146	0 315	0.744
	MIN	12.25	10.50	13.75	13.50	15.00	15.50	19.75	18.33	21.00	20.50
	MAX	13.50	13.50	17.50	17.50	19.00	19.00	20.75	21.00	21.75	22.50
	N	4	5	4	5	4	5	4	5	4	5

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)										
	SD	0.883	0.764	1.256	1.638	1.479	1.225	1.199	1.652	0 571	1.493
	MIN	11.50	12.00	14.50	14.00	16.25	17.50	18.50	20.00	21.00	21.00
	MAX	13.25	13.50	17.17	17.50	19.67	20.00	21.00	23.50	22.25	24.50
	N	3	3	4	4	4	4	4	4	4	4

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7		Day 14		Day 21		Day 28		Day 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)										
	MEAN	12.125	12.604	15.688	16.229	17.000	17.646	20.000	20.417	22.250	22.333
	SD	0.661	0.921	1.214	1.061	1 242	0.591	1.369	0.833	1 190	0.736
	MIN	11.50	11.50	15.00	14.67	16.00	16.83	18.50	19.50	21.00	21.33
	MAX	13.00	13.75	17.50	17.00	18.75	18.25	21.75	21.50	23.50	23.00
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 7		Day 14		Day 21		Day 28		Day 35	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)										
	MEAN	12.188	12.354	14.313	14.438	16.750	17.063	19.563	20.625	20.563	22.229
	SD	0.688	1.081	0.473	0.375	1.443	1.087	0.515	1.090	0 515	0.859
	MIN	11.50	11.17	14.00	14.25	15.50	16.00	19.00	19.00	20.00	21.67
	MAX	13.00	13.75	15.00	15.00	18.00	18.00	20.25	21.25	21.25	23.50
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 42		Day 49		Day 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)						
	MEAN	22.625	23.583	24.375	25.183	25.250	26.300
	SD	0.433	1.115	0.595	0.560	0.866	1 292
	MIN	22.00	22.25	24.00	24.50	24.50	25.25
	MAX	23.00	25.00	25.25	25.75	26.50	28.50
	N	4	5	4	5	4	5

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 42		Day 49		Day 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)						
	MEAN	23.042	23.688	24.104	25.188	25.292	26.000
	SD	0.220	0.591	0.458	0.688	0.846	0.791
	MIN	22.75	23.25	23.67	24.50	24.50	25.25
	MAX	23.25	24.50	24.50	26.00	26.25	27.00
	N	4	4	4	4	4	4

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 42		Day 49		Day 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)						
	MEAN	23.750	23.708	25.375	25.354	25.938	26.417
	SD	1.756	0.433	2.314	1.137	2.183	0 920
	MIN	22.00	23.25	23.75	24.17	24.25	25.67
	MAX	25.50	24.25	28.75	26.75	29.00	27.75
	N	4	4	4	4	4	4

APPENDIX NO. 40

[redacted] (b) (4)

HEIGHT MEASUREMENTS
LITTER MEAN HEIGHT MEASUREMENTS - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 42		Day 49		Day 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)						
	MEAN	22.938	23.938	24.125	24.646	24.813	25.167
	SD	1.329	1.560	1.199	1.646	1.297	1.650
	MIN	21.25	22.50	22.75	22.75	23.25	23.00
	MAX	24.00	26.00	25.25	26.75	26.00	27.00
	N	4	4	4	4	4	4

HEIGHT CHANGE BY LITTER - PUPPIES

The following abbreviation and footnote have been used throughout the appendix

--: No data
NC: Not Calculable

APPENDIX NO. 41

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)									

APPENDIX NO. 41

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)									

APPENDIX NO. 41

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)									

APPENDIX NO. 41

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)									

APPENDIX NO. 41

(b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 35 to 42		Day 42 to 49		Day 49 to 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1								

(b) (4)

APPENDIX NO. 41

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 35 to 42	Day 42 to 49	Day 49 to 56
Group No.	Litter	Pup			
2	[redacted] (b) (4)				

APPENDIX NO. 41

(b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

			Day 35 to 42		Day 42 to 49		Day 49 to 56	
Group No.	Litter No.	Pup No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3								

(b) (4)

APPENDIX NO. 41

(b) (4)

HEIGHT MEASUREMENTS CHANGE
HEIGHT CHANGE BY LITTER - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter	Pup	Day 35 to 42	Day 42 to 49	Day 49 to 56
4					

(b) (4)

LITTER MEAN HEIGHT CHANGE - PUPPIES

The following abbreviations and footnote have been used throughout the appendix and/or summary table

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

NF: No Female

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)								
	MEAN	2.188	2.967	2.250	1.933	2.875	2.967	1.250	1.367
	SD	2.065	1.719	1.137	1.114	2.046	0.960	0.645	0.944
	MIN	0.75	1.25	1.25	0.75	0.75	2.00	0.50	0.25
	MAX	5.25	5.50	3.75	3.75	4.75	4.00	2.00	2.83
	N	4	5	4	5	4	5	4	5

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)								
	MEAN	3.167	2.750	2.250	3.438	2.333	3.125	1.917	1.250
	SD	1.876	2.046	0.540	0.966	1.021	1.652	1.264	0.500
	MIN	1.25	1.00	1.50	2.50	1.33	1.00	1.00	1.00
	MAX	5.00	5.00	2.75	4.75	3.75	5.00	3.75	2.00
	N	3	3	4	4	4	4	4	4

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)								
	MEAN	3.563	3.625	1.313	1.417	3.000	2.771	2.250	1.917
	SD	1.625	1.493	0.315	0.656	0.354	0.929	1.514	0.920
	MIN	2.00	2.00	1.00	0.75	2.50	1.75	1.25	1.17
	MAX	5.75	5.50	1.75	2.17	3.25	3.75	4.50	3.25
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 7 to 14		Day 14 to 21		Day 21 to 28		Day 28 to 35	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)								
	MEAN	2.125	2.083	2.438	2.625	2.813	3.563	1.000	1.604
	SD	1.051	1.379	1.125	0.924	1.463	1.983	0.612	1.021
	MIN	1.00	0.50	1.50	1.75	1.00	1.00	0.25	0.50
	MAX	3.50	3.83	3.75	3.75	4.00	5.25	1.75	2.67
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

		Day 35 to 42		Day 42 to 49		Day 49 to 56	
Group No.	Litter No.	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
1	[redacted] (b) (4)						
	MEAN	1.313	2.150	1.750	1.600	0.875	1.117
	SD	0.515	0.802	1.021	1.098	0.323	1.063
	MIN	0.75	1.50	1.00	0.50	0.50	0.50
	MAX	1.75	3.25	3.25	3.25	1.25	3.00
	N	4	5	4	5	4	5

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 35 to 42		Day 42 to 49		Day 49 to 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
2	[redacted] (b) (4)						
	MEAN	1.250	0.813	1.063	1.500	1.188	0.813
	SD	0.677	1.008	0.554	1.061	0.427	0 239
	MIN	0.75	0.00	0.50	0.00	0.75	0.50
	MAX	2.25	2.25	1.75	2.25	1.75	1.00
	N	4	4	4	4	4	4

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 35 to 42		Day 42 to 49		Day 49 to 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
3	[redacted] (b) (4)						
	MEAN	1.500	1.375	1.625	1.646	0.563	1.063
	SD	0.577	0.777	1.331	1.203	0.375	0.427
	MIN	1.00	0.75	0.00	0.33	0.25	0.50
	MAX	2.00	2.50	3.25	3.25	1.00	1.50
	N	4	4	4	4	4	4

APPENDIX NO. 42

[redacted] (b) (4)

HEIGHT MEASUREMENTS CHANGE
LITTER MEAN HEIGHT CHANGE - PUPPIES (cm)

See Appendix No. 3 Experimental Design for group definition

Group No.	Litter No.	Day 35 to 42		Day 42 to 49		Day 49 to 56	
		FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
4	[redacted] (b) (4)						
	MEAN	2.375	1.708	1.188	0.708	0.688	0 521
	SD	1.362	0.812	0.239	0.464	0.239	0 315
	MIN	0.75	0.75	1.00	0.25	0.50	0.25
	MAX	4.00	2.50	1.50	1.33	1.00	0.83
	N	4	4	4	4	4	4

HEIGHT MEASUREMENTS - PUPPIES

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

Max: Maximum value

MIN: Minimum value

E: Excluded

Ab: Aberrant value

APPENDIX NO. 43

[redacted] (b) (4)

HEIGHT MEASUREMENTS – PUPPIES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	[redacted] (b) (4)								
	MEAN	12.05	15.09	17.00	19.91	21.41	23.50	25.14	26.23
	SD	1.47	1.63	1.70	1.59	1.14	1.36	0.84	1.71
	MIN	9.0	12.5	14.0	16.5	19.0	21.0	23.5	24.5
	MAX	14.0	18.0	19.5	22.0	23.0	25.0	26.5	31.0
	N	11	11	11	11	11	11	11	11
2	[redacted] (b) (4)								
	MEAN	12.70	14.71	18.29	21.36	22.64	23.57	25.29	26.07
	SD	1.10	1.44	1.07	1.52	1.60	0.89	0.81	0.93
	MIN	11.0	13.0	17.0	19.5	21.0	22.0	24.0	24.5
	MAX	14.0	17.5	20.0	23.5	24.5	24.5	26.0	27.5
	N	5	7	7	7	7	7	7	7

APPENDIX NO. 43

[redacted] (b) (4)

HEIGHT MEASUREMENTS - PUPPIES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
3	[redacted] (b) (4)								
	MEAN	12.61	16.06	17.56	20.39	22.22	23.72	25.22	26.33
	SD	0.89	1.24	0.95	0.86	1.03	0.87	1.23	1.03
	MIN	11.0	14.0	15.5	19.0	20.5	22.0	23.5	25.0
	MAX	14.0	17.0	19.0	22.0	23.5	24.5	27.5	28.0
	N	9	9	9	9	9	9	9	9
4	[redacted] (b) (4)								
	MEAN	12.22	14.50	17.17	20.44	22.17	23.83	24.61	25.17
	SD	1.35	0.75	1.20	1.29	1.48	1.52	1.56	1.54
	MIN	9.5	13.5	15.0	17.5	19.0	22.0	22.5	23.0
	MAX	14.5	16.0	19.0	21.5	24.0	26.0	27.0	27.0
	N	9	9	9	9	9	9	9	9

APPENDIX NO. 43

[redacted] (b) (4)

HEIGHT MEASUREMENTS - PUPPIES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
1	[redacted] (b) (4)								
	MEAN	12.75	14.94	17.19	20.06	21.31	22.63	24.38	25.25
	SD	0.89	1.76	1.79	0.50	0.37	0.83	0.83	0.96
	MIN	11.5	13.0	15.0	19.5	21.0	21.5	23.0	23.5
	MAX	14.5	18.0	19.5	21.0	22.0	24.0	25.5	26.5
	N	8	8	8	8	8	8	8	8
2	[redacted] (b) (4)								
	MEAN	12.29	15.50	17.78	20.00	21.83	23.06	24.06	25.22
	SD	0.81	1.56	1 50	1.54	1.03	0.58	0.63	0.91
	MIN	11.0	13.0	16.0	17.0	20.0	22.0	23.0	24.0
	MAX	13.5	17.5	20.0	22.5	23.5	24.0	25.0	27.0
	N	7	9	9	9	9	9	9	9

APPENDIX NO. 43

[redacted] (b) (4)

HEIGHT MEASUREMENTS - PUPPIES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 42	DAY 49	DAY 56
3	[redacted] (b) (4)								
	MEAN	12.00	15.79	17.14	20.21	22.14	23.57	25.43	25.93
	SD	0.76	1.22	1.28	1.47	1.44	1.81	2.39	2.42
	MIN	11.0	14.5	15.5	18.5	20.0	21.0	23.0	23.0
	MAX	13.0	17.5	19.0	22.5	24.0	26.0	29.5	30.0
	N	7	7	7	7	7	7	7	7
4	[redacted] (b) (4)								
	MEAN	12.29	14.21	16.57	19.64	20.64	22.79	24.00	24.64
	SD	0.76	0.39	1.51	0.63	0.80	1.78	1.38	1.35
	MIN	11.0	14.0	15.0	19.0	19.5	20.5	22.5	22.5
	MAX	13.0	15.0	19.0	20.5	21.5	26.0	26.5	26.5
	N	7	7	7	7	7	7	7	7

APPENDIX NO. 44 (b) (4)

HEIGHT MEASUREMENT CHANGES- PUPPIES

The following abbreviations and footnote have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

Max: Maximum value

MIN: Minimum value

NC: Not Calculable

APPENDIX NO. 44

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES- PUPPIES
HEIGHT CHANGE (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	[redacted] (b) (4)							
	MEAN	3.045	1.909	2.909	1.500	2.091	1.636	1.091
	SD	1.665	1.200	1.091	1.049	0.944	1.120	1.200
	MIN	0.50	0.50	1.50	0.00	1.00	0 50	0.50
	MAX	5.50	5.00	5.00	3.50	4.00	3 50	4.50
	N	11	11	11	11	11	11	11
2	[redacted] (b) (4)							
	MEAN	2.300	3.571	3.071	1.286	0.929	1.714	0.786
	SD	1.681	1.170	1.790	0.809	0.976	0.906	0.393
	MIN	0.50	2.50	0.50	0.50	0.00	0.00	0.50
	MAX	5.00	5.50	5.50	3.00	2.50	2 50	1.50
	N	5	7	7	7	7	7	7

APPENDIX NO. 44

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES- PUPPIES
HEIGHT CHANGE (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
3	[redacted] (b) (4)							
	MEAN	3.444	1.500	2.833	1.833	1.500	1.500	1.111
	SD	1.530	0.791	1.000	1.146	0.791	1.199	0.697
	MIN	1.00	0.50	1.50	0.50	0.50	0.00	0.50
	MAX	6.00	3.00	4.00	4.00	2.50	3 50	2.50
	N	9	9	9	9	9	9	9
4	[redacted] (b) (4)							
	MEAN	2.278	2.667	3.278	1.722	1.667	0.778	0.556
	SD	1.502	1.090	2.033	1.149	1.250	0.755	0.391
	MIN	0.50	1.50	0.00	0.50	0.00	0.00	0.00
	MAX	4.50	4.00	6.00	4.00	3.50	2 50	1.00
	N	9	9	9	9	9	9	9

APPENDIX NO. 44

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES- PUPPIES
HEIGHT CHANGE (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
1	[redacted] (b) (4)							
	MEAN	2.188	2.250	2.875	1.250	1.313	1.750	0.875
	SD	1.926	1.102	1.923	0.598	0.799	1.165	0.443
	MIN	0.50	1.00	0.50	0.50	0.50	0 50	0.50
	MAX	5.50	4.00	5.00	2.00	2.50	4.00	1.50
	N	8	8	8	8	8	8	8
2	[redacted] (b) (4)							
	MEAN	3.429	2.278	2.222	1.833	1.222	1.000	1.167
	SD	1.835	1.003	1.302	1.250	0.905	0.791	0.866
	MIN	1.00	0.00	0.50	0.50	0.50	0.00	0.50
	MAX	5.00	3.50	4.50	4.00	3.50	2 50	3.00
	N	7	9	9	9	9	9	9

APPENDIX NO. 44

[redacted] (b) (4)

HEIGHT MEASUREMENT CHANGES- PUPPIES
HEIGHT CHANGE (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 7 to 14	Day 14 to 21	Day 21 to 28	Day 28 to 35	Day 35 to 42	Day 42 to 49	Day 49 to 56
3	[redacted] (b) (4)							
	MEAN	3.786	1.357	3.071	1.929	1.429	1.857	0.500
	SD	1.551	0.378	0.673	1.170	0.607	1.180	0.577
	MIN	2.00	1.00	2.00	1.00	0.50	0.00	0.00
	MAX	6.50	2.00	4.00	4.50	2.00	3 50	1.50
4	[redacted] (b) (4)							
	MEAN	1.929	2.357	3.071	1.000	2.143	1.214	0.643
	SD	0.976	1.376	1.427	0.816	1.749	0.567	0.476
	MIN	1.00	1.00	1.00	0.00	0.50	0 50	0.00
	MAX	3.50	5.00	4.00	2.50	5.00	2.00	1.00
	N	7	7	7	7	7	7	7

(b) (4)

APPENDICES
F1 PUPPIES POST-WEANING

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING

The following abbreviations and footnotes have been used throughout the appendix

Only cage-side observations with abnormal findings are presented.

Post: Post Dose

Rx: Dose

DCE: Detailed Clinical Examination

UNS: Unscheduled

AM: Ante Meridiem

PM: Post Meridiem

Severity Codes:

X=Present

1=Slight

2=Moderate

A=Absent

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
1	(b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	X	.	.	X	.	.	.	.	.
		Skin Scab	Abdominal	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
1	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	X	X
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	X	.	X	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
1	[redacted]	Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	X	.	.	X	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	X	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	X	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	.	.	1	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	1	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	X	.	.	.	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Skin Scab	Abdominal	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

1012 of 1567

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	X	.	X	.	.	.	X	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	.	X	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
1	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	.	.	.	.	X	.	X	.	.	.	.
		Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 110 AM	110 PM	111 AM	111 PM	112 AM	113 AM	113 PM	114 AM	114 PM	115 AM	115 PM	116 AM	116 PM	117 AM
1	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	X
		Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	X	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	1	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	1	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Liquid		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	X	.	X	.	X	.
		Skin Red	Ear Canal Left	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Skin Scab	Penis	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	X	.	X	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
1	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft		.	.	.	.	.	X	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
1	[redacted] (b) (4)	Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	X	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	X	.	.	X	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
1	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	X	.	.	X	X
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	X	.	.	X	X	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	X	.	X	.	.	.	X	X	X	.	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	X	X	.	.	.	.	.	.	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	X	.	X
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	X	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	.	.	.	.	.	2	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	.	.	2	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	X	.	.	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	.	.	X	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	.	.	X	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	X	.	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	X	X	.	.	.	X	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
1	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	X	X	.	.	.	.	.	.	.	X	.	.	.
		Material Liquid Beige (Group Housed)		.	.	.	.	.	.	.	.	1	.	.	.	.	.
		Material Liquid Brown (Group Housed)		.	.	.	.	.	.	.	2	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Material Liquid Beige (Group Housed)		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Material Liquid Brown (Group Housed)		.	.	.	2	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	X	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	.	.	.	2	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	2	.	.	.	.	.	.
		Discharge, Yellow	Penis	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	X	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
1	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	X	.	X	.	.	X	.	.	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	X	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 197 AM	197 PM	198 AM	198 UNS	198 PM	199 AM	199 PM	200 AM	200 PM	201 AM	201 PM	202 AM	202 PM	203 AM
1	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	X	.	.	.	X	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Liquid Brown (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	2
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Liquid Brown (Group Housed)		.	.	.	.	.	.	.	.	.	2	.	.	.	.
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
1	[redacted] (b) (4)	No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	X
		Discharge, Brown	Ear Canal Left	1	.	.	.	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	1	.	.	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Ear Canal Left	X	.	.	.	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 209 PM	210 AM	210 PM	211 AM	211 PM	212 AM	212 PM	213 AM	213 PM	214 AM	215 AM	215 PM	216 AM	216 PM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 217 AM	217 PM	218 AM	218 PM	219 AM	220 AM	220 PM	221 AM	222 AM	223 AM	224 AM	224 PM	225 AM	226 AM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	.	.	.	1	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Material Undigested Food		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	X	.	.	.	.	X	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
2	[redacted] (b) (4)	Material Undigested Food		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
2	[redacted] (b) (4)	Feces Soft		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	X	.	X	.	X	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	X	.	X	.	X	X
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	X	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Liquid		.	X	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	X	.	X	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	X	.	X	.	X	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
2	[redacted] (b) (4)	Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	X	.	.	.	X	.	X	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	X	.	X	.	X	X	.	.
		Feces Soft		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO	CLINICAL SIGN	SITE	DAY 110 AM	110 PM	111 AM	111 PM	112 AM	113 AM	113 PM	114 AM	114 PM	115 AM	115 PM	116 AM	116 PM	117 AM
2	[redacted] (b) (4)	Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	X	.
		Feces Soft		.	X	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	X	X	X	.	X
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
2		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	X	.	X	.	.	.	.
		Feces Loose		.	.	X	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	X	X	X	.
	(b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	X	.	.	X	.	X	.	.	.	.	.

1040 of 1567

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO	CLINICAL SIGN	SITE	DAY 124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
2		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	X	.	.
		Feces Loose (Group Housed)		X	.	X	.	X	.	X	.	X	.	.	.	.	.
		Feces Liquid (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
2	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	X	.	X	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	X
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	X	.	.	X	.	X

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
2		Feces Red		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	X	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Material Mucoid Red		.	.	.	.	.	.	.	.	.	.	.	.	1	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	X	.	X	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Material Mucoid Red		.	.	.	.	.	.	.	.	.	.	1	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	X	.	.	X	.	X
	(b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	X	.	X	X	X	.	.	.	X	.	.	.	.
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
2		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	X	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft		.	X	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Material Mucoid Yellow		.	1	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	X	.	X	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	X	.	.	X	.	X	X	.	.	.	.	X
	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.

1044 of 1567

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
2	(b) (4)	Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Undigested Food (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	X	.	X
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	X	.	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
2	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	X	.	X
		Feces Loose (Group Housed)		X	.	.	.	.	.	X	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	.	.	.	.	X	.	.	.	X
		Limited Usage	Hindlimb Left	.	.	.	.	.	.	.	1	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	X	X	.	.	.	.	.	X	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	X	.	X	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
2		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	X	.	X	.
	(b) (4)	Feces Loose (Group Housed)		.	.	X	.	X	.	X	.	X	.	X	.	X	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Limited Usage	Hindlimb Left	.	.	.	.	.	.	.	1	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	X	.	.	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	X	X	.	X	.	X	.	X	X	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	X	X	X	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
2	(b) (4)	Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	X
		Material Mucoid Brown		.	.	.	.	.	.	.	.	.	.	.	.	.	1
		Feces Loose		.	.	.	.	.	.	X	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	X	.	X	X	.	X	.
		Feces Loose (Group Housed)		.	.	X	X	.	X	.	X	.	X	X	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 197 AM	197 PM	198 AM	198 UNS	198 PM	199 AM	199 PM	200 AM	200 PM	201 AM	201 PM	202 AM	202 PM	203 AM
2	[redacted] (b) (4)	Feces Loose (Group Housed)		X	.	X	.	.	X	.	X	.	X	.	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
2	[redacted] (b) (4)	No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Limited Usage	Hindlimb Left	1	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 209 PM	210 AM	210 PM	211 AM	211 PM	212 AM	212 PM	213 AM	213 PM	214 AM	215 AM	215 PM	216 AM	216 PM
2	[redacted]	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	X	.	.	.
		Material Dry Brown (Group Housed)		.	.	.	.	.	2	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 217 AM	217 PM	218 AM	218 PM	219 AM	220 AM	220 PM	221 AM	222 AM	223 AM	224 AM	224 PM	225 AM	226 AM
2	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	X	.	.	.	.	X
		Material Dry Brown (Group Housed)		.	.	.	.	2	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	X	.	.	.	.	.	.	X	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
2		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	X	.	.	.	.	X
	(b) (4)	Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Limited Usage	Hindlimb Left	.	.	.	.	.	.	.	1	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
2	(b) (4)	No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		Teeth Broken		.	.	.	X	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
3	[redacted]	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
3	[redacted] (b) (4)	Material Frothy Brown (Group Housed)		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Material Frothy Brown (Group Housed)		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Material Undigested Food		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
3		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
	(b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 110 AM	110 PM	111 AM	111 PM	112 AM	113 AM	113 PM	114 AM	114 PM	115 AM	115 PM	116 AM	116 PM	117 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
3	(b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	X	X	.	.
		Teeth Broken		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	X	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
3	[redacted] (b) (4)	Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	X	.	X	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	X	.	X	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	X	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	X	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	X	.	X

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
3	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	X	.	.	X	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Broken Nail/Claw	Hindpaw Left	.	.	.	.	.	.	.	.	.	X	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	X	.	.	.	.	X
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	X	.	.	.	.	X
		Skin Red	Inguinal Left	.	.	.	.	.	.	.	.	.	X	.	.	.	.
			Inguinal Right	.	.	.	.	.	.	.	.	.	X	.	.	.	.
			Pinna Left	.	.	.	.	.	.	.	.	.	X	.	.	.	.
			Pinna Right	.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
3	(b) (4)	Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
3	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	X	.	.	.	.
		Feces Liquid (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	X	.	.	.	.
		Feces Liquid (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	X	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	X	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
3		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Material Liquid Beige (Group Housed)		.	.	.	.	.	.	.	.	.	.	1	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	X	.
		Material Liquid Beige (Group Housed)		.	.	.	.	.	.	.	.	1	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
	(b) (4)	Feces Loose (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Skin Red	Pinna Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Pinna Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		X	.	.	X	.	.	.	.	.	.	.	.	X	.
		Material Dry Brown (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	X	X	.
		Material Dry Brown (Group Housed)		1	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	X	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	X	X	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	X	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	X	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	X	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 197 AM	197 PM	198 AM	198 UNS	198 PM	199 AM	199 PM	200 AM	200 PM	201 AM	201 PM	202 AM	202 PM	203 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Material Dry Brown (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	1
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Dry Brown (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	1	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	.	.	.	X	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	.	.	.	X	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
3		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Material Liquid Beige (Group Housed)		.	.	.	.	1	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Liquid Beige (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Material Frothy Beige (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Material Frothy Clear (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
	(b) (4)	Feces Soft		.	.	.	X	.	X	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Material Frothy Beige (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Material Frothy Clear (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Pinna Left	X	.	.	.	.	.	.	.	.	.	.	.	.	.
			Pinna Right	X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 209 PM	210 AM	210 PM	211 AM	211 PM	212 AM	212 PM	213 AM	213 PM	214 AM	215 AM	215 PM	216 AM	216 PM
3	(b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 217 AM	217 PM	218 AM	218 PM	219 AM	220 AM	220 PM	221 AM	222 AM	223 AM	224 AM	224 PM	225 AM	226 AM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Broken Nail/Claw	Forepaw Left	.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Skin Wound with Discharge	Forepaw Left	.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	X
		Skin, Blue	Pinna Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Skin Red	Pinna Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Pinna Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Skin Scab	Pinna Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Swelling Firm	Pinna Left	.	.	.	.	.	.	.	1	.	.	.	.	.	.
			Pinna Right	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	X	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Pinna Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Pinna Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
3	[redacted] (b) (4)	Skin Red	Pinna Left	.	.	.	X	.
			Pinna Right	.	.	.	X	.
		Skin Scab	Pinna Left	.	.	.	X	.
		Broken Nail/Claw	Forepaw Right	.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		Skin Red	Pinna Left	.	.	.	X	.
			Pinna Right	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
4	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Skin Scab	Urogenital	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	X	.	X	.	.	.
		Material Dry Brown (Group Housed)		.	.	.	.	.	.	2	.	.	.	.	.	.	.
		Skin Scab	Penis	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
4	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	X	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
4	(b) (4)	Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Skin Dry	Abdominal	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Skin Scab	Abdominal	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	X	.
		Skin Scab	Penis	.	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
4	(b) (4)	Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
4	[redacted]	Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 110 AM	110 PM	111 AM	111 PM	112 AM	113 AM	113 PM	114 AM	114 PM	115 AM	115 PM	116 AM	116 PM	117 AM
4	(b) (4)	Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	X
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Discharge, Clear	Penis	.	.	.	.	1	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		X	X	.	X	.	.	X	.	X	.	X	.	X	.
		Feces Liquid (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	X	X	.	X	.	X	.	X	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
4	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO	CLINICAL SIGN	SITE	DAY														
				131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
4		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Material Undigested Food		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	X	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	X
	(b) (4)	Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
4	[redacted] (b) (4)	Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	X	.	.	.	X	.	.	X	X	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	X	.	.	.	X	.	.	X	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	X	.	.
		Feces Loose		.	X	.	.	X	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	X	X	.	.
		Tail Kinked		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	X	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
4	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	X	.	.	X	.	.	.	.	.	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
4	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	X	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	X
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
4	[redacted] (b) (4)	Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	X	.	.	.	.	.
		Tail Kinked		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Discharge, Yellow	Penis	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Fur Thin	Tail	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
4	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	X	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	X	X	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
4	[redacted]	Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 197 AM	197 PM	198 AM	198 UNS	198 PM	199 AM	199 PM	200 AM	200 PM	201 AM	201 PM	202 AM	202 PM	203 AM
4	[redacted]	Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	X	.	.	.	.	.	X	.	X
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	X	.	X	.	X	.	X
		Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
4	[redacted] (b) (4)	No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	X	.	X	.	.	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	X	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	1	.	.	.	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	2	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	X	.	X	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Tail Kinked		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	X	.
		Discharge, Brown	Ear Canal Right	1	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO	CLINICAL SIGN	SITE	DAY 209 PM	210 AM	210 PM	211 AM	211 PM	212 AM	212 PM	213 AM	213 PM	214 AM	215 AM	215 PM	216 AM	216 PM
4	[redacted] (b) (4)	Feces Loose		X	.	X	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	X	X	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	X	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 217 AM	217 PM	218 AM	218 PM	219 AM	220 AM	220 PM	221 AM	222 AM	223 AM	224 AM	224 PM	225 AM	226 AM
4		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
	(b) (4)	Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.

1102 of 1567

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
4	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft		.	X	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	X	.	.	.	.	.	.	.	.	.
		Tail Kinked		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
4	(b) (4)	No Abnormalities Detected		.	.	.	X	.
		Feces Loose		.	X	.	.	.
		Tail Kinked		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		Discharge, Brown	Ear Canal Right	.	.	.	1	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	X	.	.	X	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
1	[redacted]	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	X	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	X	X	.	.	X	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
1	[redacted]	Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	X	X	.	.
		Broken Nail/Claw	Forepaw Right	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Skin Wound with Discharge	Forepaw Right	2	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Skin Red	Anus	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Swelling Soft	Anus	.	.	.	.	.	.	1	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
1	[redacted]	Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	X	.	.	.
		Feces Loose		.	.	.	X	.	.	.	X	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	X	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
1	[redacted]	Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
1	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Anus	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Swelling Soft	Anus	.	.	.	.	1	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces, Output		.	.	.	.	.	.	.	.	.	.	.	.	.	A
		Broken Nail/Claw	Forepaw Right	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Skin Red	Anus	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Swelling Soft	Anus	.	.	.	.	1	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Material Undigested Food		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
1	[redacted] (b) (4)	Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Material Undigested Food		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
1	[redacted] (b) (4)	Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	X	.	X
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	X	.	X	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
1		eces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		eces Loose (Group Housed)		.	X	.	.	.	.	.	X	.	.	.	.	X	.
		Material Liquid Red		1	.	.	.	.	.	.	.	.	.	.	.	.	.
		eces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		eces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		eces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	X
	(b) (4)	eces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		eces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	X	.	.	.	.

1114 of 1567

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
1	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Discharge, Brown	Ear Canal Right	.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Anus	.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Swelling Soft	Anus	.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Discharge, Brown	Ear Canal Right	.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Pinna Right	.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
1	[redacted] (b) (4)	Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
1	[redacted]	Material Mucoid Brown (Group Housed)		.	.	.	.	.	.	1	.	.	.	.	.	.	.
		Material Mucoid Brown (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
1	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Malocclusion		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Right	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Discharge, Yellow	Vulva	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
1	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	.	.	.	1	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
1	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	X	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	X	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
1	[redacted] (b) (4)	Skin Red	Ear Canal Right	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Malocclusion		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Right	1	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
1	[redacted] (b) (4)	Skin Dry	Forepaw Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Forepaw Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Malocclusion		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
1	[redacted] (b) (4)	Skin Dry	Forepaw Left	.	.	.	X	.
			Forepaw Right	.	.	.	X	.
		Skin Red	Ear Canal Left	.	.	.	X	.
			Ear Canal Right	.	.	.	X	.
		Malocclusion		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
2	(b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	X	.	.	.	.	X	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
2	[redacted]	Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	X	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
2	[redacted] (b) (4)	Feces Loose		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	X	.	.	.	X	.	.
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	X	.
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	X

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
2	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	X
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	X	.
		Undigested Food (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
2	[redacted]	Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Material Undigested Food		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				110 AM	110 PM	111 AM	111 PM	112 AM	113 AM	113 PM	114 AM	114 PM	115 AM	115 PM	116 AM	116 PM	117 AM
2	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Material Mucoid Red		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
2	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	X	.	.
		Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	X	.	X	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	X	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
2	[redacted] (b) (4)	Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	X	.	X	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	X	.	.	.	X
		Material Mucoid Red (Group Housed)		.	.	.	.	.	.	.	1	.	1	.	.	.	.
		Feces Loose		X	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	X	.	X	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	X	.	.	.	X	.	.
		Material Liquid Red		.	.	.	.	.	.	1	.	.	.	.	.	.	.
		Material Mucoid Red (Group Housed)		.	.	.	.	.	1	.	1	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	X	.	X
		Feces Loose		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	X	.	.	X	X	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	X	.	.	X	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	X	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
2	[redacted] (b) (4)	Feces Liquid		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	X	.	.	.	.	.	.	X	.	.	.	.
		Feces Liquid		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	X	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Undigested Food		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Material Liquid Beige (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Material Liquid Beige (Group Housed)		1	.	.	.	.	.	.	.	.	.	.	.	.	.
		Skin Scab	Pinna Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Skin Red	Cervical Ventral	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Skin Scab	Cervical Ventral	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Swelling Firm	Cervical Ventral	.	.	.	.	.	.	.	1	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
2		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose		.	.	.	.	.	.	X	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
	(b) (4)	Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	.	.	.	1	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
2	[redacted]	Feces Loose		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	X	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 197 AM	197 PM	198 AM	198 UNS	198 PM	199 AM	199 PM	200 AM	200 PM	201 AM	201 PM	202 AM	202 PM	203 AM
2	[redacted] (b) (4)	Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	X	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	X	.	X	.	.	.	.
		Feces Liquid		.	X	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	X	.	.	.	X
		Feces Liquid (Group Housed)		.	.	.	.	.	X	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	X	.	X	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
2	[redacted] (b) (4)	No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	X	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Liquid		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Skin Red	Cervical Ventral	X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Swelling Firm	Cervical Ventral	1	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 209 PM	210 AM	210 PM	211 AM	211 PM	212 AM	212 PM	213 AM	213 PM	214 AM	215 AM	215 PM	216 AM	216 PM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	X	.	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 217 AM	217 PM	218 AM	218 PM	219 AM	220 AM	220 PM	221 AM	222 AM	223 AM	224 AM	224 PM	225 AM	226 AM
2	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Material Liquid Yellow (Group Housed)		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Material Mucoid Yellow (Group Housed)		.	.	.	.	.	.	.	1	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Material Liquid Yellow (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Yellow (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Skin Red	Cervical Ventral	.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Swelling Firm	Cervical Ventral	.	.	.	.	.	.	.	1	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
2	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		Discharge, Green	Vulva	.	.	.	1	.
		Skin Lump	Lip	.	.	.	X	.
		Discharge, Brown	Ear Canal Left	.	.	.	1	.
			Ear Canal Right	.	.	.	1	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Skin Dry	Hindpaw Left	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Hindpaw Right	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Skin Dry	Hindpaw Left	.	.	.	.	.	.	X	.	.	.	.	.	.	.
			Hindpaw Right	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	X	.	.	X	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	X	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	X	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	X	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				110 AM	110 PM	111 AM	111 PM	112 AM	113 AM	113 PM	114 AM	114 PM	115 AM	115 PM	116 AM	116 PM	117 AM
3	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	X	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
3	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Red (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	X	.	X	.	.
		Material Mucoid Yellow (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	1
		Feces Red (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	X	.	X	.	.
		Material Mucoid Yellow (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	1

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
3	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Red (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	X	.	.	.	.	X	.	.
		Material Liquid Red (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	1	.	.
		Material Mucoid Red (Group Housed)		.	.	.	.	.	.	1	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	X	.	.	X	.	.	.	.	.	.
		Feces Red (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	X	.	.	.	.	X	.	.	.	X	X
		Material Mucoid Red		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Material Liquid Red (Group Housed)		.	.	.	.	.	.	.	.	1	.	.	.	.	.
		Material Mucoid Red (Group Housed)		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	.	.	.	.	.	.	1	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	.	.	.	.	.	.	1	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
3	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	X	.	.	.	.	.	.	X	.	X	X	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	X	.	X	.	.	X
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Material Liquid Beige		.	.	.	.	.	1	.	.	.	.	.	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	.	.	.	.	.	.	1	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Material Frothy Yellow (Group Housed)		.	.	.	.	.	.	.	.	1	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
3	(b) (4)	Feces Loose		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	X	.	.	.	.	.	.	.	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	X	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	X	.	X	.	X	.	X	.
		Feces Soft (Group Housed)		.	X	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	X	.	X	.	X	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Material Mucoid Yellow		.	.	.	.	.	.	.	.	.	.	.	1	.	.
		Material Frothy Yellow (Group Housed)		.	1	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Material Frothy Yellow (Group Housed)		.	1	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
3	(b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	.	.	.	.	.	.	.	X	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
3	(b) (4)	Feces Loose (Group Housed)		X	.	.	X	.	.	.	.	.	X	X	X	X	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	.	X	X	X	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
3	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

(b) (4)

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 197 AM	197 PM	198 AM	198 UNS	198 PM	199 AM	199 PM	200 AM	200 PM	201 AM	201 PM	202 AM	202 PM	203 AM
3	[redacted]	Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	.	X	.	X	.	X
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	X	.	X	.	X	.	X	.	X
		Feces Liquid (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Brown (Group Housed)		.	.	.	1	.	.	.	.	.	.	.	.	.	.
		Feces Liquid (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
	(b) (4)	Material Mucoid Brown (Group Housed)		.	.	.	1	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
3	[redacted] (b) (4)	No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	X	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	X	.	.	.	.	.	.	.	X	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Skin Red	Ear Canal Left	X	.	.	.	.	.	.	.	.	.	.	.	.	.
			Ear Canal Right	X	.	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 209 PM	210 AM	210 PM	211 AM	211 PM	212 AM	212 PM	213 AM	213 PM	214 AM	215 AM	215 PM	216 AM	216 PM
3	[redacted]	Feces Soft (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	X	.	X	.	X	X	.	X	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	X	.	X	.	X	X	.	.	.

1169 of 1567

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 217 AM	217 PM	218 AM	218 PM	219 AM	220 AM	220 PM	221 AM	222 AM	223 AM	224 AM	224 PM	225 AM	226 AM
3	(b) (4)	Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
3	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
3	[redacted] (b) (4)	Material Undigested Food		.	.	X	.	.
		Skin Scab	Pinna Right	.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		Skin Red	Eyelid Left	.	.	.	X	.
		Skin Red	Ear Canal Left	.	.	.	X	.
			Ear Canal Right	.	.	.	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 62 AM	62 UNS Post	62 PM	63 AM	63 DCE	63 PM	64 During Rx1	65 AM	66 AM	68 AM	69 AM	70 PM	71 AM	72 AM
4	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Undigested Food (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Skin Scab	Abdominal	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	X	X	.	X	.	.	.
		Material Dry Brown (Group Housed)		.	.	.	.	.	.	2	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 72 PM	73 AM	74 AM	75 AM	76 AM	76 PM	77 AM	77 PM	78 AM	78 PM	79 AM	79 PM	80 AM	81 AM
4	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 81 PM	82 AM	82 PM	83 AM	83 PM	84 AM	84 PM	85 AM	85 PM	86 AM	86 PM	87 AM	87 PM	88 AM
4	[redacted] (b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 88 PM	89 AM	89 PM	90 AM	90 PM	91 AM	91 DCE	91 PM	92 AM	92 PM	93 AM	93 PM	94 AM	94 PM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Broken Nail/Claw	Forepaw Right	.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Skin Scab	Abdominal	.	.	.	.	.	.	X	.	.	.	.	.	.	.
			Cervical Ventral	.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Skin Wound with Discharge	Forepaw Right	.	.	.	.	1	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	.	.	1	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	1	.	.	.	.	.	.	.
		Fur Thin	Tail	.	.	.	.	.	.	1	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY													
				95 AM	95 PM	96 AM	96 PM	97 AM	97 PM	98 AM	98 PM	99 AM	99 PM	100 AM	100 PM	101 AM	101 PM
4	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Liquid (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Material Mucoid Yellow (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	1	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

1177 of 1567

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 102 AM	102 PM	103 AM	103 PM	104 AM	104 PM	105 AM	105 PM	106 AM	106 PM	107 AM	108 AM	108 PM	109 AM
4	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Liquid (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Yellow (Group Housed)		.	.	1	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Material Liquid Yellow		.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				110 AM	110 PM	111 AM	111 PM	112 AM	113 AM	113 PM	114 AM	114 PM	115 AM	115 PM	116 AM	116 PM	117 AM
4	[redacted] (b) (4)	Feces Soft		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 117 PM	118 AM	118 PM	119 AM	119 DCE	119 PM	120 AM	120 PM	121 AM	121 PM	122 AM	122 PM	123 AM	123 PM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	X	.	X	.
		Broken Nail/Claw	Forepaw Right	.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	1	.	.	.	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	1	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	X	.	.	.	.	.
		Skin Red	Abdominal	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Ear Canal Left	.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 124 AM	124 PM	125 AM	125 PM	126 AM	126 PM	127 AM	127 PM	128 AM	128 PM	129 AM	129 PM	130 AM	130 PM
4	(b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	X
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	X	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY														
				131 AM	131 PM	132 AM	132 PM	133 AM	133 UNS Post	133 PM	134 AM	134 PM	135 AM	135 PM	136 AM	136 PM	137 AM
4		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	X	.	X	.	.	X	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
	(b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 137 PM	138 AM	138 PM	139 AM	139 PM	140 AM	140 PM	141 AM	141 PM	142 AM	142 PM	143 AM	143 PM	144 AM
4	[redacted] (b) (4)	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	X	.	.	X	X
		Feces Loose (Group Housed)		.	X	.	.	.	X	.	.	X	X	.	.	.	X

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 144 UNS Pre	144 PM	145 AM	145 UNS Pre	145 PM	146 AM	146 UNS Pre	146 PM	147 AM	147 DCE	147 PM	148 AM	148 PM	149 AM
4		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		Feces Red (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	X	.	X	.	.	X	.	X
		Material Mucoid Red (Group Housed)		.	.	.	.	.	.	1	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Red (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	X	.	.	X	.	.	.	.	.
		Material Mucoid Red (Group Housed)		1	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	X
	(b) (4)	Discharge, Brown	Ear Canal Left	.	.	.	.	.	.	.	.	.	1	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	.	.	1	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

(b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 149 PM	150 AM	150 PM	151 AM	152 AM	152 PM	153 AM	153 PM	154 AM	154 PM	155 AM	156 AM	156 PM	157 AM
4	(b) (4)	Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	X	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	X
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	X	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 158 AM	158 PM	159 AM	159 PM	160 AM	160 PM	161 AM	161 UNS	161 PM	162 AM	162 PM	163 AM	163 PM	164 AM
4	[redacted]	Feces Soft (Group Housed)		.	.	.	.	X	.	X	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		X	.	X	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted]

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 164 PM	165 AM	166 AM	166 UNS Pre	166 PM	167 AM	168 AM	168 UNS Pre	169 AM	169 PM	170 AM	170 PM	171 AM	171 PM
4	[redacted]	Feces Loose		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 172 AM	172 PM	173 AM	173 PM	174 AM	174 PM	175 AM	175 DCE	176 AM	176 PM	177 AM	177 PM	178 AM	178 PM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	X	.	.	.
		Discharge, Brown	Ear Canal Left	.	.	.	.	.	.	.	1	.	.	.	.	.	.
			Ear Canal Right	.	.	.	.	.	.	.	1	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	X	.	.	.	X	.	.	.
		Skin Red	Ear Canal Left	.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 179 AM	179 PM	180 AM	181 AM	181 PM	182 AM	182 PM	183 AM	183 PM	184 AM	185 AM	186 AM	187 AM	187 PM
4	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	X	.	.	.	.	X	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	X	.
		Feces Soft (Group Housed)		.	.	X	.	.	.	.	X	.	.	.	X	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 188 AM	188 PM	189 AM	190 AM	190 PM	191 AM	191 PM	192 AM	192 PM	193 AM	194 AM	195 AM	196 AM	196 PM
4	[redacted] (b) (4)	Feces Loose		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	X	X	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 197 AM	197 PM	198 AM	198 UNS	198 PM	199 AM	199 PM	200 AM	200 PM	201 AM	201 PM	202 AM	202 PM	203 AM
4	[redacted] (b) (4)	Feces Soft		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Material Undigested Food		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	X	.	.
		Feces Loose (Group Housed)		X	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 203 DCE	203 PM	204 AM	204 PM	205 AM	205 PM	206 AM	206 PM	207 AM	207 PM	208 AM	208 PM	209 AM	209 UNS
4	[redacted] (b) (4)	No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Soft		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	.	X	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	X	.	.	.	.	.	.	.
		No Abnormalities Detected		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Loose		.	.	.	X	.	.	.	.	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 209 PM	210 AM	210 PM	211 AM	211 PM	212 AM	212 PM	213 AM	213 PM	214 AM	215 AM	215 PM	216 AM	216 PM
4	[redacted] (b) (4)	Feces Soft (Group Housed)		.	X	.	.	.	.	.	.	.	.	.	.	.	.
		Feces Liquid		.	.	X	.	.	.	.	.	.	.	.	.	.	.
		Material Mucoid Yellow		.	.	1	.	.	.	.	.	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 217 AM	217 PM	218 AM	218 PM	219 AM	220 AM	220 PM	221 AM	222 AM	223 AM	224 AM	224 PM	225 AM	226 AM
4	[redacted] (b) (4)	Feces Soft (Group Housed)		.	.	.	.	.	.	.	.	.	X	.	.	.	.
		Feces Soft (Group Housed)		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Loose (Group Housed)		.	.	.	.	.	X	.	.	.	.	.	.	X	.
		Feces Loose (Group Housed)		.	.	X	.	.	.	.	.	.	X	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 227 AM	227 PM	228 AM	228 PM	229 AM	230 AM	231 AM	231 DCE	232 AM	232 PM	233 AM	234 AM	234 PM	235 AM
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Undigested Food (Group Housed)		.	.	.	.	X	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		Feces Liquid		.	.	.	.	.	.	.	.	.	X	.	.	X	.
		Feces Loose (Group Housed)		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		Undigested Food (Group Housed)		X	.	.	.	.	.	.	.	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.
		No Abnormalities Detected		.	.	.	.	.	.	.	X	.	.	.	.	.	.

APPENDIX NO. 45

[redacted] (b) (4)

CLINICAL OBSERVATIONS WITH SITE BY ANIMAL
F1 GENERATION - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	CLINICAL SIGN	SITE	DAY 235 PM	237 AM	238 AM	238 DCE	238 UNS
4	[redacted] (b) (4)	No Abnormalities Detected		.	.	.	X	.
		Feces Loose		X	.	.	.	.
		Feces Loose (Group Housed)		.	X	.	.	.
		No Abnormalities Detected		.	.	.	X	.
		No Abnormalities Detected		.	.	.	X	.
		Material Frothy Green		.	.	.	.	1
		Material Liquid Green		.	.	.	.	1
		No Abnormalities Detected		.	.	.	X	.

BODY WEIGHT - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations and footnote have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

*: Actual day is Day 108

APPENDIX NO. 46

(b) (4) 002

BODY WEIGHT (kg)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	Day 63	Day 70	Day 77	Day 84	Day 91	Day 98	Day 105	Day 112	Day 119	Day 126
1	(b) (4)											
	MEAN	2.734	3.210	3.590	3.870	4.265	4.830	5.525	5.845	6.090	6.720	7.110
	SD	0.165	0.212	0.251	0.313	0.390	0.422	0.624	0.589	0.608	0.659	0.587
	MIN	2 54	3.02	3.38	3.58	3.92	4.42	4.90	5.26	5.46	6.06	6.52
	MAX	2 91	3.44	3.94	4.28	4.66	5.26	6.20	6.58	6.74	7.40	7.70
	N	4	4	4	4	4	4	4	4	4	4	4
2	(b) (4)											
	MEAN	2.953	3.360	3.790	4.135	4.440	4.920	5.565	6.145	6.330	6 900	7.495
	SD	0.199	0.236	0.270	0.328	0.399	0.483	0.706	0.764	0.797	1.009	1.019
	MIN	2.70	3.02	3.56	3.76	3.94	4.36	4.84	5.46	5.52	5.92	6.56
	MAX	3 15	3.56	4.18	4.56	4.80	5.44	6.36	7.14	7.12	7.80	8.72
	N	4	4	4	4	4	4	4	4	4	4	4
3	(b) (4)											
	MEAN	2.820	3.285	3.750	4.095	4.360	4.770	5.290	5.920	6.025	6.440	7.000
	SD	0.238	0.230	0.232	0.298	0.215	0.414	0.493	0.808	0.527	0 574	0.882
	MIN	2.47	2.96	3.42	3.70	4.04	4.24	4.74	5.16	5.46	5.84	6.14
	MAX	3.01	3.50	3.94	4.40	4.50	5.18	5.84	6.76	6.64	7.10	7.92
	N	4	4	4	4	4	4	4	4	4	4	4
4	(b) (4)											
	MEAN	2.789	3.275	3.635	3.915	4.240	4.650	5.205	5.730	5.990	6 350	6.850
	SD	0.290	0.264	0.357	0.330	0.347	0.441	0.505	0.713	0.580	0.679	0.881
	MIN	2 50	3.00	3.26	3.60	3.84	4.10	4.60	4.98	5.40	5.54	5.90
	MAX	3.08	3.52	3.94	4.20	4.54	5.08	5.66	6.52	6.60	6.94	7.60
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 46

[redacted] (b) (4)

BODY WEIGHT (kg)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 133	Day 140	Day 147	Day 154	Day 161	Day 168	Day 175	Day 182	Day 189	Day 196
1	[redacted] (b) (4)										
	MEAN	7.500	7.870	8.248	8.570	9.080	9.515	9.580	9.755	10.080	10.270
	SD	0.631	0.661	0.743	0.776	0.846	0.892	0.909	0.911	0.914	0.843
	MIN	6.86	7.22	7.45	7.68	8.00	8.34	8.58	8.80	9.10	9.30
	MAX	8.18	8.44	8.92	9.36	9.94	10.40	10.38	10.64	11.00	11.22
	N	4	4	4	4	4	4	4	4	4	4
2	[redacted] (b) (4)										
	MEAN	7.775	8.110	8.445	8.930	9.160	9.530	9.970	10.360	10.500	10.615
	SD	1.067	1.052	1.236	1.124	1.078	1.149	1.152	1.283	1.312	1.113
	MIN	6.84	7.16	7.24	7.78	8.08	8.26	8.70	8.98	9.10	9.46
	MAX	8.94	9.20	9.58	10.25	10.24	10.60	11.16	11.72	12.00	11.80
	N	4	4	4	4	4	4	4	4	4	4
3	[redacted] (b) (4)										
	MEAN	7.160	7.390	7.800	8.270	8.425	8.740	9.145	9.240	9.430	9.655
	SD	0.768	0.724	0.862	1.033	0.843	0.906	0.916	1.220	1.037	1.036
	MIN	6.36	6.64	6.84	7.22	7.44	7.84	8.26	7.90	8.22	8.46
	MAX	8.04	8.20	8.72	9.30	9.34	9.78	10.18	10.58	10.56	10.88
	N	4	4	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)										
	MEAN	7.255	7.585	7.995	8.415	8.780	9.190	9.400	9.765	10.160	10.400
	SD	0.858	1.064	0.945	1.048	1.263	1.342	1.409	1.439	1.427	1.524
	MIN	6.30	6.38	6.98	7.28	7.50	7.76	8.12	8.28	8.80	8.96
	MAX	8.00	8.48	8.82	9.44	10.00	10.46	10.82	11.18	11.62	11.90
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 46

(b) (4)

BODY WEIGHT (kg)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 203	Day 210	Day 217	Day 224	Day 231	Day 238
1	(b) (4)						
	MEAN	10.720	10.660	10.740	11.005	11.195	10.890
	SD	0.816	0.837	0.796	0.919	0.869	0.899
	MIN	9.60	9.72	9.88	9.84	10.12	9.74
	MAX	11.46	11.54	11.54	11.76	12.12	11.80
	N	4	4	4	4	4	4
2	(b) (4)						
	MEAN	11.000	11.100	11.255	11.570	11.885	11.385
	SD	1.166	1.177	1.246	1.252	1.284	1.286
	MIN	9.82	10.02	10.10	10.40	10.72	10.26
	MAX	12.20	12.42	12.74	13.06	13.48	12.94
	N	4	4	4	4	4	4
3	(b) (4)						
	MEAN	9.780	9.945	10.170	10.370	10.375	10.300
	SD	1.001	0.855	1.145	1.229	1.187	1.264
	MIN	8.50	9.04	8.72	8.74	8.88	8.54
	MAX	10.82	11.02	11.44	11.68	11.68	11.54
	N	4	4	4	4	4	4
4	(b) (4)						
	MEAN	10.880	11.055	11.270	11.560	11.810	11.450
	SD	1.599	1.616	1.629	1.693	1.961	1.745
	MIN	9.34	9.60	9.70	10.02	9.98	9.82
	MAX	12.26	12.60	13.02	13.38	14.00	13.54
	N	4	4	4	4	4	4

APPENDIX NO. 46

(b) (4)

BODY WEIGHT (kg)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	Day 63	Day 70	Day 77	Day 84	Day 91	Day 98	Day 105	Day 112	Day 119	Day 126
1	(b) (4)											
	MEAN	2.621	2.770	3.005	3.310	3.580	4.135	4.645	4.905	5.195	5 595	5.890
	SD	0.290	0.265	0.242	0.300	0.301	0.382	0.597	0.442	0.545	0.618	0.510
	MIN	2 29	2.44	2.66	2.88	3.18	3.60	3.84	4.26	4.42	4.76	5.16
	MAX	3.00	3.06	3.20	3.56	3.84	4.42	5.24	5.22	5.70	6.20	6.34
	N	4	4	4	4	4	4	4	4	4	4	4
2	(b) (4)											
	MEAN	2.535	2.875	3.360	3.575	3.920	4.390	5.035	5.485	5.585	6 110	6.705
	SD	0.394	0.428	0.456	0.480	0.388	0.416	0.425	0.715	0.608	0.709	0.920
	MIN	2 17	2.46	2.92	3.06	3.52	4.04	4.50	4.82	5.02	5.30	6.12
	MAX	2.88	3.32	3.88	4.14	4.36	4.90	5.54	6.50	6.42	7.02	8.06
	N	4	4	4	4	4	4	4	4	4	4	4
3	(b) (4)											
	MEAN	2.685	2.970	3.350	3.540	3.775	4.085	4.545	5.150	5.295	5 555	6.115
	SD	0.392	0.420	0.391	0.422	0.437	0.380	0.443	0.299	0.621	0.621	0.492
	MIN	2 39	2.58	2.92	3.14	3.36	3.76	4.14	4.90	4.76	5.04	5.74
	MAX	3 26	3.56	3.86	4.06	4.36	4.60	5.10	5.56	6.06	6.32	6.82
	N	4	4	4	4	4	4	4	4	4	4	4
4	(b) (4)											
	MEAN	2.503	2.910	3.210	3.470	3.770	4.135	4.590	5.060	5.435	5.790	6.205
	SD	0.224	0.258	0.295	0.317	0.322	0.381	0.461	0.590	0.649	0 586	0.656
	MIN	2 23	2.62	2.86	3.08	3.42	3.70	4.06	4.44	4.68	5.14	5.42
	MAX	2.78	3.22	3.54	3.80	4.14	4.60	5.18	5.84	6.24	6.54	7.02
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 46

(b) (4)

BODY WEIGHT (kg)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 133	Day 140	Day 147	Day 154	Day 161	Day 168	Day 175	Day 182	Day 189	Day 196
1	(b) (4)										
	MEAN	6.180	6.450	6.720	6.980	7.365	7.780	7.710	7.945	8.040	8.155
	SD	0.475	0.476	0.603	0.576	0.589	0.592	0.471	0.500	0.444	0.557
	MIN	5 56	5.82	5.90	6.24	6.62	7.04	7.20	7.34	7.52	7.50
	MAX	6.70	6.96	7.28	7.62	8.06	8.48	8.28	8.48	8.56	8.86
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	6.870	7.160	7.445	7.780	7.955	8.175	8.525	8.815	9.035	8.985
	SD	0.879	0.820	0.906	0.972	0.973	1.024	1.066	1.147	1.205	1.205
	MIN	5 98	6.32	6.54	7.00	7.02	7.16	7.46	7.86	8.08	7.88
	MAX	8.06	8.24	8.70	9.20	9.32	9.60	10.00	10.46	10.80	10.70
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	6.200	6.370	6.650	6.953	7.090	7.425	7.730	7.775	7.965	8.055
	SD	0.712	0.712	0.833	0.795	0.914	0.901	0.976	0.766	1.047	1.155
	MIN	5 58	5.74	5.88	6.30	6.18	6.66	6.86	7.12	7.08	7.10
	MAX	7 10	7.24	7.66	7.98	8.16	8.46	8.78	8.78	9.32	9.56
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	6.560	6.920	7.143	7.535	7.938	8.280	8.385	8.580	8.865	9.015
	SD	0.634	0.770	0.805	0.785	0.989	1.115	0.920	0.924	0.958	0.945
	MIN	5.82	5.94	6.15	6.60	6.91	7.24	7.34	7.64	7.90	8.10
	MAX	7 36	7.82	8.12	8.52	9.28	9.86	9.58	9.84	10.18	10.34
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 46

(b) (4)

BODY WEIGHT (kg)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 203	Day 210	Day 217	Day 224	Day 231	Day 238
1	(b) (4)						
	MEAN	8.595	8.440	8.475	8.530	8.630	8.425
	SD	0.662	0.557	0.471	0.612	0 542	0.543
	MIN	7.80	7.76	8.00	7.86	7.94	7.78
	MAX	9.42	9.12	9.10	9.24	9.26	9.00
	N	4	4	4	4	4	4
2	(b) (4)						
	MEAN	9.170	9.260	9.455	9.650	9 930	9.555
	SD	1.193	1.159	1.219	1.267	1 329	1.401
	MIN	8.02	8.10	8.32	8.50	8.66	8.42
	MAX	10.84	10.86	11.18	11.44	11.80	11.60
	N	4	4	4	4	4	4
3	(b) (4)						
	MEAN	8.120	8.325	8.340	8.460	8 580	8.285
	SD	1.215	1.346	1.127	1.052	1 180	1.105
	MIN	7.08	7.16	7.38	7.60	7.60	7.32
	MAX	9.64	9.78	9.72	9.80	10.16	9.68
	N	4	4	4	4	4	4
4	(b) (4)						
	MEAN	9.285	9.375	9.425	9.660	9.895	9.570
	SD	1.245	1.181	1.126	1.180	1 120	1.002
	MIN	8.16	8.30	8.46	8.54	8.76	8.44
	MAX	11.06	11.06	11.04	11.32	11.32	10.86
	N	4	4	4	4	4	4

BODY WEIGHT CHANGE - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

*: Actual day is Day 98 to 108

#: Actual day is Day 108 to 112

APPENDIX NO. 47

(b) (4)

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119
1	(b) (4)									
	MEAN	0.476	0.380	0.280	0.395	0.565	0.695	0.320	0.245	0.630
	SD	0.069	0.103	0.071	0.150	0.057	0.265	0.350	0.118	0.221
	MIN	0.38	0.26	0.20	0.24	0.48	0.48	-0.16	0.16	0.42
	MAX	0.53	0.50	0.34	0.60	0.60	1.08	0.68	0.42	0.94
	N	4	4	4	4	4	4	4	4	4
2	(b) (4)									
	MEAN	0.407	0.430	0.345	0.305	0.480	0.645	0.580	0.185	0.570
	SD	0.075	0.179	0.097	0.251	0.110	0.236	0.532	0.313	0.248
	MIN	0.32	0.24	0.20	0.16	0.40	0.42	-0.02	-0.12	0.36
	MAX	0.50	0.62	0.40	0.68	0.64	0.92	1 20	0.56	0.90
	N	4	4	4	4	4	4	4	4	4
3	(b) (4)									
	MEAN	0.465	0.465	0.345	0.265	0.410	0.520	0.630	0.105	0.415
	SD	0.031	0.146	0.081	0.158	0.262	0.115	0.341	0.313	0.053
	MIN	0.44	0.26	0.28	0.04	0.20	0.38	0 26	-0.20	0.36
	MAX	0.50	0.58	0.46	0.40	0.74	0.66	0 92	0.44	0.46
	N	4	4	4	4	4	4	4	4	4
4	(b) (4)									
	MEAN	0.486	0.360	0.280	0.325	0.410	0.555	0.525	0.260	0.360
	SD	0.079	0.095	0.040	0.115	0.125	0.082	0.242	0.141	0.164
	MIN	0.42	0.26	0.26	0.18	0.26	0.48	0 32	0.08	0.14
	MAX	0.60	0.46	0.34	0.46	0.56	0.66	0.86	0.42	0.52
	N	4	4	4	4	4	4	4	4	4

APPENDIX NO. 47

(b) (4) 002

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 119 to 126	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175
1	(b) (4)								
	MEAN	0.390	0.390	0.370	0.378	0.323	0.510	0.435	0.065
	SD	0.185	0.062	0.133	0.105	0.170	0.155	0.068	0.330
	MIN	0.12	0.34	0.26	0.23	0.14	0.32	0.34	-0.32
	MAX	0.54	0.48	0.56	0.48	0.52	0.68	0.50	0.42
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	0.595	0.280	0.335	0.335	0.485	0.230	0.370	0.440
	SD	0.386	0.170	0.060	0.265	0.333	0.209	0.137	0.107
	MIN	0.14	0.08	0.26	-0.02	0.00	-0.01	0.18	0.30
	MAX	0.98	0.48	0.40	0.62	0.73	0.48	0.48	0.56
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	0.560	0.160	0.230	0.410	0.470	0.155	0.315	0.405
	SD	0.324	0.161	0.050	0.151	0.213	0.273	0.162	0.034
	MIN	0.26	-0.04	0.16	0.20	0.22	-0.14	0.08	0.36
	MAX	0.86	0.34	0.28	0.52	0.70	0.50	0.44	0.44
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	0.500	0.405	0.330	0.410	0.420	0.365	0.410	0.210
	SD	0.224	0.041	0.208	0.133	0.163	0.323	0.101	0.340
	MIN	0.26	0.36	0.08	0.30	0.30	0.12	0.26	-0.08
	MAX	0.72	0.46	0.52	0.60	0.66	0.84	0.48	0.62
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 47

(b) (4)

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 175 to 182	Day 182 to 189	Day 189 to 196	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231
1	(b) (4)								
	MEAN	0.175	0.325	0.190	0.450	-0.060	0.080	0.265	0.190
	SD	0.122	0.041	0.173	0.235	0.258	0.073	0.228	0.202
	MIN	0.04	0.28	-0.04	0.24	-0.44	0.00	-0.04	-0.10
	MAX	0.32	0.36	0.38	0.76	0.12	0.16	0.44	0.36
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	0.390	0.140	0.115	0.385	0.100	0.155	0.315	0.315
	SD	0.136	0.115	0.232	0.075	0.128	0.118	0.010	0.235
	MIN	0.28	0.00	-0.20	0.30	-0.02	0.06	0.30	0.04
	MAX	0.56	0.28	0.36	0.48	0.22	0.32	0.32	0.58
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	0.095	0.190	0.225	0.125	0.165	0.225	0.200	0.005
	SD	0.330	0.202	0.115	0.162	0.276	0.363	0.141	0.148
	MIN	-0.36	-0.02	0.06	-0.06	-0.08	-0.32	0.02	-0.20
	MAX	0.40	0.40	0.32	0.28	0.54	0.42	0.36	0.14
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	0.365	0.395	0.240	0.480	0.175	0.215	0.290	0.250
	SD	0.157	0.106	0.112	0.177	0.218	0.209	0.101	0.283
	MIN	0.16	0.28	0.14	0.36	-0.06	-0.02	0.14	-0.04
	MAX	0.54	0.52	0.38	0.74	0.38	0.42	0.36	0.62
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 47

(b) (4)

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 231 to 238
1	(b) (4)	
	MEAN	-0.305
	SD	0.057
	MIN	-0.38
	MAX	-0.26
	N	4
2	(b) (4)	
	MEAN	-0.500
	SD	0.172
	MIN	-0.72
	MAX	-0.32
	N	4
3	(b) (4)	
	MEAN	-0.075
	SD	0.303
	MIN	-0.34
	MAX	0.36
	N	4
4	(b) (4)	
	MEAN	-0.360
	SD	0.273
	MIN	-0.70
	MAX	-0.12
	N	4

APPENDIX NO. 47

(b) (4)

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119
1	(b) (4)									
	MEAN	0.149	0.235	0.305	0.270	0.555	0.510	0.260	0.290	0.400
	SD	0.479	0.114	0.060	0.089	0.096	0.247	0.360	0.158	0.314
	MIN	-0.56	0.08	0.22	0.18	0.42	0.24	-0.26	0.16	0.18
	MAX	0.47	0.32	0.36	0.38	0.64	0.84	0.56	0.48	0.86
	N	4	4	4	4	4	4	4	4	4
2	(b) (4)									
	MEAN	0.341	0.485	0.215	0.345	0.470	0.645	0.450	0.100	0.525
	SD	0.069	0.053	0.066	0.098	0.074	0.251	0.531	0.329	0.274
	MIN	0.29	0.44	0.14	0.22	0.38	0.44	-0.22	-0.26	0.28
	MAX	0.44	0.56	0.28	0.46	0.54	1.00	0.96	0.46	0.88
	N	4	4	4	4	4	4	4	4	4
3	(b) (4)									
	MEAN	0.285	0.380	0.190	0.235	0.310	0.460	0.605	0.145	0.260
	SD	0.094	0.071	0.125	0.072	0.066	0.085	0.157	0.338	0.033
	MIN	0.19	0.30	0.02	0.14	0.24	0.38	0.46	-0.20	0.22
	MAX	0.41	0.44	0.32	0.30	0.40	0.56	0.76	0.50	0.30
	N	4	4	4	4	4	4	4	4	4
4	(b) (4)									
	MEAN	0.407	0.300	0.260	0.300	0.365	0.455	0.470	0.375	0.355
	SD	0.103	0.043	0.033	0.049	0.081	0.104	0.144	0.091	0.072
	MIN	0.28	0.24	0.22	0.24	0.28	0.36	0.34	0.24	0.30
	MAX	0.52	0.34	0.30	0.34	0.46	0.58	0.66	0.44	0.46
	N	4	4	4	4	4	4	4	4	4

APPENDIX NO. 47

(b) (4)

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 119 to 126	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175
1	(b) (4)								
	MEAN	0.295	0.290	0.270	0.270	0.260	0.385	0.415	-0.070
	SD	0.348	0.155	0.012	0.151	0.105	0.120	0.057	0.278
	MIN	-0.22	0.06	0.26	0.08	0.12	0.22	0.34	-0.40
	MAX	0.54	0.40	0.28	0.44	0.34	0.50	0.48	0.16
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	0.595	0.165	0.290	0.285	0.335	0.175	0.220	0.350
	SD	0.471	0.290	0.089	0.194	0.168	0.129	0.094	0.084
	MIN	-0.04	-0.16	0.18	0.04	0.18	0.02	0.14	0.26
	MAX	1.04	0.42	0.38	0.46	0.50	0.30	0.32	0.44
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	0.560	0.085	0.170	0.280	0.303	0.138	0.335	0.305
	SD	0.220	0.273	0.035	0.124	0.099	0.191	0.143	0.108
	MIN	0.28	-0.16	0.14	0.14	0.18	-0.12	0.16	0.18
	MAX	0.78	0.36	0.22	0.42	0.42	0.34	0.50	0.44
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	0.415	0.355	0.360	0.223	0.393	0.403	0.343	0.105
	SD	0.108	0.034	0.202	0.104	0.078	0.250	0.175	0.274
	MIN	0.28	0.32	0.12	0.08	0.28	0.18	0.16	-0.28
	MAX	0.52	0.40	0.58	0.30	0.45	0.76	0.58	0.32
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 47

[redacted] (b) (4)

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 175 to 182	Day 182 to 189	Day 189 to 196	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231
1	[redacted] (b) (4)								
	MEAN	0.235	0.095	0.115	0.440	-0.155	0.035	0.055	0.100
	SD	0.081	0.075	0.205	0.114	0.112	0.152	0.179	0.198
	MIN	0.14	0.00	-0.10	0.30	-0.30	-0.12	-0.14	-0.08
	MAX	0.32	0.18	0.30	0.56	-0.04	0.24	0.26	0.38
	N	4	4	4	4	4	4	4	4
2	[redacted] (b) (4)								
	MEAN	0.290	0.220	-0.050	0.185	0.090	0.195	0.195	0.280
	SD	0.288	0.214	0.125	0.148	0.053	0.097	0.100	0.156
	MIN	-0.14	-0.08	-0.20	0.06	0.02	0.10	0.06	0.14
	MAX	0.46	0.40	0.08	0.40	0.14	0.32	0.28	0.46
	N	4	4	4	4	4	4	4	4
3	[redacted] (b) (4)								
	MEAN	0.045	0.190	0.090	0.065	0.205	0.015	0.120	0.120
	SD	0.313	0.283	0.109	0.134	0.275	0.288	0.099	0.170
	MIN	-0.38	-0.04	0.00	-0.12	-0.04	-0.36	0.00	0.00
	MAX	0.30	0.54	0.24	0.20	0.60	0.26	0.22	0.36
	N	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)								
	MEAN	0.195	0.285	0.150	0.270	0.090	0.050	0.235	0.235
	SD	0.115	0.038	0.076	0.306	0.123	0.173	0.111	0.326
	MIN	0.04	0.26	0.04	0.06	-0.02	-0.16	0.08	0.00
	MAX	0.30	0.34	0.20	0.72	0.24	0.22	0.34	0.70
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 47

(b) (4)

BODY WEIGHT CHANGE (kg)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 231 to 238
1	(b) (4)	
	MEAN	-0.205
	SD	0.168
	MIN	-0.40
	MAX	0.00
	N	4
2	(b) (4)	
	MEAN	-0.375
	SD	0.180
	MIN	-0.54
	MAX	-0.20
	N	4
3	(b) (4)	
	MEAN	-0.295
	SD	0.140
	MIN	-0.48
	MAX	-0.14
	N	4
4	(b) (4)	
	MEAN	-0.325
	SD	0.515
	MIN	-0.88
	MAX	0.36
	N	4

DAILY FOOD CONSUMPTION - F1 GENERATION – PUPPIES - POST WEANING

The following abbreviations and footnotes have been used throughout the appendix and/or summary.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

T: Technical Oversight

WF: Wet or Contaminated Food

WF1: Wet or Contaminated Food, Slight Amount (1 to 100 g) Approximately

SC1: Spillage, Contaminated with liquid or solid material, Slight Amount (1 to 100 g) Approximately

SC2: Spillage, Contaminated with liquid or solid material, Moderate Amount (101 to 200 g) Approximately

SC3: Spillage, Contaminated with liquid or solid material, Severe Amount (201 to 300 g) Approximately

#: Food spillage not recorded

APPENDIX NO. 48 (b) (4)

DAILY CAGE FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
CAGE (MALES AND FEMALES)

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	Day 57	Day 58	Day 59	Day 60	Day 61	Day 62	Day 63
1	(b) (4)								
	MEAN	145.0	170.3	201.0	199.5	251.3	242.0	278.3	264.8
	SD	37.5	37.7	37.4	18.6	25.5	22.7	35.7	45.5
	MIN	117	139	158	175	230	208	233	216
	MAX	200	223	245	220	284	255	312	304
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	167.0	161.5	195.0	190.0	217.8	243.3	264.3	279.0
	SD	28.8	23.5	42.3	19.8	33.8	46.9	57.8	55.9
	MIN	124	146	148	175	183	182	215	219
	MAX	184	196	250	219	261	296	329	339
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	SD	19.0	32.4	12.4	26.5	37.9	21.5	47.8	36.7
	MIN	69	113	188	118	165	200	163	231
	MAX	111	188	216	180	248	251	252	315
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	176.0	181.3	234.8	181.3	251.8	239.8	277.0	233.5
	SD	34.8	8.3	42.6	46.4	15.6	76.0	45.5	51.5
	MIN	125	171	180	116	242	144	221	200
	MAX	203	189	284	224	275	321	332	309
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY CAGE FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
CAGE (MALES AND FEMALES)

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 64	Day 65	Day 66	Day 67	Day 68	Day 69
1	(b) (4)						
	MEAN	239.5	285.3	294 3	329.0	294.8	294.5
	SD	37.9	11.8	53.3	54.9	28.4	50.8
	MIN	186	273	239	250	256	235
	MAX	271	300	348	377	316	350
	N	4	4	4	4	4	4
2	(b) (4)						
	MEAN	279.3	274.5	271 3	301.0	321.3	286.5
	SD	47.1	28.4	18.2	36.3	33.3	40.4
	MIN	238	252	255	255	301	228
	MAX	347	312	287	332	371	321
	N	4	4	4	4	4	4
3	(b) (4)						
	MEAN	235.3	264.8	251.8	298.3	292.0	268.3
	SD	25.4	45.4	51.3	31.6	27.3	49.4
	MIN	198	223	183	261	255	210
	MAX	254	327	292	337	315	328
	N	4	4	4	4	4	4
4	(b) (4)						
	MEAN	303.3	254.8	279.8	316.0	292.3	298.5
	SD	16.1	43.7	49.0	40.0	16.4	60.7
	MIN	291	208	228	274	273	217
	MAX	327	294	326	364	313	362
	N	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 70	Day 71	Day 72	Day 73	Day 74	Day 75	Day 76	Day 77	Day 78	Day 79
1	(b) (4)										
	MEAN	154.5	142.8	184.8	118.8	163.0	141.8	172.0	159.5	183.5	179.5
	SD	23.6	23.3	37.8	24.8	20.4	34.6	31.2	34.9	44.4	41.6
	MIN	124	125	140	96	140	111	128	127	139	137
	MAX	180	177	225	151	183	184	200	205	233	220
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	127.3	139.8	143.3	149.3	143.8	165.5	154.3	189.5	163.8	154.8
	SD	59.0	9.8	17.5	18.0	21.4	29.8	26.2	34.6	49.4	38.6
	MIN	62	127	126	124	121	128	129	156	101	115
	MAX	203	150	162	166	167	191	182	238	220	205
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	135.5	128.0	134.0	139.3	156 5	138.0	150.3	166.3	139.8	168.0
	SD	11.6	29.4	40.7	14.9	27.5	24.0	23.8	17.7	12.8	45.7
	MIN	119	85	94	118	123	113	127	149	122	138
	MAX	145	151	187	150	188	160	181	182	150	236
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	130.8	139.0	146.3	139.5	174 5	146.0	153.8	155.5	174.5	145.0
	SD	19.1	17.3	35.6	16.3	21.0	27.3	29.1	13.7	31.9	24.1
	MIN	111	114	104	126	148	116	123	147	135	123
	MAX	149	151	190	163	199	182	187	176	213	178
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 80	Day 81	Day 82	Day 83	Day 84	Day 85	Day 86	Day 87
1	(b) (4)								
	MEAN	159.8	215.0	154.5	178.3	190.0	173.0	220.5	192.5
	SD	32.8	60.3	27.0	23.6	37.0	20.4	40.7	33.7
	MIN	132	161	128	144	143	154	166	164
	MAX	200	298	192	198	230	200	258	232
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	152.3	141.0	176.3	160.5	180.3	204.8	201.8	168.3
	SD	37.0	27.9	40.5	27.5	46.6	54.1	39.9	41.1
	MIN	122	106	121	136	136	155	151	111
	MAX	200	164	208	197	245	277	236	209
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	151.8	150.0	142.3	139.8	141.8	174.0	192.8	147.0
	SD	20.9	18.3	24.2	29.6	19.0	29.6	25.3	23.0
	MIN	121	137	116	113	116	153	166	119
	MAX	165	177	174	182	160	217	223	175
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	179.8	148.8	172.3	177.5	157.3	155.5	207.5	152.3
	SD	17.4	66.4	36.7	39.0	21.9	20.6	24.4	52.5
	MIN	160	72	124	151	136	141	173	104
	MAX	202	234	213	235	187	186	228	208
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

[redacted]

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 88	Day 89	Day 90	Day 91	Day 92	Day 93	Day 94	Day 95
1	[redacted]								
	MEAN	207.8	193.3	208.8	229.3	192.3	255.8	221.8	214.3
	SD	39.7	37.9	27.7	56.1	37.5	99.2	36.8	26.5
	MIN	177	172	169	158	159	173	182	189
	MAX	261	250	232	291	240	383	255	244
	N	4	4	4	4	4	4	4	4
2	[redacted]								
	MEAN	184.8	199.5	167.5	207.5	196.0	196.5	204.5	208.0
	SD	45.8	44.5	29.7	71.6	17.7	31.6	26.0	26.4
	MIN	123	162	133	134	170	162	176	180
	MAX	226	264	201	285	208	238	229	232
	N	4	4	4	4	4	4	4	4
3	[redacted]								
	MEAN	175.3	161.3	165.8	184.0	179.0	193.5	159.8	198.8
	SD	13.3	33.6	19.7	53.9	23.4	45.9	22.2	22.2
	MIN	167	126	140	137	145	139	144	171
	MAX	195	207	184	250	195	233	192	225
	N	4	4	4	4	4	4	4	4
4	[redacted]								
	MEAN	203.3	178.8	198.8	195.5	169.5	204.5	204.8	192.0
	SD	12.2	7.6	16.6	19.7	9.1	56.1	47.9	25.0
	MIN	191	171	182	173	157	129	165	162
	MAX	220	189	214	213	178	252	274	223
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 96	Day 97	Day 98	Day 99	Day 100	Day 101	Day 102	Day 103
1	(b) (4)								
	MEAN	198.5	219.8	233.3	219.8	227.5	241.0	238.0	221.8
	SD	53.1	33.4	74.7	45.5	31.8	49.3	42.6	15.6
	MIN	128	181	151	168	193	190	194	208
	MAX	246	262	310	258	257	304	293	244
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	228.5	205.3	241.0	227.5	219.3	214.8	214.0	233.0
	SD	37.7	46.6	63.2	43.2	36.9	63.5	47.2	72.0
	MIN	177	155	171	172	182	175	172	160
	MAX	267	259	314	271	251	309	268	321
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	196.0	185.3	203.3	167.5	204.5	197.8	208.8	194.8
	SD	52.5	38.5	21.1	28.2	38.1	31.1	24.9	26.5
	MIN	128	136	175	138	167	177	180	171
	MAX	256	221	226	195	250	244	235	231
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	196.5	246.5	212.3	210.5	208.3	217.8	256.0	226.8
	SD	29.4	28.0	20.5	15.7	48.8	48.7	51.7	42.6
	MIN	165	210	197	192	149	160	183	186
	MAX	223	275	242	225	257	275	304	283
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 104	Day 105	Day 106	Day 107	Day 108	Day 109	Day 110	Day 111
1	(b) (4)								
	MEAN	242.8	259.3	242.8	233.5	196.0	237.0	233.8	214.3
	SD	25.2	46.1	31.4	31.0	24.2	25.9	35.7	44.8
	MIN	221	212	214	205	171	211	182	169
	MAX	271	305	287	274	226	264	264	262
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	218.3	229.3	230.8	260.0	220.3	259.0	243.5	259.3
	SD	49.3	52.0	70.2	56.6	43.5	72.4	50.5	45.8
	MIN	170	155	140	203	188	167	176	195
	MAX	271	269	307	338	283	337	293	298
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	173.3	207.5	223.0	199.5	208.3	247.8	210.8	215.3
	SD	24.3	48.2	34.9	35.8	24.3	37.6	34.7	52.2
	MIN	139	161	185	150	183	211	179	141
	MAX	196	275	262	233	238	300	260	263
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	232.8	206.5	236.5	227.5	201.0	214.3	239.5	221.8
	SD	51.2	36.4	39.2	51.4	16.6	14.7	54.2	42.5
	MIN	169	166	182	180	190	202	177	178
	MAX	294	253	275	284	225	235	308	280
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 112	Day 113	Day 114	Day 115	Day 116	Day 117	Day 118	Day 119
1	(b) (4)								
	MEAN	239.3	233.0	272.3	208.0	232.5	280.3	259.8	254.0
	SD	38.1	32.9	59.8	40.0	75.9	46.6	58.9	32.6
	MIN	207	201	188	160	119	212	192	222
	MAX	288	276	326	257	278	311	311	293
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	268.8	197.3	217.5	244.0	257.3	250.5	244.8	275.8
	SD	39.4	24.2	42.4	63.3	55.0	36.3	69.5	48.1
	MIN	225	178	180	176	190	199	157	222
	MAX	305	230	272	325	324	278	327	338
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	201.3	180.8	180.8	208.5	231.0	204.3	206.8	248.5
	SD	31.3	35.0	47.2	63.6	53.6	26.7	15.8	57.9
	MIN	166	143	139	155	164	169	195	186
	MAX	241	212	244	290	287	233	230	313
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	216.3	216.0	242.0	186.5	287.0	191.5	235.3	221.8
	SD	24.0	34.4	80.2	44.1	71.3	60.6	36.9	30.8
	MIN	189	180	150	127	189	133	194	185
	MAX	234	256	345	233	360	271	275	254
	N	3	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 120	Day 121	Day 122	Day 123	Day 124	Day 125	Day 126	Day 127
1	(b) (4)								
	MEAN	259.5	245.5	262.3	265.5	261.5	252.0	271.5	265.8
	SD	46.1	38.6	28.1	30.9	38.1	24.0	40.1	42.2
	MIN	198	208	236	220	226	225	240	233
	MAX	303	285	302	288	311	283	328	323
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	244.8	256.5	254.8	245.5	256.0	267.8	257.5	265.5
	SD	60.0	95.4	47.4	49.4	40.4	62.1	31.1	43.4
	MIN	156	146	216	190	199	188	227	230
	MAX	288	379	314	302	287	336	301	323
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	179.5	230.5	189.5	212.5	251.3	203.0	198.5	225.8
	SD	27.3	46.9	47.6	55.7	58.0	51.2	51.9	17.6
	MIN	157	173	132	136	182	152	135	203
	MAX	219	282	245	269	324	250	254	246
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	244.8	230.0	247.0	260.3	235.3	219.3	219.5	261.5
	SD	96.3	41.2	34.0	44.1	46.8	31.2	66.3	39.1
	MIN	138	175	200	226	166	184	176	208
	MAX	366	268	281	325	267	246	318	302
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 128	Day 129	Day 130	Day 131	Day 132	Day 133	Day 134	Day 135
1	(b) (4)								
	MEAN	235.5	284.3	293.8	264.3	270.8	263.8	274.0	287.0
	SD	50.8	29.2	71.2	31.5	56.7	35.5	18.2	53.1
	MIN	167	243	209	231	222	233	251	214
	MAX	276	305	380	305	351	315	290	341
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	285.0	271.3	252.8	271.8	220.0	248.0	215.3	227.5
	SD	82.0	86.9	44.6	52.8	55.2	21.1	39.7	66.2
	MIN	182	205	186	218	177	219	176	148
	MAX	370	399	278	337	301	266	263	302
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	253.3	223.5	202.5	238.0	185.8	230.0	223.8	219.3
	SD	32.0	47.0	29.0	8.6	16.8	36.1	47.4	59.6
	MIN	211	181	184	230	165	192	171	162
	MAX	285	284	245	250	203	277	286	289
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	250.8	240.0	234.3	255.3	217.8	263.0	255.3	279.0
	SD	43.7	35.9	31.5	29.9	55.5	51.4	44.2	22.8
	MIN	196	198	207	219	147	202	190	246
	MAX	295	281	279	291	262	316	283	297
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

[redacted]

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 136	Day 137	Day 138	Day 139	Day 140	Day 141	Day 142	Day 143
1	[redacted]								
	MEAN	282.5	276.0	260.0	298.0	244.3	277.3	254.0	253.3
	SD	80.1	34.4	75.8	25.5	49.6	45.9	42.3	23.1
	MIN	220	244	182	273	190	240	202	229
	MAX	400	324	353	321	309	343	289	280
	N	4	4	4	4	4	4	4	4
2	[redacted]								
	MEAN	277.0	242.3	248.3	258.5	257.3	236.3	244.3	242.8
	SD	79.7	26.3	54.3	70.3	49.6	65.2	69.1	31.2
	MIN	206	221	168	173	210	172	163	208
	MAX	371	275	284	345	325	321	332	281
	N	4	4	4	4	4	4	4	4
3	[redacted]								
	MEAN	231.3	215.3	245.0	223.3	242.3	205.5	235.0	226.0
	SD	23.9	45.2	41.2	43.6	74.4	47.2	75.7	35.6
	MIN	198	175	209	174	144	163	149	182
	MAX	255	279	304	280	311	257	328	269
	N	4	4	4	4	4	4	4	4
4	[redacted]								
	MEAN	249.3	265.5	252.3	234.3	240.3	290.5	258.8	248.8
	SD	52.6	59.1	37.6	41.7	38.1	73.0	33.1	46.8
	MIN	204	180	212	191	196	224	218	193
	MAX	314	316	293	270	289	372	290	307
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 144	Day 145	Day 146	Day 147	Day 148	Day 149	Day 150	Day 151
1	(b) (4)								
	MEAN	240.8	233.0	288.5	268.5	297.0	284.0	281.8	292.0
	SD	29.5	47.3	35.8	68.3	38.1	52.9	15.5	27.5
	MIN	220	187	235	203	249	209	264	274
	MAX	284	297	310	329	330	325	298	333
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	246.3	220.3	270.8	299.3	249.3	225.0	208.3	235.0
	SD	30.9	15.5	64.9	58.5	17.6	34.1	34.4	54.2
	MIN	201	201	179	228	224	191	181	158
	MAX	267	238	332	359	265	260	258	285
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	237.5	214.3	245.3	195.5	249.0	222.3	233.3	189.3
	SD	28.6	48.2	47.2	62.3	120.4	43.0	59.3	23.4
	MIN	196	180	200	152	107	165	184	167
	MAX	260	285	309	285	400	263	314	215
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	239.0	249.8	264.8	225.8	229.5	295.8	252.5	237.0
	SD	77.6	66.2	30.4	80.2	35.9	26.5	68.8	39.4
	MIN	128	201	225	111	192	258	190	179
	MAX	296	347	298	298	277	319	342	266
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 152	Day 153	Day 154	Day 155	Day 156	Day 157	Day 158	Day 159
1	(b) (4)								
	MEAN	249.8	283.5	268.8	268.8	258.0	257.5	283.0	235.5
	SD	29.7	58.7	58.7	28.3	57.8	26.2	36.6	60.9
	MIN	218	226	184	232	210	237	231	178
	MAX	285	364	319	300	337	294	315	299
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	265.5	253.5	324.3	263.3	237.0	257.8	265.8	287.8
	SD	30.8	42.2	62.8	8.7	46.3	35.0	26.4	44.6
	MIN	228	202	245	253	199	218	237	253
	MAX	294	301	394	274	303	300	292	353
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	218.3	218.5	265.8	237.0	222.3	230.3	235.8	197.8
	SD	22.4	30.7	83.4	48.5	37.8	44.9	42.8	17.6
	MIN	188	192	177	186	199	174	178	172
	MAX	242	248	347	289	266	284	278	211
	N	4	4	4	4	3	4	4	4
4	(b) (4)								
	MEAN	273.3	229.5	241.0	282.0	252.5	273.8	254.0	249.3
	SD	40.8	67.1	43.1	41.6	72.0	35.4	23.7	25.4
	MIN	228	175	189	237	154	228	232	232
	MAX	320	325	287	336	319	314	282	287
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 160	Day 161	Day 162	Day 163	Day 164	Day 165	Day 166	Day 167
1	(b) (4)								
	MEAN	278.0	268.8	297.0	303.8	260.8	277.0	292.8	227.3
	SD	55.6	73.2	67.9	48.7	46.8	52.3	11.4	60.0
	MIN	195	198	213	231	201	220	277	164
	MAX	312	360	370	332	305	346	302	307
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	288.8	271.8	263.3	258.5	239.3	223.3	255.5	264.8
	SD	56.4	39.5	70.9	24.6	35.2	40.2	27.4	53.6
	MIN	213	215	174	237	212	175	235	186
	MAX	349	302	344	290	291	262	295	299
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	245.0	237.0	209.0	198.5	223.5	213.0	232.0	221.3
	SD	26.5	44.8	50.9	41.4	69.9	45.8	62.9	26.5
	MIN	206	186	161	160	142	156	166	191
	MAX	262	279	267	246	298	268	300	253
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	249.3	267.5	260.8	257.5	251.8	261.3	263.0	241.5
	SD	74.0	90.3	49.1	43.1	41.9	58.4	78.0	64.0
	MIN	174	159	217	195	202	211	177	160
	MAX	333	372	331	288	303	345	346	314
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 168	Day 169	Day 170	Day 171	Day 172	Day 173	Day 174	Day 175
1	(b) (4)								
	MEAN	256.3	238.8	266.3	260.3	251.8	236.0	247.5	288.3
	SD	22.7	42.3	42.5	20.2	59.3	43.3	56.1	45.0
	MIN	230	184	206	235	215	197	199	223
	MAX	285	281	302	283	340	298	328	324
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	288.8	317.5	294.8	248.8	243.0	246.8	280.8	268.8
	SD	39.3	67.8	71.3	53.5	26.5	65.1	42.8	44.4
	MIN	261	232	245	182	204	156	217	205
	MAX	347	383	397	311	263	295	309	308
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	196.3	229.5	245.5	233.5	229.0	245.3	232.0	186.0
	SD	92.9	47.1	16.5	82.9	20.7	26.2	49.0	77.2
	MIN	97	178	233	135	206	206	169	95
	MAX	318	287	269	321	254	261	281	255
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	276.5	265.3	258.3	283.5	277.5	235.8	231.0	228.3
	SD	53.1	81.4	43.3	59.3	40.3	55.6	37.5	97.1
	MIN	234	206	196	214	229	155	192	141
	MAX	347	385	290	343	320	282	279	348
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 176	Day 177	Day 178	Day 179	Day 180	Day 181	Day 182	Day 183
1	(b) (4)								
	MEAN	274.5	249.3	276.0	292.8	265.5	229.5	276.3	251.3
	SD	52.1	81.0	28.4	36.4	28.1	62.0	58.4	49.6
	MIN	197	164	251	257	228	161	204	213
	MAX	309	336	314	327	288	307	347	322
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	276.8	240.3	251.8	234.0	316.3	263.8	276.8	322.3
	SD	64.5	64.6	64.8	46.1	50.1	56.3	42.7	62.9
	MIN	218	180	188	186	243	193	221	245
	MAX	362	300	342	292	356	311	317	396
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	190.3	240.5	257.5	186.8	252.5	232.3	226.5	275.0
	SD	104.3	82.6	53.5	19.9	50.6	39.8	34.5	55.3
	MIN	41	186	197	173	196	195	179	225
	MAX	284	363	319	216	319	275	261	346
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	272.5	258.5	291.0	266.8	276.3	290.5	239.3	248.0
	SD	91.8	46.7	65.9	74.3	58.9	57.6	60.3	43.5
	MIN	150	197	203	186	214	235	175	209
	MAX	370	310	354	366	351	368	314	301
	N	4	4	4	4	4	4	4	4

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 184	Day 185	Day 186	Day 187	Day 188	Day 189	Day 190	Day 191
1	(b) (4)								
	MEAN	292.0	252.0	267.0	190.5	248.8	267.8	233.3	304.0
	SD	64.5	43.3	38.4	69.5	8.2	33.4	48.1	55.3
	MIN	227	206	235	115	244	225	189	230
	MAX	381	296	312	283	261	299	294	355
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	290.0	305.3	233.8	227.8	235.5	300.5	284.5	233.5
	SD	52.2	60.1	81.4	66.9	28.1	77.2	74.3	58.5
	MIN	228	256	148	172	196	197	235	191
	MAX	351	385	340	324	262	384	395	320
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	260.3	260.0	255.5	234.5	183.8	246.3	203.3	219.8
	SD	85.2	64.9	44.0	52.1	47.5	77.9	33.8	47.3
	MIN	215	203	212	180	141	164	179	169
	MAX	388	328	311	301	245	338	253	261
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	308.0	256.0	293.0	251.8	277.3	210.8	296.3	250.8
	SD	94.1	60.8	20.6	39.7	75.5	27.1	74.3	28.1
	MIN	174	191	263	196	189	188	235	215
	MAX	382	336	310	290	344	250	399	277
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 192	Day 193	Day 194	Day 195	Day 196	Day 197	Day 198	Day 199
1	(b) (4)								
	MEAN	248.3	288.3	269.5	228.3	268.0	265.8	240.5	270.0
	SD	47.7	27.9	21.3	34.4	61.6	57.5	33.4	63.5
	MIN	194	266	251	182	202	217	191	201
	MAX	303	325	293	259	350	344	264	354
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	314.8	201.5	246.5	212.5	287.5	249.8	200.0	266.0
	SD	50.4	27.6	43.1	69.9	64.1	83.0	87.1	69.5
	MIN	263	172	196	123	199	133	110	166
	MAX	384	231	296	285	345	326	313	318
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	272.3	214.3	195.0	252.5	229.5	172.3	273.0	222.8
	SD	67.6	65.6	123.2	47.7	46.6	22.0	42.6	53.5
	MIN	195	155	17	195	174	149	229	146
	MAX	359	308	293	311	288	200	317	270
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	265.3	260.8	257.0	262.3	273.5	258.0	252.8	272.8
	SD	55.1	47.9	36.5	56.8	46.5	86.7	54.0	40.8
	MIN	191	215	212	208	230	134	192	228
	MAX	320	314	301	339	326	332	323	323
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 200	Day 201	Day 202	Day 203	Day 204	Day 205	Day 206	Day 207
1	(b) (4)								
	MEAN	247.0	196.0	279.8	230.3	296.3	225.0	239.0	269.0
	SD	46.5	52.6	23.7	54.2	78.6	35.1	71.2	30.1
	MIN	183	147	252	158	221	185	139	232
	MAX	294	262	306	288	400	266	299	294
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	220.8	282.3	305.0	280.0	274.3	206.0	282.5	269.8
	SD	33.2	80.3	65.4	63.0	83.9	68.3	62.2	61.1
	MIN	176	198	220	233	206	122	215	181
	MAX	256	390	376	373	396	287	360	315
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	197.8	224.5	185.8	232.3	226.8	243.8	220.5	165.8
	SD	39.3	83.8	45.1	143.8	129.5	81.3	40.4	110.1
	MIN	164	155	140	24	88	154	176	1
	MAX	254	341	247	347	400	332	269	229
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	247.0	257.8	281.5	246.8	295.3	287.5	267.3	254.0
	SD	47.5	50.4	57.7	37.0	50.0	85.3	79.7	68.6
	MIN	202	207	218	197	231	178	183	165
	MAX	302	310	344	280	353	360	370	309
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 208	Day 209	Day 210	Day 211	Day 212	Day 213	Day 214	Day 215
1	(b) (4)								
	MEAN	257.8	234.5	257.5	249.0	279.3	256.0	256.3	233.3
	SD	55.8	98.3	109.6	45.8	70.9	42.4	53.6	44.2
	MIN	203	140	124	195	238	193	205	171
	MAX	313	370	391	304	385	283	331	272
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	218.3	277.8	277.5	204.5	225.8	251.5	305.0	262.5
	SD	19.6	76.5	59.0	49.9	55.0	68.0	68.7	85.1
	MIN	202	221	247	144	158	189	210	157
	MAX	244	387	366	262	273	347	374	334
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	221.5	213.5	208.5	177.8	216.5	239.8	184.3	229.5
	SD	57.2	82.2	64.4	33.9	38.0	48.1	121.6	48.2
	MIN	183	136	164	144	175	176	13	178
	MAX	305	286	304	216	265	277	287	279
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	250.5	275.0	234.0	257.5	277.3	241.0	242.0	252.5
	SD	58.0	91.5	31.4	76.8	51.4	36.8	20.8	52.2
	MIN	191	172	204	147	206	203	223	201
	MAX	330	393	264	324	320	291	270	315
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 216	Day 217	Day 218	Day 219	Day 220	Day 221	Day 222	Day 223
1	(b) (4)								
	MEAN	235.5	273.3	235.8	245.3	239.8	286.3	230.3	214.8
	SD	82.4	60.8	59.3	35.3	41.5	72.1	38.0	68.2
	MIN	130	220	179	217	217	237	189	114
	MAX	324	360	314	291	302	392	278	264
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	216.0	264.5	271.8	242.5	220.3	297.0	262.5	258.8
	SD	68.0	84.1	66.0	42.2	97.5	82.9	70.6	47.4
	MIN	130	183	175	213	112	194	197	192
	MAX	296	341	324	304	349	397	327	301
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	238.5	250.5	230.8	205.5	242.0	229.7	257.0	228.3
	SD	63.4	45.6	77.1	21.8	37.6	88.6	84.1	62.2
	MIN	151	201	164	177	206	162	194	175
	MAX	289	311	342	230	281	330	381	318
	N	4	4	4	4	3	3	4	4
4	(b) (4)								
	MEAN	281.8	243.0	279.3	265.5	218.8	265.0	246.3	289.3
	SD	95.3	59.6	64.6	61.2	76.9	77.7	110.2	33.8
	MIN	148	186	212	202	113	155	161	260
	MAX	369	323	339	348	287	330	400	330
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 224	Day 225	Day 226	Day 227	Day 228	Day 229	Day 230	Day 231
1	(b) (4)								
	MEAN	225.8	245.3	287.0	199.3	235.5	233.5	238.3	194.8
	SD	44.1	19.7	86.5	61.1	35.0	16.7	36.6	52.2
	MIN	182	227	191	121	208	216	204	128
	MAX	280	273	365	267	284	255	290	245
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	256.3	243.0	250.5	236.8	252.0	240.8	284.3	273.8
	SD	50.2	79.2	45.4	36.3	71.0	59.4	75.1	74.3
	MIN	208	193	221	190	189	163	220	206
	MAX	314	361	317	266	354	304	371	376
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	225.5	170.8	203.0	222.3	241.8	209.5	170.5	213.8
	SD	45.5	84.9	90.7	37.4	26.1	30.7	26.9	47.2
	MIN	178	48	100	174	212	168	132	156
	MAX	286	231	309	257	274	242	191	263
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	291.0	253.8	280.8	223.8	210.8	222.5	225.0	260.5
	SD	57.1	45.6	65.5	33.8	53.2	78.5	84.8	19.7
	MIN	245	201	200	177	132	105	111	235
	MAX	364	303	336	256	245	267	316	277
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 232	Day 233	Day 234	Day 235	Day 236	Day 237
1	(b) (4)						
	MEAN	228.0	189.3	235.5	249.0	225.0	222.8
	SD	70.9	36.8	42.4	51.2	21.5	30.0
	MIN	169	145	193	181	205	186
	MAX	331	235	293	305	251	258
	N	4	4	4	4	4	4
2	(b) (4)						
	MEAN	255.3	220.3	247.3	259.3	207.3	205.8
	SD	39.1	49.5	57.5	42.3	76.9	59.6
	MIN	222	177	192	196	133	162
	MAX	300	289	324	285	312	293
	N	4	4	4	4	4	4
3	(b) (4)						
	MEAN	189.5	200.8	230.8	161.3	179.5	208.5
	SD	22.7	31.6	69.6	35.0	41.6	64.5
	MIN	156	168	142	117	124	140
	MAX	204	244	312	200	224	265
	N	4	4	4	4	4	4
4	(b) (4)						
	MEAN	259.0	236.0	255.3	212.8	211.8	234.0
	SD	86.3	44.1	20.1	111.7	32.1	64.4
	MIN	169	173	236	53	167	146
	MAX	365	276	278	305	242	295
	N	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 70	Day 71	Day 72	Day 73	Day 74	Day 75	Day 76	Day 77	Day 78	Day 79
1	(b) (4)										
	SD	17.2	5.5	27.1	21.8	21.5	23.7	25.8	46.3	40.4	25.8
	MIN	100	98	109	68	110	110	106	94	82	108
	MAX	136	111	168	115	161	164	162	205	169	167
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	117.5	126.5	125.3	114.0	137.8	133.0	142.8	161.8	148.8	145.5
	SD	23.7	26.5	31.5	6.9	7.5	21.6	9.7	15.1	21.7	2.6
	MIN	93	98	92	108	129	106	131	147	118	143
	MAX	142	162	166	124	147	156	153	180	167	149
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	98.3	101.5	106.8	87.8	121.3	125.8	115.5	131.3	114.5	141.3
	SD	19.0	9.1	28.1	26.5	24.2	31.2	32.0	14.1	31.1	41.4
	MIN	78	92	77	66	92	88	90	115	75	109
	MAX	123	112	144	125	144	161	162	144	144	202
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	124.3	123.5	123.8	105.8	148.5	124.0	141.0	145.0	156.0	147.8
	SD	35.1	11.7	21.2	24.9	29.0	21.2	16.6	36.0	33.4	37.6
	MIN	81	109	108	92	115	108	122	117	115	94
	MAX	162	133	154	143	184	154	161	194	196	179
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 80	Day 81	Day 82	Day 83	Day 84	Day 85	Day 86	Day 87
1	(b) (4)								
	MEAN	136.8	153.5	151.3	145.3	159.5	135.3	170.8	164.3
	SD	30.7	27.3	17.9	18.2	33.3	18.9	23.0	32.3
	MIN	102	123	133	123	113	121	141	121
	MAX	169	177	173	166	192	161	196	198
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	137.8	141.0	143.3	163.5	177.8	177.0	190.5	159.5
	SD	26.5	28.2	22.4	8.9	9.8	18.9	33.0	14.6
	MIN	99	110	112	156	165	149	163	149
	MAX	159	170	161	175	189	190	237	181
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	SD	39.5	20.5	35.3	26.0	17.8	13.4	22.8	32.3
	MIN	86	115	61	90	108	116	134	98
	MAX	179	158	140	152	150	145	181	168
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	158.5	155.3	147.0	165.0	156.8	150.3	179.0	167.8
	SD	40.0	46.9	26.4	32.1	30.7	20.3	25.2	27.0
	MIN	116	113	108	120	134	120	154	131
	MAX	209	215	166	196	202	163	209	196
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 88	Day 89	Day 90	Day 91	Day 92	Day 93	Day 94	Day 95
1	(b) (4)								
	MEAN	166.5	174.8	161.8	177.0	158.8	182.0	192.5	179.0
	SD	25.4	29.1	18.5	46.5	37.3	40.2	62.2	24.5
	MIN	132	149	141	113	120	131	132	143
	MAX	188	214	184	224	204	229	266	198
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	161.3	151.8	163.8	187.8	182.0	178.0	189.8	180.3
	SD	33.1	33.5	31.5	34.0	10.0	4.8	17.6	19.9
	MIN	113	123	123	154	171	173	165	153
	MAX	183	198	199	219	191	183	205	195
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	143.3	151.0	124.0	131.3	148.3	143.0	168.5	171.3
	SD	10.4	35.1	20.3	9.5	2.2	21.0	13.8	28.3
	MIN	129	123	102	120	146	123	151	144
	MAX	154	202	151	141	151	167	181	208
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	174.3	166.5	159.0	162.3	180.0	188.5	185.8	181.0
	SD	26.7	34.6	25.3	21.7	21.0	14.9	50.0	45.3
	MIN	135	132	128	147	161	172	130	138
	MAX	193	211	190	193	210	208	241	238
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 96	Day 97	Day 98	Day 99	Day 100	Day 101	Day 102	Day 103
1	(b) (4)								
	MEAN	186.3	197.0	206.0	177.8	183.3	201.0	209.3	181.0
	SD	26.1	37.2	52.5	32.4	45.6	29.3	25.6	17.0
	MIN	159	143	146	145	128	162	172	163
	MAX	215	227	273	215	234	231	230	204
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	211.3	188.0	215.3	217.3	207.0	184.5	210.5	178.8
	SD	45.5	45.7	30.5	42.9	30.0	45.1	24.8	44.6
	MIN	176	136	179	160	166	159	181	128
	MAX	278	245	246	264	238	252	236	227
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	171.3	151.5	159.3	160.8	163.0	163.3	185.5	175.3
	SD	13.5	23.4	22.6	45.1	13.0	19.8	20.6	28.0
	MIN	158	123	135	97	151	145	166	150
	MAX	188	180	179	203	177	185	212	208
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	198.0	189.8	181.5	191.8	189.8	203.3	193.5	204.0
	SD	38.5	45.3	10.5	20.1	54.6	33.1	65.4	35.4
	MIN	145	146	166	164	119	154	114	162
	MAX	233	246	188	207	249	225	274	245
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 104	Day 105	Day 106	Day 107	Day 108	Day 109	Day 110	Day 111
1	(b) (4)								
	MEAN	214.3	190.0	193.0	190.5	146.0	186.8	209.3	179.0
	SD	36.6	50.5	21.7	30.3	20.1	15.8	53.7	25.5
	MIN	164	145	165	158	120	169	135	158
	MAX	248	257	213	231	169	207	256	216
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	196.5	204.5	206.8	213.0	217.0	241.8	211.5	219.0
	SD	24.2	31.6	46.3	39.7	62.1	61.0	28.7	32.6
	MIN	162	171	159	188	163	186	172	195
	MAX	218	246	270	272	292	326	236	267
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	170.0	161.0	175.8	173.8	188.5	186.8	192.3	192.8
	SD	27.8	28.7	17.6	7.4	20.4	21.2	35.8	20.9
	MIN	143	131	156	166	172	158	146	164
	MAX	195	198	192	181	218	205	233	211
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	218.3	188.8	216.0	218.3	199.0	208.3	222.5	219.3
	SD	22.3	24.7	36.3	31.5	46.6	30.9	33.5	45.7
	MIN	197	157	179	182	142	181	187	176
	MAX	239	215	266	258	250	251	266	264
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 112	Day 113	Day 114	Day 115	Day 116	Day 117	Day 118	Day 119
1	(b) (4)								
	MEAN	233.0	182.8	222.0	203.5	217.5	202.8	175.5	182.0
	SD	37.0	24.1	83.7	42.4	61.0	40.9	45.2	13.8
	MIN	191	161	161	153	155	148	123	166
	MAX	280	206	340	253	301	246	232	195
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	256.8	169.8	200.0	226.5	246.0	213.8	199.3	235.8
	SD	41.0	61.4	50.1	44.7	25.1	28.6	53.0	76.4
	MIN	215	85	149	190	227	188	140	156
	MAX	313	221	245	291	283	245	255	339
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	209.3	172.3	169.3	183.3	172.8	184.3	186.0	207.0
	SD	40.4	54.6	57.8	30.7	11.4	25.3	68.4	20.1
	MIN	161	119	133	150	162	153	142	192
	MAX	259	237	255	221	184	209	288	236
4	(b) (4)								
	MEAN	236.0	217.8	219.8	193.8	266.8	171.0	208.3	210.8
	SD	9.6	16.5	53.7	46.4	52.0	48.5	42.3	13.7
	MIN	225	205	161	137	202	105	173	196
	MAX	247	242	272	248	318	208	269	229
	N	4	4	4	4	4	4	4	4

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 120	Day 121	Day 122	Day 123	Day 124	Day 125	Day 126	Day 127
1	(b) (4)								
	MEAN	212.3	204.8	200.3	226.5	210.3	207.3	174.5	179.3
	SD	50.6	30.4	66.6	53.2	32.3	33.6	34.6	6.1
	MIN	145	163	154	186	172	166	125	174
	MAX	256	236	297	304	237	243	205	188
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	SD	69.1	58.6	66.9	39.3	51.2	44.9	47.3	56.4
	MIN	146	196	151	202	172	177	153	155
	MAX	304	322	309	287	283	286	264	290
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	177.0	191.0	173.3	189.8	203.8	183.8	189.8	190.0
	SD	36.1	45.1	52.7	30.0	53.5	33.0	29.2	19.9
	MIN	153	124	130	158	164	155	150	171
	MAX	230	221	241	226	282	231	218	218
	N	4	4	4	4	4	4	4	4
4	(b) (4) C1								
	MEAN	223.5	196.3	237.8	207.8	225.5	244.5	223.8	226.3
	SD	28.2	35.5	22.9	27.6	67.0	36.6	38.6	53.3
	MIN	199	150	209	185	146	220	187	177
	MAX	258	232	265	248	282	298	271	302
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 128	Day 129	Day 130	Day 131	Day 132	Day 133	Day 134	Day 135
1	(b) (4)								
	MEAN	229.3	213.8	236.3	183.3	216.0	187.0	202.0	213.3
	SD	42.4	14.8	37.8	19.6	38.5	14.3	17.5	24.1
	MIN	183	199	189	159	189	172	191	187
	MAX	279	233	274	204	273	206	228	244
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	245.3	231.8	250.5	241.0	223.8	230.3	227.8	255.5
	SD	53.5	37.6	35.9	55.2	62.5	26.9	29.6	34.1
	MIN	192	190	223	204	137	204	195	224
	MAX	313	280	302	323	276	259	264	303
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	216.5	187.0	188.5	213.0	184.5	212.0	177.0	194.3
	SD	34.4	44.5	37.5	20.2	57.7	36.0	23.5	29.9
	MIN	197	147	155	197	112	162	145	167
	MAX	268	246	239	242	247	242	196	231
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	231.0	234.3	233.0	243.8	234.8	214.8	249.5	229.5
	SD	9.0	30.6	42.7	24.6	63.5	22.0	32.7	42.1
	MIN	222	205	201	218	149	189	215	189
	MAX	243	268	296	277	302	242	290	282
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 136	Day 137	Day 138	Day 139	Day 140	Day 141	Day 142	Day 143
1	(b) (4)								
	MEAN	216.0	207.8	212.3	219.5	202.5	227.8	201.5	194.5
	SD	32.3	17.7	23.0	24.1	12.8	37.1	30.5	11.6
	MIN	179	191	184	203	190	187	182	183
	MAX	255	228	236	255	220	264	247	205
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	233.8	216.0	199.8	217.0	231.0	214.0	243.8	214.3
	SD	22.7	46.4	20.8	20.6	45.4	40.3	19.3	56.5
	MIN	216	158	183	187	167	170	225	184
	MAX	266	271	227	232	273	267	270	299
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	173.0	175.8	175.0	213.5	210.8	199.5	176.5	187.0
	SD	20.1	46.1	35.2	6.2	45.0	15.7	18.8	35.9
	MIN	147	115	134	208	172	176	159	150
	MAX	194	220	220	222	267	208	203	223
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	238.3	220.3	232.5	260.5	239.0	237.8	243.0	229.0
	SD	21.3	35.3	18.1	48.1	47.9	20.7	31.3	24.5
	MIN	217	174	206	202	180	215	200	194
	MAX	264	257	246	315	279	265	269	250
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 144	Day 145	Day 146	Day 147	Day 148	Day 149	Day 150	Day 151
1	(b) (4)								
	MEAN	167.8	169.8	237.3	200.5	220.5	227.5	200.5	226.8
	SD	18.2	43.9	33.3	16.6	27.7	25.0	25.3	33.1
	MIN	145	104	217	176	188	201	171	199
	MAX	186	195	287	213	245	261	229	271
2	(b) (4)								
	SD	50.0	21.6	36.4	41.1	33.1	55.7	29.8	34.1
	MIN	148	175	193	190	157	157	185	171
	MAX	260	225	279	274	231	279	240	245
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	215.5	201.8	202.8	179.5	199.8	206.5	206.8	167.3
	SD	32.7	46.0	12.5	20.2	51.0	39.1	35.3	27.0
	MIN	195	156	185	165	150	179	185	128
	MAX	264	265	212	209	269	262	259	190
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	223.5	228.3	202.0	205.0	216.0	255.3	217.8	204.0
	SD	27.8	16.1	20.9	54.9	41.3	44.4	33.1	36.6
	MIN	184	213	184	123	186	207	190	171
	MAX	249	245	226	240	277	314	265	244
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 152	Day 153	Day 154	Day 155	Day 156	Day 157	Day 158	Day 159
1	(b) (4)								
	MEAN	215.8	219.0	189.5	199.5	188.8	199.8	203.8	184.5
	SD	8.1	7.1	5.2	24.6	29.7	15.6	26.0	22.5
	MIN	208	209	182	164	171	180	165	165
	MAX	227	224	194	217	233	215	220	213
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	252.5	222.0	255.5	223.5	202.3	232.0	207.0	226.8
	SD	21.7	15.1	48.9	43.7	32.9	46.5	29.1	33.6
	MIN	225	203	200	165	176	167	185	189
	MAX	277	239	315	271	247	266	249	257
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	170.5	203.5	209.5	193.5	202.0	180.8	206.8	200.3
	SD	13.0	14.6	15.9	8.6	38.4	45.8	42.5	21.7
	MIN	161	187	188	186	169	136	167	174
	MAX	189	219	226	205	257	230	266	227
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	209.5	208.8	231.0	250.0	238.5	256.5	215.5	236.3
	SD	29.6	44.0	60.8	17.6	16.8	39.1	28.2	32.5
	MIN	168	148	164	232	216	223	176	190
	MAX	238	249	299	273	256	313	243	263
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 160	Day 161	Day 162	Day 163	Day 164	Day 165	Day 166	Day 167
1	(b) (4)								
	MEAN	205.8	227.3	206.3	200.5	219.0	201.0	208.5	224.5
	SD	11.2	37.3	26.8	20.3	7.6	48.4	21.9	34.0
	MIN	197	177	171	172	211	136	193	193
	MAX	222	267	229	216	229	250	240	270
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	233.0	229.0	204.0	235.3	220.8	212.0	187.0	250.8
	SD	55.7	34.3	27.5	51.6	31.8	32.2	16.6	34.5
	MIN	175	206	165	184	187	183	163	219
	MAX	303	280	229	292	256	254	201	297
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	195.5	222.0	186.8	199.3	216.5	190.5	224.0	211.3
	SD	69.2	45.6	32.1	19.5	59.7	29.5	27.1	10.8
	MIN	100	178	150	181	162	163	197	203
	MAX	262	286	217	225	301	217	260	227
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	217.5	240.5	241.8	250.5	220.5	219.0	289.8	236.0
	SD	48.9	11.7	52.5	34.3	40.2	46.9	73.1	26.6
	MIN	170	230	196	217	178	156	230	207
	MAX	286	256	293	296	266	264	386	261
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 168	Day 169	Day 170	Day 171	Day 172	Day 173	Day 174	Day 175
1	(b) (4)								
	SD	6.2	20.7	27.4	19.4	27.9	13.3	38.2	11.1
	MIN	186	209	178	168	194	182	152	214
	MAX	200	257	238	209	253	214	245	238
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	237.5	273.5	254.8	260.5	215.3	206.0	236.3	241.3
	SD	38.4	52.9	44.3	53.0	55.2	35.3	48.0	51.2
	MIN	208	211	195	208	165	176	183	168
	MAX	294	334	302	321	288	247	295	284
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	222.0	165.3	226.3	220.3	196.5	209.0	221.5	212.5
	SD	16.9	27.1	60.4	27.0	67.2	46.1	61.2	10.4
	MIN	200	142	148	187	141	164	163	197
	MAX	238	198	295	253	281	271	307	219
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	244.3	228.0	247.0	261.0	232.8	226.5	210.0	210.3
	SD	31.2	38.2	43.6	47.8	36.5	35.2	23.1	43.7
	MIN	214	171	193	194	198	179	185	158
	MAX	282	252	297	307	278	257	238	265
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 176	Day 177	Day 178	Day 179	Day 180	Day 181	Day 182	Day 183
1	(b) (4)								
	MEAN	222.3	206.3	223.3	211.8	227.0	196.8	206.8	190.5
	SD	19.1	28.8	7.3	28.7	14.8	23.9	44.0	43.7
	MIN	204	165	213	174	218	166	154	143
	MAX	246	231	229	241	249	219	260	236
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	243.0	229.8	238.3	209.3	235.5	247.0	255.5	266.8
	SD	33.0	49.4	31.0	40.3	63.6	56.1	70.3	46.0
	MIN	212	185	197	166	156	193	181	218
	MAX	286	274	270	263	305	312	341	329
3	(b) (4)								
	MEAN	191.0	200.5	205.3	188.8	209.3	210.3	205.3	220.0
	SD	21.3	46.0	56.4	18.4	48.6	25.7	25.2	61.1
	MIN	166	149	161	173	158	181	168	178
	MAX	212	261	288	215	271	243	223	310
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	212.3	228.5	255.5	230.0	210.8	232.5	221.0	239.8
	SD	48.6	18.8	33.0	46.2	56.5	15.5	44.6	34.6
	MIN	147	207	224	196	169	212	176	192
	MAX	263	252	295	297	293	246	266	272
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 184	Day 185	Day 186	Day 187	Day 188	Day 189	Day 190	Day 191
1	(b) (4)								
	MEAN	189.0	201.0	192.0	172.5	195.3	214.3	203.8	213.8
	SD	33.4	39.3	3.2	24.7	22.0	29.3	39.5	27.5
	MIN	152	160	188	150	166	176	169	199
	MAX	225	249	195	199	217	247	258	255
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	224.5	268.0	207.5	208.8	223.0	283.5	245.0	238.0
	SD	77.6	42.7	59.1	65.0	50.2	56.3	52.6	74.9
	MIN	170	224	128	138	166	210	184	154
	MAX	335	309	254	295	287	346	310	318
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	197.5	240.5	215.8	200.5	177.0	186.3	182.0	208.5
	SD	29.9	48.0	43.6	32.3	65.3	37.8	18.6	53.2
	MIN	161	209	179	168	117	155	166	164
	MAX	234	312	274	236	266	240	207	278
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	297.5	214.5	252.8	264.0	223.5	205.8	232.3	214.3
	SD	38.4	62.3	27.3	46.0	24.4	40.0	58.0	58.7
	MIN	260	125	221	213	197	151	171	136
	MAX	351	268	285	319	256	236	304	265
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

[redacted]

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 192	Day 193	Day 194	Day 195	Day 196	Day 197	Day 198	Day 199
1	[redacted]								
	MEAN	201.0	236.0	207.8	182.0	197.0	178.5	204.5	202.0
	SD	32.5	27.8	17.3	23.1	38.9	17.5	41.2	35.2
	MIN	154	207	190	150	163	156	152	166
	MAX	229	273	231	202	249	197	245	245
	N	4	4	4	4	4	4	4	4
2	[redacted]								
	MEAN	221.5	162.0	230.3	199.8	217.0	210.0	186.8	219.5
	SD	52.5	25.8	64.0	26.1	46.1	29.8	37.7	59.4
	MIN	184	135	165	174	167	177	150	151
	MAX	298	190	311	232	272	249	238	287
	N	4	4	4	4	4	4	4	4
3	[redacted]								
	MEAN	200.0	179.0	170.5	197.0	203.3	188.5	189.5	200.8
	SD	57.5	57.0	29.9	17.9	10.7	69.8	31.3	56.0
	MIN	159	116	141	180	190	133	153	138
	MAX	285	254	212	222	216	290	229	274
	N	4	4	4	4	4	4	4	4
4	[redacted]								
	MEAN	241.0	221.0	244.8	210.0	217.8	226.0	199.5	237.3
	SD	27.3	48.7	42.9	43.9	103.1	58.6	55.5	25.1
	MIN	205	173	209	154	91	150	149	210
	MAX	271	281	298	251	315	287	272	270
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 200	Day 201	Day 202	Day 203	Day 204	Day 205	Day 206	Day 207
1	(b) (4)								
	MEAN	191.0	214.5	203.0	200.5	172.8	180.3	219.0	194.5
	SD	26.5	46.4	35.5	37.4	31.4	17.0	50.0	32.7
	MIN	159	162	169	148	144	157	191	158
	MAX	224	261	247	236	212	196	294	237
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	200.8	253.8	237.5	257.3	211.3	151.3	203.0	228.8
	SD	11.2	35.6	61.3	42.1	44.8	101.5	27.7	58.9
	MIN	186	208	185	208	182	0	176	170
	MAX	213	288	323	298	278	215	235	307
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	189.3	244.8	184.3	209.0	205.8	190.8	181.3	200.5
	SD	20.2	103.3	69.6	22.7	51.5	47.8	44.1	73.8
	MIN	161	179	110	178	147	142	133	127
	MAX	209	399	278	230	271	253	237	303
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	213.0	232.8	204.5	180.0	250.5	231.3	194.5	213.3
	SD	38.1	17.5	37.3	47.2	31.1	39.4	49.0	21.3
	MIN	175	208	149	134	206	198	144	189
	MAX	265	249	228	246	273	287	237	238
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 208	Day 209	Day 210	Day 211	Day 212	Day 213	Day 214	Day 215
1									
	MEAN	172.5	231.0	172.3	195.0	202.5	168.3	200.3	164.3
	SD	39.2	56.1	58.1	26.2	30.6	27.1	30.8	32.8
	MIN	146	159	105	169	183	143	157	130
	MAX	230	292	242	220	248	196	226	207
	N	4	4	4	4	4	4	4	4
2									(b) (4)
	MEAN	195.0	219.3	259.0	212.0	204.5	219.8	217.8	237.5
	SD	32.2	53.8	58.3	43.2	10.6	30.8	42.1	40.9
	MIN	152	150	185	178	192	191	159	200
	MAX	227	279	326	270	216	258	258	291
	N	4	4	4	4	4	4	4	4
3									
	MEAN	187.3	198.0	150.5	190.3	170.5	201.8	168.3	187.3
	SD	25.1	26.7	32.6	44.7	7.2	32.3	32.3	18.5
	MIN	162	174	117	155	164	169	136	167
	MAX	222	234	190	255	180	246	213	210
	N	4	4	4	4	4	4	4	4
4									(b) (4)
	MEAN	196.3	273.3	219.0	188.0	224.3	213.3	202.8	228.8
	SD	30.7	66.9	33.7	35.3	33.8	16.6	61.4	31.5
	MIN	169	180	180	139	187	190	134	203
	MAX	238	330	260	217	263	227	256	272
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 216	Day 217	Day 218	Day 219	Day 220	Day 221	Day 222	Day 223
1	(b) (4)								
	MEAN	216.0	164.0	202.0	179.8	184.5	188.3	190.5	188.3
	SD	57.2	45.8	24.2	39.4	47.5	16.5	29.6	37.4
	MIN	144	96	173	138	143	171	161	134
	MAX	272	195	232	220	253	206	228	213
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	214.0	236.3	206.0	211.3	191.8	249.8	220.8	235.8
	SD	52.6	38.9	48.4	29.3	34.5	57.2	70.4	50.0
	MIN	167	181	146	186	158	170	152	161
	MAX	262	265	256	253	238	299	310	266
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	215.8	135.8	181.3	181.3	185.5	218.8	201.3	174.0
	SD	24.5	51.6	28.3	50.5	24.8	23.0	29.8	63.5
	MIN	189	68	151	138	164	187	178	133
	MAX	238	192	213	251	207	242	245	268
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	210.8	202.0	253.5	224.0	186.3	196.0	244.0	267.5
	SD	72.9	27.4	38.9	51.9	29.2	43.6	56.1	21.6
	MIN	167	167	200	161	148	154	199	241
	MAX	319	231	291	288	219	257	317	288
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 224	Day 225	Day 226	Day 227	Day 228	Day 229	Day 230	Day 231
1	(b) (4)								
	MEAN	186.8	155.3	202.3	174.8	189.0	211.8	171.8	191.8
	SD	17.8	31.2	26.1	40.9	28.7	59.2	26.3	6.8
	MIN	172	109	176	123	157	145	137	182
	MAX	212	177	238	219	226	274	200	197
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	203.0	240.0	260.3	196.3	252.5	231.3	244.3	253.5
	SD	65.0	70.4	40.4	44.8	50.6	41.9	38.2	43.7
	MIN	111	153	223	134	216	188	200	226
	MAX	260	324	312	234	327	287	280	318
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	209.3	186.3	185.0	174.8	177.5	170.0	195.5	204.0
	SD	82.2	95.7	33.3	28.7	16.7	11.6	56.5	24.9
	MIN	152	97	138	136	162	159	137	176
	MAX	331	321	211	198	199	181	272	230
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	232.0	230.0	210.3	196.0	211.8	223.5	196.8	220.3
	SD	20.6	40.5	52.9	59.0	22.6	25.0	27.7	49.1
	MIN	215	186	139	147	193	202	179	160
	MAX	262	284	265	278	242	249	238	278
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

DAILY FOOD CONSUMPTION (g)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 232	Day 233	Day 234	Day 235	Day 236	Day 237
1	(b) (4)						
	MEAN	189.8	171.0	209.5	191.3	202.3	140.0
	SD	43.2	28.5	36.9	10.2	23.6	63.0
	MIN	151	131	166	180	185	62
	MAX	239	195	252	204	236	210
	N	4	4	4	4	4	4
2	(b) (4)						
	MEAN	241.5	195.5	240.8	177.3	193.0	219.3
	SD	83.3	75.7	46.4	68.7	36.3	74.6
	MIN	137	99	183	124	160	144
	MAX	328	284	295	278	242	310
	N	4	4	4	4	4	4
3	(b) (4)						
	MEAN	177.0	174.5	197.5	157.3	157.0	183.0
	SD	64.0	36.6	59.5	57.9	22.4	58.0
	MIN	118	129	133	106	133	141
	MAX	268	218	277	238	178	268
	N	4	4	4	4	4	4
4	(b) (4)						
	MEAN	209.5	182.5	222.3	185.3	203.8	167.0
	SD	44.7	43.9	24.9	74.1	61.2	75.8
	MIN	145	147	199	110	163	56
	MAX	243	245	251	273	293	224
	N	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

WEEKLY CAGE FOOD CONSUMPTION
F1 GENERATION - PUPPIES - POST WEANING (g)
CAGE (MALES AND FEMALES)

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 1	Week 2
1	(b) (4)		
	MEAN	212.5	286.0
	SD	22.5	23.3
	MIN	185	257
	MAX	238	313
	N	4	4
2	(b) (4)		
	MEAN	205.5	287.5
	SD	22.9	16.3
	MIN	191	273
	MAX	239	311
	N	4	4
3	(b) (4)		
	MEAN	176.9	269.5
	SD	4.2	10.8
	MIN	173	257
	MAX	183	283
	N	4	4
4	(b) (4)		
	MEAN	220.3	282.6
	SD	28.6	30.9
	MIN	181	248
	MAX	245	320
	N	4	4

APPENDIX NO. 48

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
1	(b) (4)								
	MEAN	153.9	175.7	198.0	218.8	232.0	230.9	246.4	257.2
	SD	16.2	31.8	29.1	42.8	37.1	28.0	40.6	29.3
	MIN	139	149	164	168	196	202	196	222
	MAX	176	214	228	263	269	258	281	283
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	146.1	162.6	186.7	206.6	224.0	243.1	240.0	257.3
	SD	23.5	26.6	35.9	32.7	46.8	45.5	42.2	48.7
	MIN	125	139	156	174	185	193	189	204
	MAX	171	192	227	239	282	304	284	316
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	140.2	151.1	165.4	185.2	192.8	216.0	201.9	216.4
	SD	19.6	8.9	13.0	28.9	21.1	26.5	23.8	25.7
	MIN	124	141	153	161	173	196	182	187
	MAX	163	162	180	221	221	253	236	243
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	147.1	164.8	179.0	201.3	223.5	221.0	226.3	236.9
	SD	15.8	16.5	10.8	23.5	31.0	21.8	31.7	40.3
	MIN	129	141	171	176	193	199	198	182
	MAX	166	178	194	228	255	242	255	269
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17	Week 18
1	(b) (4)								
	MEAN	269.4	277.3	255.9	279.5	264.2	275.3	251.0	268.0
	SD	37.1	27.8	28.2	35.0	30.1	31.8	26.9	25.6
	MIN	236	258	229	238	224	241	214	242
	MAX	319	318	284	322	295	306	272	303
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	260.5	245.3	245.4	248.0	274.9	253.8	274.3	264.5
	SD	51.2	43.9	38.8	26.3	34.2	34.4	41.8	42.3
	MIN	208	191	198	209	235	210	227	217
	MAX	330	293	293	266	318	287	328	320
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	218.2	226.8	229.4	218.0	234.2	219.2	230.1	220.8
	SD	20.5	31.2	35.2	22.6	17.5	31.3	25.2	30.2
	MIN	200	204	181	198	209	183	207	188
	MAX	237	273	265	239	247	257	258	257
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	239.9	256.9	256.0	249.0	257.4	257.6	261.1	269.1
	SD	33.5	32.1	40.7	40.1	37.8	43.5	37.0	55.7
	MIN	206	226	215	202	212	213	211	220
	MAX	275	291	302	296	289	296	298	324
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48 (b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 19	Week 20	Week 21	Week 22	Week 23	Week 24	Week 25	Week 26
1	(b) (4)								
	MEAN	254.0	262.8	252.4	250.3	252.4	246.5	237.8	220.6
	SD	30.7	26.8	19.7	32.8	10.5	9.8	22.7	11.8
	MIN	227	236	239	223	238	233	210	205
	MAX	285	295	282	296	260	255	258	232
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	270.2	256.3	258.8	258.4	249.0	259.6	251.9	238.4
	SD	46.9	47.8	34.0	54.1	49.5	45.4	50.6	47.2
	MIN	240	207	233	218	211	232	220	202
	MAX	339	321	308	337	322	327	327	308
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	242.2	229.0	215.1	217.7	213.5	237.3	206.2	197.7
	SD	27.3	26.3	26.7	20.6	27.3	30.4	17.3	18.4
	MIN	206	199	179	200	176	203	191	170
	MAX	273	252	243	246	241	271	224	209
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	267.6	257.6	263.3	268.0	255.1	258.1	243.9	238.5
	SD	43.5	35.3	41.7	45.9	41.7	47.6	39.1	36.1
	MIN	211	213	208	203	197	206	188	200
	MAX	315	295	309	303	295	322	279	279
	N	4	4	4	4	4	4	4	4

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED WEEKS
1	MEAN	242.9
	SD	24.2
	MIN	216
	MAX	268
	N	4
2	MEAN	240.6
	SD	37.3
	MIN	203
	MAX	291
	N	4
3	MEAN	209.4
	SD	21.7
	MIN	185
	MAX	235
	N	4
4	MEAN	237.5
	SD	31.8
	MIN	199
	MAX	271
	N	4

APPENDIX NO. 48

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
1	(b) (4)								
	MEAN	127.3	146.0	161.8	181.8	196.1	184.9	205.3	206.2
	SD	11.2	18.0	22.2	34.2	27.3	17.8	25.4	20.9
	MIN	112	119	134	134	156	159	169	176
	MAX	137	159	187	208	216	198	229	223
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	128.1	148.8	168.8	188.1	201.4	216.2	216.0	230.7
	SD	13.4	9.0	13.6	21.2	24.2	37.9	35.3	47.3
	MIN	118	138	157	163	181	192	183	182
	MAX	148	160	184	214	230	273	263	295
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	108.1	125.6	136.8	155.0	168.1	181.5	182.4	189.4
	SD	18.9	11.2	12.1	10.6	14.3	16.5	35.8	20.9
	MIN	90	118	126	145	153	167	154	178
	MAX	135	142	149	166	186	204	234	221
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	127.3	153.5	164.8	183.6	197.4	210.3	216.2	220.9
	SD	16.5	21.3	19.0	29.1	25.8	22.9	12.8	13.3
	MIN	109	133	142	160	163	177	203	202
	MAX	145	183	186	224	223	229	231	233
	N	4	4	4	4	4	4	4	4

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17	Week 18
1	(b) (4)								
	MEAN	204.6	208.3	200.1	215.8	195.9	212.4	203.2	215.7
	SD	14.6	6.8	5.9	16.4	5.8	6.5	6.7	7.6
	MIN	191	200	192	196	190	204	197	209
	MAX	225	214	206	236	203	219	212	226
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	234.4	225.7	221.3	222.8	225.7	219.8	240.5	234.9
	SD	44.0	12.6	31.2	29.1	32.4	23.5	37.2	36.6
	MIN	186	213	199	193	197	197	204	194
	MAX	293	242	268	250	272	252	293	277
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	195.6	188.6	199.1	190.5	198.3	207.2	208.7	202.5
	SD	18.0	22.2	24.4	24.3	30.0	26.6	36.1	20.5
	MIN	175	162	172	171	164	184	183	179
	MAX	218	210	227	226	233	244	260	228
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	232.4	235.0	228.9	216.6	235.0	242.6	235.6	225.7
	SD	21.4	28.5	10.8	26.6	18.0	18.7	14.3	24.5
	MIN	203	199	219	196	220	225	218	208
	MAX	254	268	239	256	260	267	252	262
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 19	Week 20	Week 21	Week 22	Week 23	Week 24	Week 25	Week 26
1	(b) (4)								
	MEAN	192.4	208.4	198.6	195.8	188.4	185.3	184.5	185.1
	SD	4.6	14.7	12.9	11.9	12.6	6.1	9.2	8.8
	MIN	189	189	183	180	177	177	172	172
	MAX	199	224	212	208	200	191	193	192
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	236.3	225.7	217.9	209.4	223.5	221.6	232.5	217.3
	SD	44.0	43.4	22.8	32.2	18.9	30.9	36.9	52.3
	MIN	193	190	194	168	208	199	198	176
	MAX	297	278	244	241	251	266	283	294
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	208.1	189.0	200.0	196.1	183.5	182.5	185.5	178.6
	SD	38.6	21.7	41.4	30.9	16.4	7.9	38.8	21.4
	MIN	176	172	169	167	172	173	151	165
	MAX	261	219	260	238	207	192	241	210
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	244.7	224.1	218.7	219.9	212.4	224.8	214.3	198.6
	SD	17.0	26.0	28.2	28.3	28.2	3.9	11.5	11.0
	MIN	225	200	194	186	183	222	202	187
	MAX	266	261	253	256	248	230	224	214
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 48

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED WEEKS
1	MEAN	191.8
	SD	8.0
	MIN	180
	MAX	198
	N	4
2	MEAN	212.8
	SD	28.6
	MIN	189
	MAX	253
	N	4
3	MEAN	181.7
	SD	21.2
	MIN	166
	MAX	211
	N	4
4	MEAN	211.8
	SD	15.8
	MIN	197
	MAX	234
	N	4

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
1	MEAN	140.6	160.8	179.9	200.3	214.0	207.9	225.9	231.7
	SD	19.2	28.7	30.8	40.9	35.7	32.8	38.3	36.0
	MIN	112	119	134	134	156	159	169	176
	MAX	176	214	228	263	269	258	281	283
	N	8	8	8	8	8	8	8	8
2	MEAN	137.1	155.7	177.7	197.4	212.7	229.7	228.0	244.0
	SD	20.2	19.8	26.9	27.4	36.5	41.3	38.2	46.6
	MIN	118	138	156	163	181	192	183	182
	MAX	171	192	227	239	282	304	284	316
	N	8	8	8	8	8	8	8	8
3	MEAN	124.2	138.4	151.1	170.1	180.5	198.8	192.2	202.9
	SD	24.7	16.5	19.2	25.8	21.3	27.5	30.0	26.0
	MIN	90	118	126	145	153	167	154	178
	MAX	163	162	180	221	221	253	236	243
	N	8	8	8	8	8	8	8	8
4	MEAN	137.2	159.1	171.9	192.5	210.4	215.6	221.2	228.9
	SD	18.3	18.6	16.2	26.3	29.8	21.5	23.0	29.1
	MIN	109	133	142	160	163	177	198	182
	MAX	166	183	194	228	255	242	255	269
	N	8	8	8	8	8	8	8	8

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 11	Week 12	Week 13	Week 14	Week 15	Week 16	Week 17	Week 18
1	MEAN	237.0	242.8	228.0	247.6	230.1	243.9	227.1	241.8
	SD	43.4	41.4	35.2	42.4	41.7	39.8	31.3	32.9
	MIN	191	200	192	196	190	204	197	209
	MAX	319	318	284	322	295	306	272	303
	N	8	8	8	8	8	8	8	8
2	MEAN	247.5	235.5	233.4	235.4	250.3	236.8	257.4	249.7
	SD	46.3	31.7	35.0	29.0	40.5	32.8	40.8	39.9
	MIN	186	191	198	193	197	197	204	194
	MAX	330	293	293	266	318	287	328	320
	N	8	8	8	8	8	8	8	8
3	MEAN	206.9	207.7	214.3	204.3	216.2	213.2	219.4	211.7
	SD	21.6	32.3	32.4	26.2	29.7	27.6	31.1	25.8
	MIN	175	162	172	171	164	183	183	179
	MAX	237	273	265	239	247	257	260	257
	N	8	8	8	8	8	8	8	8
4	MEAN	236.1	246.0	242.4	232.8	246.2	250.1	248.4	247.4
	SD	26.4	30.5	31.1	36.0	29.9	32.0	29.3	46.1
	MIN	203	199	215	196	212	213	211	208
	MAX	275	291	302	296	289	296	298	324
	N	8	8	8	8	8	8	8	8

APPENDIX NO. 48

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Week 19	Week 20	Week 21	Week 22	Week 23	Week 24	Week 25	Week 26
1	MEAN	223.2	235.6	225.5	223.0	220.4	215.9	211.1	202.8
	SD	38.7	35.3	32.6	37.0	35.9	33.5	32.7	21.3
	MIN	189	189	183	180	177	177	172	172
	MAX	285	295	282	296	260	255	258	232
	N	8	8	8	8	8	8	8	8
2	MEAN	253.2	241.0	238.3	233.9	236.2	240.6	242.2	227.8
	SD	45.8	45.3	34.6	48.8	37.3	41.3	42.3	47.5
	MIN	193	190	194	168	208	199	198	176
	MAX	339	321	308	337	322	327	327	308
	N	8	8	8	8	8	8	8	8
3	MEAN	225.1	209.0	207.6	206.9	198.5	209.9	195.8	188.2
	SD	35.9	30.9	33.2	26.9	26.3	35.8	29.9	21.1
	MIN	176	172	169	167	172	173	151	165
	MAX	273	252	260	246	241	271	241	210
	N	8	8	8	8	8	8	8	8
4	MEAN	256.2	240.9	241.0	243.9	233.8	241.4	229.1	218.6
	SD	32.9	33.8	40.7	43.7	40.1	36.0	31.0	32.6
	MIN	211	200	194	186	183	206	188	187
	MAX	315	295	309	303	295	322	279	279
	N	8	8	8	8	8	8	8	8

APPENDIX NO. 48

(b) (4)

WEEKLY FOOD CONSUMPTION (g)
F1 GENERATION – PUPPIES – POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	COMBINED WEEKS
1	MEAN	217.4
	SD	32.0
	MIN	180
	MAX	268
	N	8
2	MEAN	226.7
	SD	34.2
	MIN	189
	MAX	291
	N	8
3	MEAN	195.5
	SD	24.8
	MIN	166
	MAX	235
	N	8
4	MEAN	224.6
	SD	27.0
	MIN	197
	MAX	271
	N	8

APPENDIX NO. 49

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations and footnote have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

^: Data was recorded without decimal

E: Excluded

Ab: Aberrant value

APPENDIX NO. 49

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	[redacted]											
	MEAN	26.25	27.63	27.88	28.13	29.00	29.00	28.75	29.13	29.50	30.25	31.50
	SD	0.65	0.48	0.25	0.25	1.00	1.00	0.29	0.25	0.41	0.65	0.91
	MIN	25.5	27.0	27.5	28.0	28.5	28.5	28.5	29.0	29.0	29.5	30.5
	MAX	27.0	28.0	28.0	28.5	30.5	30.5	29.0	29.5	30.0	31.0	32.5
	N	4	4	4	4	4	4	4	4	4	4	4
2	[redacted]											
	MEAN	27.00	26.50	26.88	27.38	29.00	29.38	29.75	30.00	30.13	30.88	31.88
	SD	0.91	0.91	1.11	0.75	0.71	0.48	0.50	0.00	0.25	0.25	0.85
	MIN	26.0	25.5	25.5	26.5	28.0	29.0	29.0	30.0	30.0	30.5	31.0
	MAX	28.0	27.5	28.0	28.0	29.5	30.0	30.0	30.0	30.5	31.0	33.0
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
[redacted] (b) (4)												
	MEAN	26.75	27.00	28.75	28.75	29.25	29.25	29.63	29.63	29.88	31.00	30.88
	SD	0.96	1.22	1.04	1.04	0.50	0.29	0.48	0.48	0.25	1.22	0.85
	MIN	26.0	26.0	27.5	27.5	29.0	29.0	29.0	29.0	29.5	29.5	30.0
	MAX	28.0	28.5	30.0	30.0	30.0	29.5	30.0	30.0	30.0	32.0	32.0
4	[redacted] (b) (4)											
	MEAN	26.00	26.25	28.38	28.00	28.25	28.38	29.13	29.25	29.63	30.63	30.75
	SD	0.82	1.26	1.44	1.22	1.04	0.85	0.75	0.87	0.75	1.11	1.32
	MIN	25.0	25.0	26.5	26.5	27.0	27.5	28.5	28.5	29.0	29.0	29.0
	MAX	27.0	28.0	29.5	29.5	29.5	29.5	30.0	30.0	30.5	31.5	32.0
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	[redacted]										
	MEAN	31.13	31.75	32.13	33.00	33.13	33.50	33.75	34.13	34.25	34.38
	SD	0.85	0.29	0.48	1.15	1.03	1.15	1.19	1.11	0.87	0.63
	MIN	30.0	31.5	31.5	32.0	32.0	32.5	32.5	32.5	33.0	33.5
	MAX	32.0	32.0	32.5	34.0	34.0	34.5	35.0	35.0	35.0	35.0
	N	4	4	4	4	4	4	4	4	4	4
2	[redacted]										
	MEAN	32.50	31.75	32.00	32.25	32.38	32.88	33.13	34.38	34.50	34.75
	SD	1.87	1.32	1.29	1.32	1.11	1.03	0.85	1.11	1.00	1.19
	MIN	30.5	30.0	30.5	30.5	31.0	31.5	32.0	33.5	34.0	34.0
	MAX	35.0	33.0	33.5	33.5	33.5	34.0	34.0	36.0	36.0	36.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
3	[redacted]										
	SD	1.93	1.26	1.31	1.32	1.18	1.18	0.85	1.32	1.32	1.58
	MIN	30.5	30.5	31.0	31.0	32.0	32.0	32.5	32.5	32.5	32.5
	MAX	34.5	33.5	34.0	34.0	34.5	34.5	34.5	35.5	35.5	36.0
	N	4	4	4	4	4	4	4	4	4	4
4	[redacted]										
	MEAN	31.25	31.63	32.00	32.63	33.00	33.00	33.38	33.38	33.63	34.00
	SD	1.55	1.60	1.47	1.97	1.83	1.83	1.89	1.89	1.70	1.47
	MIN	29.5	30.0	30.5	31.0	31.0	31.0	31.5	31.5	31.5	32.5
	MAX	33.0	33.0	33.5	35.0	35.0	35.0	35.0	35.0	35.0	35.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	[redacted]						
	MEAN	34.38	34.75	34.50	34.88	34.88	35.13
	SD	0.63	1.04	0.71	0.48	0.48	0.48
	MIN	33.5	33.5	33.5	34.5	34.5	34.5
	MAX	35.0	36.0	35.0	35.5	35.5	35.5
	N	4	4	4	4	4	4
2	[redacted]						
	MEAN	34.88	34.88	35.13	35.38	35.88	36.25
	SD	1.11	1.11	1.11	1.03	0.85	0.96
	MIN	34.0	34.0	34.0	34.0	35.0	35.0
	MAX	36.5	36.5	36.5	36.5	37.0	37.0
	N	4	4	4	4	4	4

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
3	[redacted]						
	MEAN	34.13	34.38	34.63	34.38	34.63	34.63
	SD	1.49	1.38	1.11	1.38	1.60	1.60
	MIN	32.5	33.0	33.5	33.0	33.0	33.0
	MAX	36.0	36.0	36.0	36.0	36.0	36.0
	N	4	4	4	4	4	4
4	[redacted]						
	MEAN	34.13	33.75	33.63	33.75	33.75	33.75
	SD	1.31	1.19	1.70	1.66	1.66	1.66
	MIN	33.0	33.0	32.0	32.0	32.0	32.0
	MAX	35.5	35.5	36.0	36.0	36.0	36.0
	N	4	4	4	4	4	4

APPENDIX NO. 49

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	(b) (4)											
	MEAN	25.88	26.88	26.13	26.88	26.88	27.13	27.13	27.63	28.50	29.13	29.88
	SD	0.85	1.44	0.48	0.48	0.48	0.48	0.48	0.48	1.15	1.11	0.25
	MIN	25.0	25.0	25.5	26.5	26.5	26.5	26.5	27.0	27.5	27.5	29.5
	MAX	27.0	28.0	26.5	27.5	27.5	27.5	27.5	28.0	29.5	30.0	30.0
	N	4	4	4	4	4	4	4	4	4	4	4
2	(b) (4)											
	MEAN	25.50	25.75	25.88	26.63	27.38	28.13	28.38	28.50	28.63	28.88	29.88
	SD	0.91	1.50	1.44	1.03	1.25	1.11	1.03	0.82	0.85	0.48	0.48
	MIN	24.5	25.0	25.0	25.5	26.0	27.0	27.0	27.5	27.5	28.5	29.5
	MAX	26.5	28.0	28.0	28.0	29.0	29.5	29.5	29.5	29.5	29.5	30.5
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
3	[redacted] (b) (4)											
	MEAN	25.75	25.88	27.75	26.75	26.88	27.25	27.88	27.88	28.13	29.00	29.50
	SD	0.87	0.25	2.36	1.19	1.18	0.96	0.75	0.75	0.75	1.08	0.71
	MIN	25.0	25.5	26.0	26.0	26.0	26.5	27.0	27.0	27.5	27.5	29.0
	MAX	27.0	26.0	31.0	28.5	28.5	28.5	28.5	28.5	29.0	30.0	30.5
	N	4	4	4	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)											
	MEAN	25.00	25.00	27.00	27.00	27.13	27.25	27.38	27.50	27.88	28.63	29.13
	SD	1.00	1.08	1.91	0.58	0.75	0.65	0.48	0.71	0.48	0.48	0.48
	MIN	24.0	24.0	25.5	26.5	26.5	26.5	27.0	27.0	27.5	28.0	28.5
	MAX	26.0	26.5	29.5	27.5	28.0	28.0	28.0	28.5	28.5	29.0	29.5
	N	3	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	[redacted]										
	MEAN	29.63	30.00	30.50	31.00	31.00	31.25	31.75	32.00	32.13	32.25
	SD	1.11	0.41	0.58	0.71	0.71	1.19	1.04	0.91	0.75	0.65
	MIN	28.0	29.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5	31.5
	MAX	30.5	30.5	31.0	32.0	32.0	33.0	33.0	33.0	33.0	33.0
	N	4	4	4	4	4	4	4	4	4	4
2	[redacted]										
	MEAN	30.63	30.50	31.00	31.13	31.13	31.13	32.00	32.38	32.50	32.75
	SD	1.89	0.41	0.71	0.63	0.63	0.63	1.41	1.11	1.00	1.50
	MIN	28.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5	32.0	32.0
	MAX	33.0	31.0	32.0	32.0	32.0	32.0	34.0	34.0	34.0	35.0
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
3	[redacted]										
	MEAN	30.13	30.25	30.38	30.63	30.88	30.88	31.25	31.63	31.63	32.13
	SD	0.63	0.65	0.63	0.48	0.48	0.48	0.87	1.11	1.11	1.38
	MIN	29.5	29.5	29.5	30.0	30.5	30.5	30.5	30.5	30.5	30.5
	MAX	31.0	31.0	31.0	31.0	31.5	31.5	32.0	33.0	33.0	33.5
	N	4	4	4	4	4	4	4	4	4	4
4	[redacted]										
	MEAN	29.75	30.50	30.50	31.00	31.00	31.38	32.00	32.13	32.38	32.88
	SD	0.50	0.71	0.71	0.82	0.82	1.49	1.08	0.95	1.11	1.18
	MIN	29.5	29.5	29.5	30.0	30.0	30.0	31.0	31.5	31.5	32.0
	MAX	30.5	31.0	31.0	32.0	32.0	33.5	33.5	33.5	34.0	34.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 49

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	(b) (4)						
	MEAN	32.25	33.63	33.00	33.25	33.25	33.75
	SD	0.65	2.02	1.22	1.04	1.04	0.87
	MIN	31.5	31.5	31.5	32.0	32.0	33.0
	MAX	33.0	36.0	34.5	34.5	34.5	34.5
	N	4	4	4	4	4	4
2	(b) (4)						
	MEAN	32.75	32.75	33.25	33.25	34.00	34.00
	SD	1.50	1.50	1.32	1.32	1.47	1.47
	MIN	32.0	32.0	32.0	32.0	32.5	32.5
	MAX	35.0	35.0	35.0	35.0	36.0	36.0
	N	4	4	4	4	4	4

APPENDIX NO. 49

[redacted]

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
3	[redacted]						
	MEAN	32.25	32.38	32.88	32.38	32.38	32.50
	SD	1.19	1.11	1.75	1.11	1.11	0.91
	MIN	31.0	31.0	31.0	31.0	31.0	31.5
	MAX	33.5	33.5	35.0	33.5	33.5	33.5
	N	4	4	4	4	4	4
4	[redacted]						
	MEAN	32.88	33.50	33.25	33.25	33.25	33.38
	SD	1.18	1.73	1.04	1.04	1.04	1.03
	MIN	32.0	32.0	32.0	32.0	32.0	32.0
	MAX	34.5	36.0	34.5	34.5	34.5	34.5
	N	4	4	4	4	4	4

APPENDIX NO. 49

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
SEX COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119
1	MEAN	26.06	27.25	27.00	27.50	27.94	28.06	27.94	28.38	29.00	29.69
	SD	0.73	1.07	1.00	0.76	1.35	1.24	0.94	0.88	0.96	1.03
	MIN	25.0	25.0	25.5	26.5	26.5	26.5	26.5	27.0	27.5	27.5
	MAX	27.0	28.0	28.0	28.5	30.5	30.5	29.0	29.5	30.0	31.0
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	26.25	26.13	26.38	27.00	28.19	28.75	29.06	29.25	29.38	29.88
	SD	1.16	1.22	1.30	0.93	1.28	1.04	1.05	0.96	0.99	1.13
	MIN	24.5	25.0	25.0	25.5	26.0	27.0	27.0	27.5	27.5	28.5
	MAX	28.0	28.0	28.0	28.0	29.5	30.0	30.0	30.0	30.5	31.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	26.25	26.44	28.25	27.75	28.06	28.25	28.75	28.75	29.00	30.00
	SD	1.00	1.02	1.77	1.49	1.52	1.25	1.10	1.10	1.07	1.51
	MIN	25.0	25.5	26.0	26.0	26.0	26.5	27.0	27.0	27.5	27.5
	MAX	28.0	28.5	31.0	30.0	30.0	29.5	30.0	30.0	30.0	32.0
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	25.57	25.63	27.69	27.50	27.69	27.81	28.25	28.38	28.75	29.63
	SD	0.98	1.27	1.73	1.04	1.03	0.92	1.10	1.19	1.10	1.33
	MIN	24.0	24.0	25.5	26.5	26.5	26.5	27.0	27.0	27.5	28.0
	MAX	27.0	28.0	29.5	29.5	29.5	29.5	30.0	30.0	30.5	31.5
	N	7	8	8	8	8	8	8	8	8	8

(b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
SEX COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 126	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189
1	MEAN	30.69	30.38	30.88	31.31	32.00	32.06	32.38	32.75	33.06	33.19
	SD	1.07	1.22	0.99	1.00	1.39	1.40	1.62	1.49	1.47	1.36
	MIN	29.5	28.0	29.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5
	MAX	32.5	32.0	32.0	32.5	34.0	34.0	34.5	35.0	35.0	35.0
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	30.88	31.56	31.13	31.50	31.69	31.75	32.00	32.56	33.38	33.50
	SD	1.25	2.01	1.13	1.10	1.13	1.07	1.22	1.24	1.48	1.41
	MIN	29.5	28.5	30.0	30.5	30.5	30.5	30.5	31.0	31.5	32.0
	MAX	33.0	35.0	33.0	33.5	33.5	33.5	34.0	34.0	36.0	36.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	30.19	31.25	31.00	31.25	31.44	31.88	31.88	32.31	32.69	32.69
	SD	1.03	1.79	1.22	1.34	1.27	1.36	1.36	1.39	1.60	1.60
	MIN	29.0	29.5	29.5	29.5	30.0	30.5	30.5	30.5	30.5	30.5
	MAX	32.0	34.5	33.5	34.0	34.0	34.5	34.5	34.5	35.5	35.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	29.94	30.50	31.06	31.25	31.81	32.00	32.19	32.69	32.75	33.00
	SD	1.27	1.34	1.29	1.34	1.65	1.69	1.77	1.60	1.54	1.49
	MIN	28.5	29.5	29.5	29.5	30.0	30.0	30.0	31.0	31.5	31.5
	MAX	32.0	33.0	33.0	33.5	35.0	35.0	35.0	35.0	35.0	35.0
	N	8	8	8	8	8	8	8	8	8	8

APPENDIX NO. 49

[redacted] (b) (4)

HEAD CIRCUMFERENCE MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
SEX COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 196	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238	COMBINED DAYS
1	MEAN	33.31	33.31	34.19	33.75	34.06	34.06	34.44	30.91
	SD	1.28	1.28	1.60	1.22	1.15	1.15	0.98	1.01
	MIN	31.5	31.5	31.5	31.5	32.0	32.0	33.0	29.4
	MAX	35.0	35.0	36.0	35.0	35.5	35.5	35.5	32.1
	N	8	8	8	8	8	8	8	8
2	MEAN	33.75	33.81	33.81	34.19	34.31	34.94	35.13	31.12
	SD	1.65	1.67	1.67	1.51	1.58	1.50	1.66	1.17
	MIN	32.0	32.0	32.0	32.0	32.0	32.5	32.5	29.6
	MAX	36.5	36.5	36.5	36.5	36.5	37.0	37.0	32.9
	N	8	8	8	8	8	8	8	8
3	MEAN	33.06	33.19	33.38	33.75	33.38	33.50	33.56	30.81
	SD	1.70	1.60	1.58	1.65	1.58	1.75	1.66	1.26
	MIN	30.5	31.0	31.0	31.0	31.0	31.0	31.5	28.9
	MAX	36.0	36.0	36.0	36.0	36.0	36.0	36.0	32.7
	N	8	8	8	8	8	8	8	8
4	MEAN	33.44	33.50	33.63	33.44	33.50	33.50	33.56	30.71
	SD	1.37	1.34	1.38	1.32	1.31	1.31	1.29	1.05
	MIN	32.0	32.0	32.0	32.0	32.0	32.0	32.0	29.4
	MAX	35.5	35.5	36.0	36.0	36.0	36.0	36.0	32.4
	N	8	8	8	8	8	8	8	8

HEAD CIRCUMFERENCE MEASUREMENT CHANGES - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

NC: Not Calculable

APPENDIX NO. 50 (b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	(b) (4)										
	MEAN	1.38	0.25	0.25	0.88	0.00	-0.25	0.38	0.38	0.75	1.25
	SD	1.03	0.50	0.29	0.75	0.00	0.87	0.25	0.48	0.65	1.04
	MIN	0.0	0.0	0.0	0.5	0.0	-1.5	0.0	0.0	0.0	0.0
	MAX	2.5	1.0	0.5	2.0	0.0	0.5	0.5	1.0	1.5	2.5
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	-0.50	0.38	0.50	1.63	0.38	0.38	0.25	0.13	0.75	1.00
	SD	0.58	0.75	0.41	0.63	0.48	0.48	0.50	0.25	0.29	1.08
	MIN	-1.0	-0.5	0.0	1.0	0.0	0.0	0.0	0.0	0.5	0.0
	MAX	0.0	1.0	1.0	2.5	1.0	1.0	1.0	0.5	1.0	2.5
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	0.25	1.75	0.00	0.50	0.00	0.38	0.00	0.25	1.13	-0.13
	SD	1.04	2.06	0.00	0.71	0.41	0.48	0.00	0.29	1.03	0.95
	MIN	-1.0	0.0	0.0	0.0	-0.5	0.0	0.0	0.0	0.0	-1.5
	MAX	1.5	4.0	0.0	1.5	0.5	1.0	0.0	0.5	2.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	0.25	2.13	-0.38	0.25	0.13	0.75	0.13	0.38	1.00	0.13
	SD	1.26	1.70	1.89	0.29	0.25	0.65	0.25	0.25	1.08	0.85
	MIN	-1.0	0.5	-3.0	0.0	0.0	0.0	0.0	0.0	0.0	-1.0
	MAX	2.0	4.5	1.5	0.5	0.5	1.5	0.5	0.5	2.5	1.0
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 50

(b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	(b) (4)										
	MEAN	-0.38	0.63	0.38	0.88	0.13	0.38	0.25	0.38	0.13	0.13
	SD	1.49	0.75	0.48	0.75	0.25	0.25	0.29	0.75	0.25	0.25
	MIN	-2.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	1.0	1.5	0.5	0.5	0.5	1.5	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	0.63	-0.75	0.25	0.25	0.13	0.50	0.25	1.25	0.13	0.25
	SD	2.46	1.50	0.29	0.29	0.25	0.41	0.29	0.87	0.25	0.29
	MIN	-2.5	-2.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0
	MAX	3.5	1.0	0.5	0.5	0.5	1.0	0.5	2.0	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	1.50	-0.63	0.38	0.13	0.63	0.00	0.50	0.38	0.00	0.25
	SD	1.15	1.11	0.25	0.25	0.25	0.00	0.41	0.48	0.00	0.29
	MIN	0.5	-2.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	0.5	0.5	1.0	0.0	1.0	1.0	0.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	0.50	0.38	0.38	0.63	0.38	0.00	0.38	0.00	0.25	0.38
	SD	0.41	0.48	0.48	0.63	0.48	0.00	0.48	0.00	0.50	0.48
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.0	1.0	1.5	1.0	0.0	1.0	0.0	1.0	1.0
	N	4	4	4	4	4	4	4	4	4	4

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238	COMBINED DAYS
1	(b) (4)							
	MEAN	0.00	0.38	-0.25	0.38	0.00	0.25	0.34
	SD	0.00	0.75	0.50	0.48	0.00	0.50	0.04
	MIN	0.0	0.0	-1.0	0.0	0.0	0.0	0.3
	MAX	0.0	1.5	0.0	1.0	0.0	1.0	0.4
	N	4	4	4	4	4	4	4
2	(b) (4)							
	MEAN	0.13	0.00	0.25	0.25	0.50	0.38	0.36
	SD	0.25	0.00	0.50	0.50	0.41	0.75	0.04
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.3
	MAX	0.5	0.0	1.0	1.0	1.0	1.5	0.4
	N	4	4	4	4	4	4	4
3	(b) (4)							
	MEAN	0.13	0.25	0.25	-0.25	0.25	0.00	0.30
	SD	0.25	0.29	0.50	0.50	0.50	0.00	0.06
	MIN	0.0	0.0	0.0	-1.0	0.0	0.0	0.3
	MAX	0.5	0.5	1.0	0.0	1.0	0.0	0.4
	N	4	4	4	4	4	4	4
4	(b) (4)							
	MEAN	0.13	-0.38	-0.13	0.13	0.00	0.00	0.30
	SD	0.25	1.11	0.63	0.25	0.00	0.00	0.05
	MIN	0.0	-2.0	-1.0	0.0	0.0	0.0	0.2
	MAX	0.5	0.5	0.5	0.5	0.0	0.0	0.3
	N	4	4	4	4	4	4	4

APPENDIX NO. 50 (b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	(b) (4)										
	MEAN	1.00	-0.75	0.75	0.00	0.25	0.00	0.50	0.88	0.63	0.75
	SD	1.47	1.19	0.65	0.00	0.50	0.00	0.71	0.75	1.25	1.19
	MIN	-0.5	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	3.0	0.5	1.5	0.0	1.0	0.0	1.5	1.5	2.5	2.5
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	0.25	0.13	0.75	0.75	0.75	0.25	0.13	0.13	0.25	1.00
	SD	1.04	0.25	0.65	0.29	1.19	0.50	0.25	0.25	0.50	0.91
	MIN	-1.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.5	0.5	1.5	1.0	2.5	1.0	0.5	0.5	1.0	2.0
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	0.13	1.88	-1.00	0.13	0.38	0.63	0.00	0.25	0.88	0.50
	SD	0.75	2.25	2.35	0.25	0.25	0.48	0.00	0.29	0.75	0.71
	MIN	-1.0	0.0	-4.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	0.5	5.0	0.5	0.5	0.5	1.0	0.0	0.5	1.5	1.5
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	0.00	2.00	0.00	0.13	0.13	0.13	0.13	0.38	0.75	0.50
	SD	1.80	1.68	2.16	0.25	0.25	0.25	0.25	0.48	0.29	0.41
	MIN	-2.0	1.0	-3.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0
	MAX	1.5	4.5	2.0	0.5	0.5	0.5	0.5	1.0	1.0	1.0
	N	3	4	4	4	4	4	4	4	4	4

APPENDIX NO. 50 (b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	(b) (4)										
	MEAN	-0.25	0.38	0.50	0.50	0.00	0.25	0.50	0.25	0.13	0.13
	SD	1.19	0.75	0.41	0.41	0.00	0.50	0.71	0.29	0.25	0.25
	MIN	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	0.5	1.5	1.0	1.0	0.0	1.0	1.5	0.5	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	0.75	-0.13	0.50	0.13	0.00	0.00	0.88	0.38	0.13	0.25
	SD	2.33	1.75	0.58	0.25	0.00	0.00	1.75	1.70	0.25	0.50
	MIN	-2.0	-2.0	0.0	0.0	0.0	0.0	0.0	-2.0	0.0	0.0
	MAX	3.5	2.0	1.0	0.5	0.0	0.0	3.5	2.0	0.5	1.0
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	0.63	0.13	0.13	0.25	0.25	0.00	0.38	0.38	0.00	0.50
	SD	0.25	0.25	0.25	0.29	0.29	0.00	0.48	0.48	0.00	0.41
	MIN	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	0.5	0.5	0.5	0.5	0.0	1.0	1.0	0.0	1.0
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	0.63	0.75	0.00	0.50	0.00	0.38	0.63	0.13	0.25	0.50
	SD	0.48	0.87	0.00	0.71	0.00	0.75	0.48	0.25	0.29	0.41
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	0.0	1.5	0.0	1.5	1.0	0.5	0.5	1.0
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 50 (b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238	COMBINED DAYS
1	(b) (4)							
	MEAN	0.00	1.38	-0.63	0.25	0.00	0.50	0.30
	SD	0.00	1.60	1.03	0.29	0.00	0.58	0.04
	MIN	0.0	0.0	-1.5	0.0	0.0	0.0	0.3
	MAX	0.0	3.0	0.5	0.5	0.0	1.0	0.4
	N	4	4	4	4	4	4	4
2	(b) (4)							
	MEAN	0.00	0.00	0.50	0.00	0.75	0.00	0.33
	SD	0.00	0.00	0.71	0.41	0.65	0.00	0.04
	MIN	0.0	0.0	0.0	-0.5	0.0	0.0	0.3
	MAX	0.0	0.0	1.5	0.5	1.5	0.0	0.4
	N	4	4	4	4	4	4	4
3	(b) (4)							
	MEAN	0.13	0.13	0.50	-0.50	0.00	0.13	0.26
	SD	0.48	0.25	1.00	1.00	0.00	0.25	0.02
	MIN	-0.5	0.0	0.0	-2.0	0.0	0.0	0.3
	MAX	0.5	0.5	2.0	0.0	0.0	0.5	0.3
	N	4	4	4	4	4	4	4
4	(b) (4)							
	MEAN	0.00	0.63	-0.25	0.00	0.00	0.13	0.33
	SD	0.00	0.75	0.87	0.00	0.00	0.25	0.03
	MIN	0.0	0.0	-1.5	0.0	0.0	0.0	0.3
	MAX	0.0	1.5	0.5	0.0	0.0	0.5	0.4
	N	4	4	4	4	4	4	4

APPENDIX NO. 50

(b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	1.19	-0.25	0.50	0.44	0.13	-0.13	0.44	0.63	0.69	1.00
	SD	1.19	1.00	0.53	0.68	0.35	0.58	0.50	0.64	0.92	1.07
	MIN	-0.5	-2.0	0.0	0.0	0.0	-1.5	0.0	0.0	0.0	0.0
	MAX	3.0	1.0	1.5	2.0	1.0	0.5	1.5	1.5	2.5	2.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	-0.13	0.25	0.63	1.19	0.56	0.31	0.19	0.13	0.50	1.00
	SD	0.88	0.53	0.52	0.65	0.86	0.46	0.37	0.23	0.46	0.93
	MIN	-1.0	-0.5	0.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.5	1.0	1.5	2.5	2.5	1.0	1.0	0.5	1.0	2.5
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	0.19	1.81	-0.50	0.31	0.19	0.50	0.00	0.25	1.00	0.19
	SD	0.84	2.00	1.63	0.53	0.37	0.46	0.00	0.27	0.85	0.84
	MIN	-1.0	0.0	-4.5	0.0	-0.5	0.0	0.0	0.0	0.0	-1.5
	MAX	1.5	5.0	0.5	1.5	0.5	1.0	0.0	0.5	2.0	1.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.14	2.06	-0.19	0.19	0.13	0.44	0.13	0.38	0.88	0.31
	SD	1.38	1.57	1.89	0.26	0.23	0.56	0.23	0.35	0.74	0.65
	MIN	-2.0	0.5	-3.0	0.0	0.0	0.0	0.0	0.0	0.0	-1.0
	MAX	2.0	4.5	2.0	0.5	0.5	1.5	0.5	1.0	2.5	1.0
	N	7	8	8	8	8	8	8	8	8	8

(b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	-0.31	0.50	0.44	0.69	0.06	0.31	0.38	0.31	0.13	0.13
	SD	1.25	0.71	0.42	0.59	0.18	0.37	0.52	0.53	0.23	0.23
	MIN	-2.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	1.0	1.5	0.5	1.0	1.5	1.5	0.5	0.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	0.69	-0.44	0.38	0.19	0.06	0.25	0.56	0.81	0.13	0.25
	SD	2.22	1.55	0.44	0.26	0.18	0.38	1.21	1.33	0.23	0.38
	MIN	-2.5	-2.0	0.0	0.0	0.0	0.0	0.0	-2.0	0.0	0.0
	MAX	3.5	2.0	1.0	0.5	0.5	1.0	3.5	2.0	0.5	1.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	1.06	-0.25	0.25	0.19	0.44	0.00	0.44	0.38	0.00	0.38
	SD	0.90	0.85	0.27	0.26	0.32	0.00	0.42	0.44	0.00	0.35
	MIN	0.5	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	0.5	0.5	1.0	0.0	1.0	1.0	0.0	1.0
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.56	0.56	0.19	0.56	0.19	0.19	0.50	0.06	0.25	0.44
	SD	0.42	0.68	0.37	0.62	0.37	0.53	0.46	0.18	0.38	0.42
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.0	1.5	1.0	1.5	1.0	1.5	1.0	0.5	1.0	1.0
	N	8	8	8	8	8	8	8	8	8	8

APPENDIX NO. 50

(b) (4)

HEAD CIRCUMFERENCE CHANGE, F1, POST WEANING
HEAD CIRCUMFERENCE CHANGES (cm)
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238	COMBINED DAYS
1	MEAN	0.00	0.88	-0.44	0.31	0.00	0.38	0.32
	SD	0.00	1.27	0.78	0.37	0.00	0.52	0.04
	MIN	0.0	0.0	-1.5	0.0	0.0	0.0	0.3
	MAX	0.0	3.0	0.5	1.0	0.0	1.0	0.4
	N	8	8	8	8	8	8	8
2	MEAN	0.06	0.00	0.38	0.13	0.63	0.19	0.34
	SD	0.18	0.00	0.58	0.44	0.52	0.53	0.04
	MIN	0.0	0.0	0.0	-0.5	0.0	0.0	0.3
	MAX	0.5	0.0	1.5	1.0	1.5	1.5	0.4
	N	8	8	8	8	8	8	8
3	MEAN	0.13	0.19	0.38	-0.38	0.13	0.06	0.28
	SD	0.35	0.26	0.74	0.74	0.35	0.18	0.05
	MIN	-0.5	0.0	0.0	-2.0	0.0	0.0	0.3
	MAX	0.5	0.5	2.0	0.0	1.0	0.5	0.4
	N	8	8	8	8	8	8	8
4	MEAN	0.06	0.13	-0.19	0.06	0.00	0.06	0.31
	SD	0.18	1.03	0.70	0.18	0.00	0.18	0.04
	MIN	0.0	-2.0	-1.5	0.0	0.0	0.0	0.2
	MAX	0.5	1.5	0.5	0.5	0.0	0.5	0.4
	N	8	8	8	8	8	8	8

APPENDIX NO. 51 (b) (4)

HEIGHT MEASUREMENTS - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations and footnote have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

^: Data was recorded without decimal.

APPENDIX NO. 51

(b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	(b) (4)											
	MEAN	26.00	27.63	29.00	29.25	30.75	31.25	32.00	33.75	34.38	35.63	37.13
	SD	0.00	1.65	1.58	1.32	1.55	1.19	0.91	1.55	1.65	2.17	1.65
	MIN	26.0	26.5	27.0	27.5	29.0	30.0	31.0	32.5	32.5	32.5	35.0
	MAX	26.0	30.0	30.5	30.5	32.5	32.5	33.0	36.0	36.0	37.5	39.0
	N	4	4	4	4	4	4	4	4	4	4	4
2	(b) (4)											
	MEAN	26.25	26.63	29.88	31.38	31.25	31.88	32.50	32.88	35.25	36.13	38.50
	SD	0.87	2.78	3.40	1.70	1.19	1.44	0.71	1.11	1.89	2.02	3.34
	MIN	25.5	24.0	26.5	30.0	30.0	30.0	32.0	32.0	34.0	34.5	35.5
	MAX	27.5	30.5	33.5	33.5	32.5	33.5	33.5	34.5	38.0	39.0	42.5
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 51

(b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
3	(b) (4)											
	MEAN	26.00	25.63	30.63	31.63	31.75	32.50	32.38	34.38	35.38	35.63	36.38
	SD	1.41	0.95	4.33	1.18	1.50	0.71	0.75	1.11	1.49	1.60	2.14
	MIN	25.0	25.0	25.5	30.0	30.0	31.5	31.5	33.0	34.0	34.5	35.0
	MAX	28.0	27.0	35.5	32.5	33.0	33.0	33.0	35.5	37.5	38.0	39.5
	N	4	4	4	4	4	4	4	4	4	4	4
4	(b) (4)											
	MEAN	25.25	25.50	28.88	30.25	30.88	31.38	32.13	32.75	33.63	34.75	34.50
	SD	1.71	1.29	3.52	1.85	0.85	1.38	0.85	1.32	1.31	1.55	2.27
	MIN	23.0	24.0	25.0	27.5	30.0	30.0	31.0	31.5	32.5	32.5	32.5
	MAX	27.0	27.0	33.5	31.5	32.0	33.0	33.0	34.5	35.0	36.0	37.5
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 51

[redacted]

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	[redacted]										
	MEAN	37.13	37.25	37.38	40.13	38.25	38.88	39.25	39.63	40.63	41.00
	SD	0.48	0.50	0.63	2.78	1.04	1.03	1.50	1.80	1.31	1.47
	MIN	36.5	36.5	36.5	37.5	37.0	38.0	38.0	38.0	39.5	39.5
	MAX	37.5	37.5	38.0	43.0	39.5	40.0	41.0	42.0	42.0	42.5
	N	4	4	4	4	4	4	4	4	4	4
2	[redacted]										
	MEAN	39.13	38.13	38.88	39.00	39.25	40.00	40.25	40.88	41.13	41.50
	SD	3.40	1.93	2.43	2.35	2.18	2.12	2.06	2.43	2.14	2.27
	MIN	35.5	37.0	37.5	37.5	38.0	38.0	38.5	38.5	39.5	39.5
	MAX	42.5	41.0	42.5	42.5	42.5	42.5	42.5	44.0	44.0	44.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 51

[redacted]

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
3	[redacted]										
	MEAN	37.50	37.50	37.75	38.00	40.38	39.00	39.25	39.88	40.00	40.75
	SD	2.92	2.04	1.76	1.78	2.17	1.41	1.32	1.97	1.78	2.02
	MIN	35.0	35.5	36.0	36.0	38.5	37.0	37.5	37.5	38.0	38.0
	MAX	40.5	39.5	39.5	39.5	43.5	40.0	40.5	41.5	41.5	42.5
4	[redacted]										
	MEAN	35.63	36.00	37.25	38.38	38.75	39.63	40.13	40.25	40.50	40.75
	SD	2.32	2.16	1.66	2.29	0.87	1.25	1.84	1.85	1.63	1.85
	MIN	32.5	33.0	36.0	36.0	38.0	38.0	38.0	38.0	38.5	38.5
	MAX	38.0	38.0	39.5	41.0	39.5	41.0	42.5	42.5	42.5	43.0
	N	4	4	4	4	4	4	4	4	4	4

[redacted]

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	[redacted]						
	MEAN	41.13	43.00	42.13	42.25	42.25	43.38
	SD	1.65	2.58	2.17	1.85	1.85	1.18
	MIN	39.5	40.0	40.0	40.5	40.5	42.5
	MAX	43.0	46.0	44.0	44.5	44.5	45.0
	N	4	4	4	4	4	4
2	[redacted]						
	MEAN	41.63	41.75	42.75	42.38	42.75	43.13
	SD	2.14	2.02	2.33	1.70	1.44	0.95
	MIN	40.0	40.0	40.5	41.0	41.0	42.5
	MAX	44.5	44.5	45.0	44.5	44.5	44.5
	N	4	4	4	4	4	4

APPENDIX NO. 51

[redacted]

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
3	[redacted]						
	MEAN	41.00	41.13	42.50	41.63	41.63	41.75
	SD	2.12	2.25	0.71	1.93	1.93	1.94
	MIN	38.0	38.0	41.5	39.0	39.0	39.0
	MAX	42.5	43.0	43.0	43.5	43.5	43.5
	N	4	4	4	4	4	4
4	[redacted]						
	MEAN	40.88	41.63	41.63	41.88	41.88	42.25
	SD	1.84	2.06	2.06	1.65	1.65	2.10
	MIN	38.5	39.0	39.0	40.0	40.0	40.0
	MAX	43.0	43.5	43.5	43.5	43.5	44.5
	N	4	4	4	4	4	4

APPENDIX NO. 51

(b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
1	(b) (4)											
	MEAN	25.00	27.25	28.75	28.50	29.88	30.13	30.88	31.63	33.00	33.88	35.00
	SD	1.22	2.25	2.96	2.74	1.60	1.60	1.49	2.02	1.08	1.31	1.96
	MIN	23.5	25.5	26.0	25.5	28.5	28.5	29.0	30.0	32.0	32.5	33.0
	MAX	26.5	30.5	32.0	31.5	31.5	31.5	32.5	34.5	34.5	35.0	37.5
	N	4	4	4	4	4	4	4	4	4	4	4
2	(b) (4)											
	MEAN	25.38	26.75	29.13	29.88	30.13	31.38	31.75	32.63	34.00	34.88	36.88
	SD	1.38	1.55	1.70	1.11	0.75	1.49	1.94	1.97	2.68	2.06	2.29
	MIN	24.0	25.0	27.0	28.5	29.5	29.5	29.5	31.0	31.0	33.0	33.5
	MAX	27.0	28.5	30.5	31.0	31.0	33.0	34.0	35.0	37.5	37.5	38.5
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 51

[redacted] (b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119	DAY 126
3	[redacted] (b) (4)											
	MEAN	26.50	26.13	29.75	30.25	30.88	31.25	31.50	32.38	34.38	34.63	34.75
	SD	2.52	1.03	2.40	2.18	1.49	1.19	1.00	1.38	1.03	0.75	0.65
	MIN	24.0	25.0	27.5	28.5	29.5	30.5	31.0	31.0	33.5	34.0	34.0
	MAX	30.0	27.0	32.5	33.0	33.0	33.0	33.0	34.0	35.5	35.5	35.5
	N	4	4	4	4	4	4	4	4	4	4	4
4	[redacted]											
	MEAN	24.75	25.25	28.38	29.63	30.38	30.75	31.38	32.13	33.50	34.63	33.88
	SD	0.96	0.87	2.59	2.25	1.03	1.04	1.31	1.75	1.08	0.95	0.95
	MIN	24.0	24.0	26.0	26.5	29.5	29.5	29.5	30.0	32.0	34.0	32.5
	MAX	26.0	26.0	31.5	31.5	31.5	32.0	32.5	34.0	34.5	36.0	34.5
	N	4	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 51

[redacted]

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
1	[redacted]										
	MEAN	34.88	35.75	35.88	38.63	36.50	38.63	39.13	39.50	39.75	39.25
	SD	1.18	0.87	1.44	3.90	1.47	2.32	2.39	2.86	2.47	1.71
	MIN	34.0	35.0	35.0	35.0	35.0	35.5	36.0	36.0	37.0	37.0
	MAX	36.5	37.0	38.0	42.0	38.0	41.0	41.0	42.5	42.5	41.0
	N	4	4	4	4	4	4	4	4	4	4
2	[redacted]										
	MEAN	37.88	37.38	37.38	37.50	37.75	38.63	39.00	39.38	39.63	40.13
	SD	2.95	2.06	2.06	2.12	2.22	3.07	2.94	2.56	2.29	2.43
	MIN	35.5	35.5	35.5	35.5	35.5	35.5	36.0	36.5	37.0	37.0
	MAX	42.0	40.0	40.0	40.0	40.5	41.5	42.0	42.0	42.0	42.5
	N	4	4	4	4	4	4	4	4	4	4

[redacted] (b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189	DAY 196
3	[redacted] (b) (4)										
	MEAN	37.25	37.75	38.00	37.50	39.75	38.25	38.63	38.75	38.75	39.63
	SD	2.06	1.44	1.15	1.00	2.63	0.96	0.85	0.65	0.65	0.75
	MIN	35.0	36.5	37.0	37.0	37.5	37.5	37.5	38.0	38.0	39.0
	MAX	39.0	39.0	39.0	39.0	43.5	39.5	39.5	39.5	39.5	40.5
	N	4	4	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)										
	MEAN	34.63	35.13	35.50	37.38	36.50	38.38	39.25	39.25	39.38	40.00
	SD	0.48	0.48	0.71	3.77	0.58	1.11	1.32	1.32	1.25	0.71
	MIN	34.0	34.5	34.5	35.0	36.0	37.5	38.0	38.0	38.0	39.5
	MAX	35.0	35.5	36.0	43.0	37.0	40.0	41.0	41.0	41.0	41.0
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 51

[redacted]

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
1	[redacted]						
	MEAN	39.50	40.25	40.88	40.50	40.50	41.38
	SD	1.29	2.06	2.02	1.47	1.47	1.49
	MIN	38.0	38.0	38.5	38.5	38.5	39.5
	MAX	41.0	43.0	43.0	42.0	42.0	43.0
	N	4	4	4	4	4	4
2	[redacted]						
	MEAN	40.13	40.25	40.50	40.88	41.13	41.13
	SD	2.43	2.60	2.20	1.75	1.65	1.65
	MIN	37.0	37.0	38.0	39.0	39.0	39.0
	MAX	42.5	43.0	43.0	43.0	43.0	43.0
	N	4	4	4	4	4	4

(b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238
3	(b) (4)						
	MEAN	40.00	40.25	41.00	40.88	40.88	40.88
	SD	0.71	0.29	1.35	0.75	0.75	0.75
	MIN	39.5	40.0	40.0	40.5	40.5	40.5
	MAX	41.0	40.5	43.0	42.0	42.0	42.0
	N	4	4	4	4	4	4
4	(b) (4)						
	MEAN	40.25	41.13	41.13	41.00	41.13	41.50
	SD	0.87	1.80	0.85	1.22	1.31	1.22
	MIN	39.5	39.5	40.0	40.0	40.0	40.0
	MAX	41.5	43.5	42.0	42.5	42.5	42.5
	N	4	4	4	4	4	4

(b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56	DAY 63	DAY 70	DAY 77	DAY 84	DAY 91	DAY 98	DAY 105	DAY 112	DAY 119
1	MEAN	25.50	27.44	28.88	28.88	30.31	30.69	31.44	32.69	33.69	34.75
	SD	0.96	1.84	2.20	2.03	1.53	1.44	1.29	2.02	1.49	1.91
	MIN	23.5	25.5	26.0	25.5	28.5	28.5	29.0	30.0	32.0	32.5
	MAX	26.5	30.5	32.0	31.5	32.5	32.5	33.0	36.0	36.0	37.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	25.81	26.69	29.50	30.63	30.69	31.63	32.13	32.75	34.63	35.50
	SD	1.16	2.09	2.52	1.55	1.10	1.38	1.41	1.49	2.25	2.00
	MIN	24.0	24.0	26.5	28.5	29.5	29.5	29.5	31.0	31.0	33.0
	MAX	27.5	30.5	33.5	33.5	32.5	33.5	34.0	35.0	38.0	39.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	26.25	25.88	30.19	30.94	31.31	31.88	31.94	33.38	34.88	35.13
	SD	1.91	0.95	3.27	1.78	1.46	1.13	0.94	1.58	1.30	1.27
	MIN	24.0	25.0	25.5	28.5	29.5	30.5	31.0	31.0	33.5	34.0
	MAX	30.0	27.0	35.5	33.0	33.0	33.0	33.0	35.5	37.5	38.0
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	25.00	25.38	28.63	29.94	30.63	31.06	31.75	32.44	33.56	34.69
	SD	1.31	1.03	2.88	1.94	0.92	1.18	1.10	1.47	1.12	1.19
	MIN	23.0	24.0	25.0	26.5	29.5	29.5	29.5	30.0	32.0	32.5
	MAX	27.0	27.0	33.5	31.5	32.0	33.0	33.0	34.5	35.0	36.0
	N	8	8	8	8	8	8	8	8	8	8

(b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 126	DAY 133	DAY 140	DAY 147	DAY 154	DAY 161	DAY 168	DAY 175	DAY 182	DAY 189
1	MEAN	36.06	36.00	36.50	36.63	39.38	37.38	38.75	39.19	39.56	40.19
	SD	2.03	1.46	1.04	1.30	3.24	1.51	1.67	1.85	2.21	1.89
	MIN	33.0	34.0	35.0	35.0	35.0	35.0	35.5	36.0	36.0	37.0
	MAX	39.0	37.5	37.5	38.0	43.0	39.5	41.0	41.0	42.5	42.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	37.69	38.50	37.75	38.13	38.25	38.50	39.31	39.63	40.13	40.38
	SD	2.79	3.02	1.89	2.23	2.22	2.19	2.55	2.45	2.45	2.20
	MIN	33.5	35.5	35.5	35.5	35.5	35.5	35.5	36.0	36.5	37.0
	MAX	42.5	42.5	41.0	42.5	42.5	42.5	42.5	42.5	44.0	44.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	35.56	37.38	37.63	37.88	37.75	40.06	38.63	38.94	39.31	39.38
	SD	1.70	2.34	1.64	1.38	1.36	2.26	1.19	1.08	1.49	1.41
	MIN	34.0	35.0	35.5	36.0	36.0	37.5	37.0	37.5	37.5	38.0
	MAX	39.5	40.5	39.5	39.5	39.5	43.5	40.0	40.5	41.5	41.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	34.19	35.13	35.56	36.38	37.88	37.63	39.00	39.69	39.75	39.94
	SD	1.65	1.64	1.52	1.51	2.94	1.38	1.28	1.56	1.58	1.47
	MIN	32.5	32.5	33.0	34.5	35.0	36.0	37.5	38.0	38.0	38.0
	MAX	37.5	38.0	38.0	39.5	43.0	39.5	41.0	42.5	42.5	42.5
	N	8	8	8	8	8	8	8	8	8	8

(b) (4)

HEIGHT MEASUREMENTS (cm)
F1 GENERATION - PUPPIES - POST WEANING
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	DAY 196	DAY 203	DAY 210	DAY 217	DAY 224	DAY 231	DAY 238	COMBINED DAYS
1	MEAN	40.13	40.31	41.63	41.50	41.38	41.38	42.38	36.02
	SD	1.75	1.62	2.62	2.05	1.81	1.81	1.64	1.22
	MIN	37.0	38.0	38.0	38.5	38.5	38.5	39.5	33.9
	MAX	42.5	43.0	46.0	44.0	44.5	44.5	45.0	37.8
	N	8	8	8	8	8	8	8	8
2	MEAN	40.81	40.88	41.00	41.63	41.63	41.94	42.13	36.60
	SD	2.30	2.26	2.30	2.42	1.79	1.68	1.64	1.64
	MIN	37.0	37.0	37.0	38.0	39.0	39.0	39.0	34.1
	MAX	44.5	44.5	44.5	45.0	44.5	44.5	44.5	39.5
	N	8	8	8	8	8	8	8	8
3	MEAN	40.19	40.50	40.69	41.75	41.25	41.25	41.31	36.34
	SD	1.53	1.56	1.56	1.28	1.41	1.41	1.44	0.97
	MIN	38.0	38.0	38.0	40.0	39.0	39.0	39.0	35.3
	MAX	42.5	42.5	43.0	43.0	43.5	43.5	43.5	38.2
	N	8	8	8	8	8	8	8	8
4	MEAN	40.38	40.56	41.38	41.38	41.44	41.50	41.88	35.80
	SD	1.36	1.37	1.81	1.48	1.43	1.44	1.64	1.09
	MIN	38.5	38.5	39.0	39.0	40.0	40.0	40.0	34.5
	MAX	43.0	43.0	43.5	43.5	43.5	43.5	44.5	37.7
	N	8	8	8	8	8	8	8	8

HEIGHT MEASUREMENT CHANGES - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum value

MIN: Minimum value

APPENDIX NO. 52 (b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	(b) (4)										
	MEAN	1.63	1.38	0.25	1.50	0.50	0.75	1.75	0.63	1.25	1.50
	SD	1.65	2.32	0.29	2.38	0.41	0.50	1.19	0.95	1.89	1.22
	MIN	0.5	-1.5	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0
	MAX	4.0	3.5	0.5	5.0	1.0	1.0	3.0	2.0	4.0	2.5
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	0.38	3.25	1.50	-0.13	0.63	0.63	0.38	2.38	0.88	2.38
	SD	3.52	4.63	1.78	0.63	0.75	0.95	0.48	1.03	0.85	2.78
	MIN	-3.5	-3.0	0.0	-1.0	0.0	0.0	0.0	1.5	0.0	0.5
	MAX	5.0	7.0	3.5	0.5	1.5	2.0	1.0	3.5	2.0	6.5
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	-0.38	5.00	1.00	0.13	0.75	-0.13	2.00	1.00	0.25	0.75
	SD	1.80	3.54	4.55	1.25	1.19	0.25	1.35	0.82	0.29	0.65
	MIN	-3.0	0.5	-4.0	-1.5	0.0	-0.5	0.0	0.0	0.0	0.0
	MAX	1.0	8.5	7.0	1.5	2.5	0.0	3.0	2.0	0.5	1.5
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	0.25	3.38	1.38	0.63	0.50	0.75	0.63	0.88	1.13	-0.25
	SD	2.22	3.09	2.59	1.89	1.00	0.65	0.95	0.85	1.31	1.66
	MIN	-3.0	1.0	-2.5	-1.5	0.0	0.0	0.0	0.0	0.0	-2.5
	MAX	2.0	7.5	3.0	3.0	2.0	1.5	2.0	2.0	3.0	1.5
	N	4	4	4	4	4	4	4	4	4	4

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	(b) (4)										
	MEAN	0.00	0.13	0.13	2.75	-1.88	0.63	0.38	0.38	1.00	0.38
	SD	1.47	0.25	0.25	2.90	3.42	0.48	0.48	0.48	0.71	0.48
	MIN	-2.0	0.0	0.0	0.0	-5.0	0.0	0.0	0.0	0.0	0.0
	MAX	1.5	0.5	0.5	5.5	2.0	1.0	1.0	1.0	1.5	1.0
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	0.63	-1.00	0.75	0.13	0.25	0.75	0.25	0.63	0.25	0.38
	SD	5.50	2.74	0.65	0.25	0.29	1.50	0.29	0.75	0.50	0.25
	MIN	-7.0	-4.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	6.0	2.0	1.5	0.5	0.5	3.0	0.5	1.5	1.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	1.13	0.00	0.25	0.25	2.38	-1.38	0.25	0.63	0.13	0.75
	SD	1.65	1.08	0.29	0.29	3.47	3.42	0.29	0.75	0.25	0.65
	MIN	0.0	-1.5	0.0	0.0	0.0	-6.5	0.0	0.0	0.0	0.0
	MAX	3.5	1.0	0.5	0.5	7.5	0.5	0.5	1.5	0.5	1.5
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	1.13	0.38	1.25	1.13	0.38	0.88	0.50	0.13	0.25	0.25
	SD	1.11	0.25	1.32	1.65	2.69	0.75	0.71	0.25	0.29	0.29
	MIN	0.0	0.0	0.0	0.0	-3.0	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	3.0	3.5	3.5	1.5	1.5	0.5	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 52 (b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238	COMBINED DAYS
1	(b) (4)							
	MEAN	0.13	1.88	-0.88	0.13	0.00	1.13	0.67
	SD	0.25	1.93	2.39	0.85	0.00	0.75	0.05
	MIN	0.0	0.0	-3.5	-1.0	0.0	0.5	0.6
	MAX	0.5	4.0	2.0	1.0	0.0	2.0	0.7
	N	4	4	4	4	4	4	4
2	(b) (4)							
	MEAN	0.13	0.13	1.00	-0.38	0.38	0.38	0.65
	SD	0.25	0.25	1.35	1.11	0.75	0.75	0.05
	MIN	0.0	0.0	0.0	-2.0	0.0	0.0	0.6
	MAX	0.5	0.5	3.0	0.5	1.5	1.5	0.7
	N	4	4	4	4	4	4	4
3	(b) (4)							
	MEAN	0.25	0.13	1.38	-0.88	0.00	0.13	0.61
	SD	0.29	0.25	2.43	2.10	0.00	0.25	0.08
	MIN	0.0	0.0	0.0	-4.0	0.0	0.0	0.5
	MAX	0.5	0.5	5.0	0.5	0.0	0.5	0.7
	N	4	4	4	4	4	4	4
4	(b) (4)							
	MEAN	0.13	0.75	0.00	0.25	0.00	0.38	0.65
	SD	0.25	0.87	0.00	0.50	0.00	0.75	0.09
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.5
	MAX	0.5	2.0	0.0	1.0	0.0	1.5	0.8
	N	4	4	4	4	4	4	4

APPENDIX NO. 52

(b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	(b) (4)										
	MEAN	2.25	1.50	-0.25	1.38	0.25	0.75	0.75	1.38	0.88	1.13
	SD	3.18	4.53	1.32	1.25	0.29	0.96	0.96	1.25	1.44	2.69
	MIN	0.5	-4.0	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	-2.0
	MAX	7.0	6.5	1.0	3.0	0.5	2.0	2.0	3.0	3.0	4.5
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	1.38	2.38	0.75	0.25	1.25	0.38	0.88	1.38	0.88	2.00
	SD	2.50	1.89	1.19	0.50	1.19	0.48	0.63	1.31	1.03	2.61
	MIN	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	4.0	4.5	2.5	1.0	2.5	1.0	1.5	2.5	2.0	5.5
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	-0.38	3.63	0.50	0.63	0.38	0.25	0.88	2.00	0.25	0.13
	SD	2.06	3.35	3.89	1.70	0.48	0.29	0.85	0.71	0.29	0.48
	MIN	-3.0	0.5	-4.0	-1.5	0.0	0.0	0.0	1.0	0.0	-0.5
	MAX	1.5	7.0	5.5	2.0	1.0	0.5	2.0	2.5	0.5	0.5
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	0.50	3.13	1.25	0.75	0.38	0.63	0.75	1.38	1.13	-0.75
	SD	1.78	2.29	1.32	1.50	0.48	0.75	0.87	1.55	1.31	1.85
	MIN	-2.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	-3.5
	MAX	2.0	6.0	3.0	3.0	1.0	1.5	2.0	3.5	2.5	0.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 52 (b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	(b) (4)										
	MEAN	-0.13	0.88	0.13	2.75	-2.13	2.13	0.50	0.38	0.25	-0.50
	SD	1.65	0.48	0.63	3.40	3.84	1.18	0.71	0.75	0.50	1.35
	MIN	-2.5	0.5	-0.5	0.0	-6.5	0.5	0.0	0.0	0.0	-2.5
	MAX	1.0	1.5	1.0	7.0	2.0	3.0	1.5	1.5	1.0	0.5
	N	4	4	4	4	4	4	4	4	4	4
2	(b) (4)										
	MEAN	1.00	-0.50	0.00	0.13	0.25	0.88	0.38	0.38	0.25	0.50
	SD	3.24	1.00	0.00	0.25	0.29	1.44	0.25	0.48	0.29	0.41
	MIN	-3.0	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	4.5	0.0	0.0	0.5	0.5	3.0	0.5	1.0	0.5	1.0
	N	4	4	4	4	4	4	4	4	4	4
3	(b) (4)										
	MEAN	2.50	0.50	0.25	-0.50	2.25	-1.50	0.38	0.13	0.00	0.88
	SD	2.61	0.71	0.29	1.00	2.87	3.00	0.48	0.25	0.00	0.48
	MIN	0.0	0.0	0.0	-2.0	0.5	-6.0	0.0	0.0	0.0	0.5
	MAX	5.0	1.5	0.5	0.0	6.5	0.0	1.0	0.5	0.0	1.5
	N	4	4	4	4	4	4	4	4	4	4
4	(b) (4)										
	MEAN	0.75	0.50	0.38	1.88	-0.88	1.88	0.88	0.00	0.13	0.63
	SD	0.65	0.00	0.48	3.42	4.13	1.55	0.48	0.00	0.25	0.75
	MIN	0.0	0.5	0.0	0.0	-7.0	0.5	0.5	0.0	0.0	0.0
	MAX	1.5	0.5	1.0	7.0	2.0	4.0	1.5	0.0	0.5	1.5
	N	4	4	4	4	4	4	4	4	4	4

APPENDIX NO. 52 (b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238	COMBINED DAYS
1	(b) (4)							
	MEAN	0.25	0.75	0.63	-0.38	0.00	0.88	0.63
	SD	0.50	0.96	1.70	1.11	0.00	1.18	0.02
	MIN	0.0	0.0	-1.0	-2.0	0.0	0.0	0.6
	MAX	1.0	2.0	3.0	0.5	0.0	2.5	0.7
	N	4	4	4	4	4	4	4
2	(b) (4)							
	MEAN	0.00	0.13	0.25	0.38	0.25	0.00	0.61
	SD	0.00	0.25	0.50	0.48	0.50	0.00	0.04
	MIN	0.0	0.0	0.0	0.0	0.0	0.0	0.6
	MAX	0.0	0.5	1.0	1.0	1.0	0.0	0.7
	N	4	4	4	4	4	4	4
3	(b) (4)							
	MEAN	0.38	0.25	0.75	-0.13	0.00	0.00	0.55
	SD	0.25	0.65	1.50	0.63	0.00	0.00	0.10
	MIN	0.0	-0.5	0.0	-1.0	0.0	0.0	0.4
	MAX	0.5	1.0	3.0	0.5	0.0	0.0	0.6
	N	4	4	4	4	4	4	4
4	(b) (4)							
	MEAN	0.25	0.88	0.00	-0.13	0.13	0.38	0.64
	SD	0.29	1.75	1.87	0.95	0.25	0.48	0.06
	MIN	0.0	0.0	-2.5	-1.5	0.0	0.0	0.6
	MAX	0.5	3.5	2.0	0.5	0.5	1.0	0.7
	N	4	4	4	4	4	4	4

APPENDIX NO. 52

(b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 56 to 63	Day 63 to 70	Day 70 to 77	Day 77 to 84	Day 84 to 91	Day 91 to 98	Day 98 to 105	Day 105 to 112	Day 112 to 119	Day 119 to 126
1	MEAN	1.94	1.44	0.00	1.44	0.38	0.75	1.25	1.00	1.06	1.31
	SD	2.37	3.33	0.93	1.76	0.35	0.71	1.13	1.10	1.57	1.94
	MIN	0.5	-4.0	-2.0	0.0	0.0	0.0	0.0	0.0	0.0	-2.0
	MAX	7.0	6.5	1.0	5.0	1.0	2.0	3.0	3.0	4.0	4.5
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	0.88	2.81	1.13	0.06	0.94	0.50	0.63	1.88	0.88	2.19
	SD	2.88	3.31	1.46	0.56	0.98	0.71	0.58	1.22	0.88	2.51
	MIN	-3.5	-3.0	0.0	-1.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	5.0	7.0	3.5	1.0	2.5	2.0	1.5	3.5	2.0	6.5
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	-0.38	4.31	0.75	0.38	0.56	0.06	1.44	1.50	0.25	0.44
	SD	1.79	3.27	3.93	1.41	0.86	0.32	1.21	0.89	0.27	0.62
	MIN	-3.0	0.5	-4.0	-1.5	0.0	-0.5	0.0	0.0	0.0	-0.5
	MAX	1.5	8.5	7.0	2.0	2.5	0.5	3.0	2.5	0.5	1.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.38	3.25	1.31	0.69	0.44	0.69	0.69	1.13	1.13	-0.50
	SD	1.87	2.52	1.91	1.58	0.73	0.65	0.84	1.19	1.22	1.65
	MIN	-3.0	0.5	-2.5	-1.5	0.0	0.0	0.0	0.0	0.0	-3.5
	MAX	2.0	7.5	3.0	3.0	2.0	1.5	2.0	3.5	3.0	1.5
	N	8	8	8	8	8	8	8	8	8	8

APPENDIX NO. 52

(b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 126 to 133	Day 133 to 140	Day 140 to 147	Day 147 to 154	Day 154 to 161	Day 161 to 168	Day 168 to 175	Day 175 to 182	Day 182 to 189	Day 189 to 196
1	MEAN	-0.06	0.50	0.13	2.75	-2.00	1.38	0.44	0.38	0.63	-0.06
	SD	1.45	0.53	0.44	2.93	3.37	1.16	0.56	0.58	0.69	1.05
	MIN	-2.5	0.0	-0.5	0.0	-6.5	0.0	0.0	0.0	0.0	-2.5
	MAX	1.5	1.5	1.0	7.0	2.0	3.0	1.5	1.5	1.5	1.0
	N	8	8	8	8	8	8	8	8	8	8
2	MEAN	0.81	-0.75	0.38	0.13	0.25	0.81	0.31	0.50	0.25	0.44
	SD	4.18	1.93	0.58	0.23	0.27	1.36	0.26	0.60	0.38	0.32
	MIN	-7.0	-4.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	MAX	6.0	2.0	1.5	0.5	0.5	3.0	0.5	1.5	1.0	1.0
	N	8	8	8	8	8	8	8	8	8	8
3	MEAN	1.81	0.25	0.25	-0.13	2.31	-1.44	0.31	0.38	0.06	0.81
	SD	2.15	0.89	0.27	0.79	2.95	2.98	0.37	0.58	0.18	0.53
	MIN	0.0	-1.5	0.0	-2.0	0.0	-6.5	0.0	0.0	0.0	0.0
	MAX	5.0	1.5	0.5	0.5	7.5	0 5	1.0	1.5	0.5	1.5
	N	8	8	8	8	8	8	8	8	8	8
4	MEAN	0.94	0.44	0.81	1.50	-0.25	1.38	0.69	0.06	0.19	0.44
	SD	0.86	0.18	1.03	2.52	3.30	1.25	0.59	0.18	0.26	0.56
	MIN	0.0	0.0	0.0	0.0	-7.0	0.0	0.0	0.0	0.0	0.0
	MAX	2.5	0.5	3.0	7.0	3.5	4.0	1.5	0.5	0.5	1.5
	N	8	8	8	8	8	8	8	8	8	8

APPENDIX NO. 52

(b) (4)

HEIGHT CHANGE, F1, POST WEANING
HEIGHT CHANGES (cm)
SEXES COMBINED

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 196 to 203	Day 203 to 210	Day 210 to 217	Day 217 to 224	Day 224 to 231	Day 231 to 238	COMBINED DAYS
1	MEAN	0.19	1.31	-0.13	-0.13	0.00	1.00	0.65
	SD	0.37	1.53	2.08	0.95	0.00	0.93	0.04
	MIN	0.0	0.0	-3.5	-2.0	0.0	0.0	0.6
	MAX	1.0	4.0	3.0	1.0	0.0	2.5	0.7
	N	8	8	8	8	8	8	8
2	MEAN	0.06	0.13	0.63	0.00	0.31	0.19	0.63
	SD	0.18	0.23	1.03	0.89	0.59	0.53	0.05
	MIN	0.0	0.0	0.0	-2.0	0.0	0.0	0.6
	MAX	0.5	0.5	3.0	1.0	1.5	1.5	0.7
	N	8	8	8	8	8	8	8
3	MEAN	0.31	0.19	1.06	-0.50	0.00	0.06	0.58
	SD	0.26	0.46	1.90	1.49	0.00	0.18	0.09
	MIN	0.0	-0.5	0.0	-4.0	0.0	0.0	0.4
	MAX	0.5	1.0	5.0	0.5	0.0	0.5	0.7
	N	8	8	8	8	8	8	8
4	MEAN	0.19	0.81	0.00	0.06	0.06	0.38	0.65
	SD	0.26	1.28	1.22	0.73	0.18	0.58	0.07
	MIN	0.0	0.0	-2.5	-1.5	0.0	0.0	0.5
	MAX	0.5	3.5	2.0	1.0	0.5	1.5	0.8
	N	8	8	8	8	8	8	8

APPENDIX NO. 53

(b) (4)

BODY TEMPERATURE
F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

APPENDIX NO. 53 (b) (4)

BODY TEMPERATURE (RECTAL) (Degree Celsius)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	(b) (4)								
	MEAN	38.18	38.30	38.45	38.30	38.43	38.15	38.18	38.63
	SD	0.05	0.14	0.24	0 27	0.48	0.34	0.10	0.17
	MIN	38.1	38.2	38.2	38.1	38.0	37.7	38.1	38.4
	MAX	38.2	38.5	38.7	38.7	39.1	38.5	38.3	38.8
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	38.18	38.40	38.30	38.40	38.45	38.10	38.10	38.90
	SD	0.15	0.22	0.12	0 36	0.47	0.24	0.41	0.28
	MIN	38.1	38.1	38.2	38.1	38.1	37.8	37.5	38.7
	MAX	38.4	38.6	38.4	38.9	39.1	38.4	38.4	39.3
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	38.20	38.33	38.53	38.53	38.35	38.15	38.15	38.65
	SD	0.22	0.21	0.13	0 17	0.24	0.24	0.31	0.30
	MIN	37.9	38.1	38.4	38.3	38.1	37.9	37.8	38.4
	MAX	38.4	38.5	38.7	38.7	38.6	38.4	38.5	39.0
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	38.33	38.45	38.38	38.38	38.55	38.50	38.25	38.68
	SD	0.58	0.25	0.25	0 10	0.29	0.18	0.25	0.15
	MIN	37.7	38.1	38.1	38.3	38.2	38.3	38.0	38.5
	MAX	39.1	38.7	38.7	38.5	38.9	38.7	38.6	38.8
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 53

[redacted] (b) (4)

BODY TEMPERATURE (RECTAL) (Degree Celsius)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	[redacted] (b) (4)								
	MEAN	38.15	38.43	38.30	38.28	38.53	38.40	38.35	39.00
	SD	0.25	0.21	0.12	0 26	0.22	0.12	0.42	0.39
	MIN	37.8	38.2	38.2	37.9	38.3	38.3	37.8	38.6
	MAX	38.4	38.6	38.4	38.5	38.8	38.5	38.8	39.5
	N	4	4	4	4	4	4	4	4
2	[redacted] (b) (4)								
	MEAN	38.33	38.45	38.40	38.50	38.65	38.40	38.33	38.75
	SD	0.71	0.13	0.14	0 37	0.13	0.08	0.36	0.13
	MIN	37.7	38.3	38.3	38.1	38.5	38.3	38.0	38.6
	MAX	39.2	38.6	38.6	38.9	38.8	38.5	38.8	38.9
	N	4	4	4	4	4	4	4	4
3	[redacted] (b) (4)								
	MEAN	38.28	38.25	38.33	38.43	38.35	38.28	38.25	38.75
	SD	0.32	0.38	0.17	0 19	0.17	0.13	0.33	0.44
	MIN	38.0	38.0	38.1	38.3	38.2	38.1	37.9	38.4
	MAX	38.6	38.8	38.5	38.7	38.6	38.4	38.7	39.3
	N	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)								
	MEAN	38.40	38.30	38.35	38.30	38.45	38.38	38.18	38.50
	SD	0.62	0.14	0.13	0.41	0.37	0.21	0.15	0.14
	MIN	37.9	38.2	38.2	38.0	38.0	38.1	38.0	38.3
	MAX	39.3	38.5	38.5	38.9	38.8	38.6	38.3	38.6
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 54

(b) (4)

HEART RATE
F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

APPENDIX NO. 54

(b) (4)

HEART RATE (Beats/min)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	(b) (4)								
	MEAN	181.0	173.0	160.0	154.0	145.0	131.0	148.0	128.0
	SD	2.0	14.0	10.3	5.2	19.4	16.5	32.2	9.8
	MIN	180	152	148	148	116	116	120	116
	MAX	184	180	172	160	156	152	188	140
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	201.0	186.0	177.0	152.0	158.0	146.0	144.0	141.0
	SD	24.5	16.5	13.2	15.0	31.7	27.4	37.2	27.8
	MIN	184	164	164	132	116	124	92	112
	MAX	236	204	192	168	192	184	180	172
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	169.0	188.0	148.0	135.0	135.0	128.0	117.0	127.0
	SD	8.2	6.5	15.3	11.5	15.4	8.6	17.1	19.4
	MIN	160	180	136	128	120	120	96	116
	MAX	180	196	168	152	156	140	136	156
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	165.0	149.0	162.0	132.0	129.0	131.0	119.0	124.0
	SD	31.2	20.0	6.9	24.0	12.4	3.8	15.1	11.8
	MIN	120	120	152	96	112	128	104	112
	MAX	188	164	168	144	140	136	140	140
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 54

(b) (4)

HEART RATE (Beats/min)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	(b) (4)								
	MEAN	174.0	178.0	158.0	163.0	154.0	136.0	139.0	128.0
	SD	6.9	20.3	6.9	6.0	13.7	10.8	25.2	18.8
	MIN	168	164	152	160	140	128	120	108
	MAX	184	208	168	172	172	152	176	144
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	178.0	176.0	155.0	143.0	141.0	137.0	122.0	125.0
	SD	11.5	5.7	18.6	10.0	13.2	15.4	20.0	13.2
	MIN	164	168	132	132	132	128	100	112
	MAX	192	180	172	156	160	160	148	140
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	183.0	163.0	133.0	128.0	120.0	114.0	113.0	119.0
	SD	22.9	6.8	13.2	9.2	25.5	4.0	6.0	28.9
	MIN	156	156	120	120	96	112	108	92
	MAX	204	172	148	136	144	120	120	160
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	195.0	171.0	152.0	132.0	139.0	143.0	133.0	118.0
	SD	33.4	20.0	17.3	26.5	8.2	20.5	22.9	12.4
	MIN	172	144	128	96	128	116	112	100
	MAX	244	192	168	160	148	164	160	128
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 55

(b) (4)

RESPIRATORY RATE
F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation
MIN: Minimum
MAX: Maximum
N: Number of Animals
Resp: Respiration

APPENDIX NO. 55

(b) (4)

RESPIRATORY RATE (Resp/min)
F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	(b) (4)								
	MEAN	62.0	68.0	60.0	41.0	48.0	41.0	45.0	40.0
	SD	19.2	9.8	15.7	8.9	19.0	8.9	10.5	3.3
	MIN	44	56	44	28	36	32	36	36
	MAX	88	80	80	48	76	52	56	44
	N	4	4	4	4	4	4	4	4
2	(b) (4)								
	MEAN	68.0	60.0	50.0	37.0	44.0	38.0	34.0	49.0
	SD	11.8	3.3	5.2	12.8	6.5	6.9	2.3	21.3
	MIN	56	56	44	28	36	32	32	32
	MAX	80	64	56	56	52	48	36	80
	N	4	4	4	4	4	4	4	4
3	(b) (4)								
	MEAN	69.0	61.0	52.0	39.0	37.0	36.0	36.0	38.0
	SD	14.4	8.2	8.0	3.8	6.8	3.3	6.5	10.1
	MIN	48	52	48	36	28	32	28	28
	MAX	80	72	64	44	44	40	44	52
	N	4	4	4	4	4	4	4	4
4	(b) (4)								
	MEAN	62.0	64.0	55.0	38.0	41.0	35.0	39.0	41.0
	SD	16.8	6.5	3.8	12.4	12.8	6.0	6.0	6.8
	MIN	44	56	52	28	28	28	32	32
	MAX	80	72	60	56	52	40	44	48
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 55

[redacted] (b) (4)

RESPIRATORY RATE (Resp/min)
F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	Day 63	Day 91	Day 119	Day 147	Day 175	Day 203	Day 231	Day 238
1	[redacted] (b) (4)								
	MEAN	55.0	54.0	46.0	40.0	44.0	39.0	38.0	34.0
	SD	9.5	12.4	6.9	9.2	6.5	3.8	10.1	8.3
	MIN	48	36	36	32	36	36	28	24
	MAX	68	64	52	48	52	44	52	44
	N	4	4	4	4	4	4	4	4
2	[redacted] (b) (4)								
	MEAN	63.0	60.0	44.0	38.0	49.0	34.0	35.0	39.0
	SD	8.9	9.8	7.3	10.6	12.4	5.2	8.9	6.8
	MIN	52	52	36	28	32	28	28	32
	MAX	72	72	52	52	60	40	48	48
	N	4	4	4	4	4	4	4	4
3	[redacted] (b) (4)								
	MEAN	59.0	54.0	50.0	35.0	39.0	31.0	36.0	36.0
	SD	15.4	5.2	5.2	3.8	11.5	3.8	4.6	9.8
	MIN	44	48	44	32	32	28	32	28
	MAX	76	60	56	40	56	36	40	48
	N	4	4	4	4	4	4	4	4
4	[redacted] (b) (4)								
	MEAN	75.0	57.0	54.0	40.0	42.0	49.0	50.0	38.0
	SD	14.0	5.0	13.3	10.8	10.6	7.6	10.1	7.7
	MIN	60	52	44	32	32	44	36	32
	MAX	92	64	72	56	56	60	60	48
	N	4	4	4	4	4	4	4	4

APPENDIX NO. 56 (b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations and footnote have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum

MIN: Minimum

U: Unscheduled

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
	(b) (4)									
1		Day 56	5.64	126	0.41	71.9	22.4	312	13.2	290
		Day 112	6.30	139	0.43	67.9	22.0	324	12.9	277
		Day 168	7.02	157	0.49	69.3	22.4	323	12.7	229
		Day 224	7.58	171	0.52	69.2	22.6	327	14.2	247
		Day 56	5.22	115	0.37	71.8	22.0	306	13.8	475
		Day 112	6.27	140	0.43	68.8	22.3	324	13.7	451
		Day 168	6.31	146	0.44	69.5	23.2	334	13.3	339
		Day 224	6.37	145	0.44	69.5	22.7	327	14.4	324
		Day 56	5.25	117	0.37	70.8	22.3	315	13.9	309
		Day 112	5.82	134	0.41	69.8	22.9	329	13.9	318
		Day 168	5.68	135	0.41	71.5	23.8	333	12.4	268
		Day 224	6.94	166	0.49	71.2	24.0	337	13.1	202
		Day 56	5.26	114	0.36	68.9	21.6	314	14.3	342
		Day 112	5.87	130	0.40	68.8	22.1	321	13.2	347
		Day 168	6.59	151	0.46	69.7	22.9	328	12.3	224
		Day 224	7.36	168	0.50	68.6	22.8	332	13.2	230
2		Day 56	5.99	127	0.41	67.8	21.3	313	14.1	329
		Day 112	6.25	133	0.41	65.1	21.3	328	13.1	274
		Day 168	6.85	152	0.46	67.2	22.2	330	13.0	296
		Day 224	7.64	171	0.51	66.7	22.4	335	12.9	229
		Day 56	5.54	118	0.38	68.0	21.4	314	14.3	269
		Day 112	5.79	128	0.40	69.0	22.1	321	13.6	254
		Day 168	6.39	149	0.44	68.7	23.2	338	12.4	240
		Day 224	6.84	158	0.48	69.9	23.0	329	13.8	184
		Day 56	5.30	106	0.35	65.9	19.9	302	17.1	386
		Day 112	5.58	113	0.36	64.1	20.3	317	14.8	367
		Day 168	6.19	132	0.40	64.9	21.3	329	13.9	322
		Day 224	6.89	149	0.45	65.3	21.6	331	14.1	266
		Day 56	5.72	120	0.38	66.9	21.0	313	15.3	311
		Day 112	6.46	140	0.43	66.4	21.7	327	13.1	288
		Day 168	7.28	162	0.49	67.8	22.2	328	12.3	238
		Day 224	7.97	175	0.54	67.7	21.9	324	13.5	219

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
3	(b) (4)	Day 56	5.37	114	0.36	67.9	21.3	313	13.8	354
		Day 112	6.18	134	0.41	66.8	21.6	324	12.8	330
		Day 168	6.31	141	0.42	66.4	22.3	336	12.4	229
		Day 224	6.55	146	0.43	66.1	22.3	337	13.5	245
		Day 56	4.65	106	0.33	71.0	22.8	321	13.4	328
		Day 112	5.88	135	0.42	71.4	23.0	322	13.0	397
		Day 168	6.50	155	0.46	70.7	23.8	336	12.5	342
		Day 224	6.86	162	0.49	71.1	23.6	332	13.6	294
		Day 56	5.23	115	0.37	71.1	22.0	310	13.2	252
		Day 112	5.71	126	0.39	67.8	22.1	326	12.5	258
		Day 168	6.97	157	0.48	68.7	22.5	327	12.2	228
		Day 224	7.07	159	0.49	69.5	22.6	324	12.0	189
		Day 56	5.56	121	0.39	70.7	21.7	307	14.3	391
		Day 112	5.90	130	0.40	67.0	22.1	329	13.1	292
		Day 168	6.29	143	0.43	68.5	22.7	331	13.1	278
		Day 224	6.86	157	0.47	68.1	22.9	336	12.6	211
4		Day 56	5.07	104	0.35	69.1	20.4	295	14.7	384
		Day 112	6.18	131	0.41	66.2	21.2	321	13.3	393
		Day 168	5.84	135	0.40	68.6	23.2	338	12.5	311
		Day 224	7.31	170	0.51	69.4	23.2	335	12.2	268
		Day 56	4.76	106	0.34	70.5	22.2	314	12.7	363
		Day 112	5.54	122	0.38	67.7	22.1	326	12.4	398
		Day 168	5.57	126	0.39	69.2	22.5	326	12.1	300
		Day 224	6.31	147	0.44	69.6	23.3	336	12.3	259
		Day 56	5.49	121	0.38	69.4	22.0	317	13.5	429
		Day 112	6.33	141	0.43	68.6	22.2	324	13.0	382
		Day 168	7.30	164	0.51	69.4	22.5	324	12.2	267
		Day 224	7.56	174	0.53	69.6	23.0	331	13.3	253
		Day 56 (Unscheduled)	5.29U	110U	0.35U	65.5U	20.7U	316U	15.2U	360U
		Day 112	5.88	126	0.38	65.4	21.4	328	13.5	340
		Day 168	6.42	146	0.43	67.4	22.7	337	13.6	329
		Day 224	7.07	161	0.48	68.5	22.7	332	14.2	243

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	(b) (4)	Day 56	11.94	6.77	4.35	0 59	0.14	0.05	0.05
		Day 112	11.33	5.81	4.77	0.47	0.19	0.05	0.05
		Day 168	9.69	5.21	3.63	0.47	0.21	0.08	0.08
		Day 224	10.28	6.25	3.28	0.43	0.16	0.10	0.07
		Day 56	10.04	4.78	4.14	0.65	0.29	0.07	0.11
		Day 112	10.61	5.33	4.22	0.60	0.37	0.04	0.05
		Day 168	8.01	4.09	2.98	0 59	0.26	0.05	0.04
		Day 224	9.59	5.87	2.91	0.44	0.26	0.07	0.03
		Day 56	10.36	4.99	4.65	0.42	0.16	0.06	0.08
		Day 112	8.27	4.15	3.41	0 37	0.29	0.02	0.02
		Day 168	9.04	4.57	3.31	0 54	0.57	0.03	0.02
		Day 224	6.78	3.37	2.63	0 26	0.45	0.05	0.02
		Day 56	12.06	6.38	4.65	0.77	0.17	0.04	0.05
		Day 112	12.44	6.34	4.84	0.70	0.48	0.04	0.05
		Day 168	9.65	4.97	3.59	0 55	0.49	0.03	0.02
		Day 224	8.76	4.67	3.10	0 38	0.54	0.05	0.02
2		Day 56	11.37	5.61	5.00	0 38	0.23	0.06	0.08
		Day 112	11.07	6.00	4.16	0 55	0.22	0.06	0.08
		Day 168	13.23	8.55	3.37	0.87	0.24	0.10	0.11
		Day 224	10.78	6.27	3.65	0.42	0.31	0.06	0.07
		Day 56	11.09	6.23	4.05	0 54	0.16	0.05	0.06
		Day 112	11.46	6.95	3.67	0 52	0.24	0.05	0.04
		Day 168	9.58	5.46	3.37	0.43	0.25	0.04	0.03
		Day 224	9.44	6.02	2.61	0.41	0.31	0.06	0.03
		Day 56	9.63	3.75	4.95	0 54	0.29	0.04	0.06
		Day 112	9.91	5.12	3.64	0.70	0.34	0.04	0.08
		Day 168	10.71	5.97	3.69	0.67	0.29	0.04	0.04
		Day 224	8.68	4.58	3.31	0.43	0.29	0.05	0.02
		Day 56	12.99	7.11	4.98	0.61	0.20	0.04	0.05
		Day 112	14.20	7.60	5.55	0 59	0.29	0.09	0.07
		Day 168	9.72	4.91	3.94	0 50	0.28	0.06	0.03
		Day 224	10.75	6.22	3.57	0.43	0.40	0.07	0.05

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
3	(b) (4)	Day 56	8.70	3.93	4.02	0.46	0.22	0.03	0.04
		Day 112	8.91	5.07	3.08	0 50	0.21	0.04	0.02
		Day 168	7.54	3.68	2.95	0 55	0.25	0.06	0.05
		Day 224	6.66	3.74	2.20	0 36	0.28	0.05	0.02
		Day 56	11.58	5.92	4.82	0 54	0.18	0.05	0.07
		Day 112	14.05	7.28	5.31	0 90	0.37	0.10	0.09
		Day 168	12.12	6.54	4.44	0.61	0.32	0.10	0.09
		Day 224	13.88	8.67	3.99	0.61	0.42	0.15	0.04
		Day 56	10.57	5.14	4.62	0 39	0.33	0.04	0.05
		Day 112	11.28	6.32	3.91	0 59	0.36	0.05	0.05
		Day 168	9.44	4.63	3.83	0.46	0.41	0.05	0.07
		Day 224	9.40	5.22	3.14	0 51	0.44	0.04	0.05
		Day 56	16.33	10.07	4.99	0 92	0.22	0.05	0.08
		Day 112	9.18	4.77	3.77	0 36	0.23	0.02	0.03
		Day 168	10.08	5.88	3.32	0.49	0.29	0.05	0.04
		Day 224	10.55	6.13	3.60	0.48	0.26	0.05	0.03
4		Day 56	10.73	4.91	4.73	0.75	0.26	0.05	0.04
		Day 112	9.76	4.26	4.79	0.47	0.15	0.05	0.03
		Day 168	7.58	3.66	3.24	0.44	0.17	0.04	0.03
		Day 224	8.06	4.14	3.25	0.41	0.20	0.04	0.03
		Day 56	9.79	5.33	3.64	0 55	0.21	0.03	0.05
		Day 112	13.12	7.71	4.29	0.69	0.32	0.06	0.05
		Day 168	9.39	5.11	3.39	0 51	0.30	0.03	0.04
		Day 224	10.06	6.08	3.11	0 53	0.29	0.02	0.03
		Day 56	13.15	6.48	5.23	0 96	0.35	0.05	0.08
		Day 112	14.18	6.98	5.79	0.88	0.39	0.07	0.07
		Day 168	9.73	4.83	3.78	0 56	0.45	0.07	0.05
		Day 224	9.32	5.19	3.13	0 50	0.40	0.07	0.03
		Day 56 (Unscheduled)	9.19U	4.35U	4.03U	0.50U	0.22U	0.04U	0.04U
		Day 112	11.02	5.54	4.64	0.46	0.26	0.06	0.06
		Day 168	6.68	2.87	3.34	0 28	0.12	0.04	0.03
		Day 224	9.84	5.61	3.34	0 55	0.24	0.08	0.02

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	(b) (4)	Day 56	56.7	36.4	4.9	1.2	0.4	0.4	148.2	2.6
		Day 112	51.3	42.1	4.1	1.7	0.4	0.4	121.0	1.9
		Day 168	53.8	37.5	4.9	2.2	0.8	0.8	137.1	2.0
		Day 224	60.8	31.9	4.2	1.5	1.0	0.6	83.8	1.1
		Day 56	47.6	41.2	6.5	2.9	0.7	1 1	201.0	3.9
		Day 112	50.2	39.8	5.6	3.5	0.4	0 5	112.2	1.8
		Day 168	51.0	37.2	7.4	3.2	0.7	0 5	62.0	1.0
		Day 224	61.3	30.3	4.6	2.7	0.8	0 3	37.6	0.6
		Day 56	48.2	44.9	4.1	1.5	0.5	0.8	167.4	3.2
		Day 112	50.2	41.2	4.5	3.5	0.3	0 3	137.7	2.4
		Day 168	50.5	36.7	6.0	6.3	0.3	0 2	57.5	1.0
		Day 224	49.7	38.9	3.8	6.6	0.8	0 2	38.3	0.6
		Day 56	52.9	38.5	6.4	1.4	0.3	0 5	152.6	2.9
		Day 112	51.0	38.9	5.6	3.8	0.3	0.4	85.1	1.5
		Day 168	51.5	37.2	5.7	5.1	0.3	0 2	75.7	1.1
		Day 224	53.3	35.3	4.3	6.2	0.6	0 2	29.0	0.4
2		Day 56	49.4	44.0	3.4	2.0	0.5	0.7	176.5	2.9
		Day 112	54.2	37.5	5.0	2.0	0.6	0.7	80.7	1.3
		Day 168	64.6	25.5	6.6	1.8	0.7	0.8	77.1	1.1
		Day 224	58.1	33.9	3.9	2.9	0.6	0.6	52.3	0.7
		Day 56	56.1	36.5	4.8	1.5	0.5	0.6	105.8	1.9
		Day 112	60.6	32.0	4.5	2.1	0.4	0 3	86.4	1.5
		Day 168	56.9	35.2	4.5	2.6	0.4	0 3	65.7	1.0
		Day 224	63.7	27.6	4.4	3.3	0.7	0 3	42.0	0.6
		Day 56	38.9	51.4	5.6	3.0	0.4	0.6	183.5	3.5
		Day 112	51.6	36.8	7.0	3.5	0.4	0.8	95.3	1.7
		Day 168	55.7	34.5	6.3	2.7	0.4	0.4	83.9	1.4
		Day 224	52.8	38.1	5.0	3.3	0.6	0 3	59.7	0.9
		Day 56	54.7	38.3	4.7	1.5	0.3	0.4	156.2	2.7
		Day 112	53.5	39.1	4.2	2.1	0.7	0 5	97.5	1.5
		Day 168	50.5	40.5	5.2	2.9	0.6	0 3	64.0	0.9
		Day 224	57.9	33.2	4.0	3.7	0.7	0.4	51.9	0.7

APPENDIX NO. 56

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
3	(b) (4)	Day 56	45.1	46.2	5.3	2.5	0.4	0 5	158.7	3.0
		Day 112	56.9	34.6	5.6	2.3	0.4	0 2	81.6	1.3
		Day 168	48.8	39.1	7.3	3.3	0.8	0.6	47.5	0.8
		Day 224	56.2	33.1	5.4	4.2	0.8	0 3	25.4	0.4
		Day 56	51.1	41.6	4.7	1.5	0.5	0.6	98.9	2.1
		Day 112	51.8	37.8	6.4	2.6	0.7	0.6	124.6	2.1
		Day 168	54.0	36.7	5.1	2.7	0.8	0.8	69.9	1.1
		Day 224	62.5	28.8	4.4	3.0	1.1	0 3	47.1	0.7
		Day 56	48.6	43.7	3.7	3.1	0.4	0 5	117.7	2.2
		Day 112	56.0	34.7	5.3	3.2	0.4	0 5	63.8	1.1
		Day 168	49.0	40.5	4.8	4.3	0.5	0.8	54.2	0.8
		Day 224	55.5	33.4	5.5	4.7	0.4	0 5	49.7	0.7
		Day 56	61.7	30.6	5.6	1.3	0.3	0 5	145.5	2.6
		Day 112	52.0	41.1	3.9	2.5	0.3	0 3	75.0	1.3
		Day 168	58.3	33.0	4.8	2.9	0.5	0.4	78.7	1.3
		Day 224	58.1	34.2	4.5	2.5	0.5	0 3	41.9	0.6
4		Day 56	45.7	44.0	7.0	2.5	0.4	0.4	125.0	2.5
		Day 112	43.7	49.0	4.8	1.6	0.6	0 3	38.9	0.6
		Day 168	48.3	42.8	5.8	2.2	0.5	0.4	34.4	0.6
		Day 224	51.3	40.3	5.0	2.5	0.5	0 3	45.7	0.6
		Day 56	54.4	37.2	5.6	2.1	0.3	0 5	94.6	2.0
		Day 112	58.8	32.7	5.2	2.4	0.4	0.4	73.5	1.3
		Day 168	54.4	36.1	5.5	3.2	0.3	0 5	56.7	1.0
		Day 224	60.4	30.9	5.3	2.9	0.2	0 3	37.5	0.6
		Day 56	49.3	39.7	7.3	2.7	0.4	0.6	135.3	2.5
		Day 112	49.3	40.8	6.2	2.7	0.5	0 5	101.3	1.6
		Day 168	49.6	38.8	5.7	4.6	0.8	0 5	78.3	1.1
		Day 224	55.7	33.6	5.4	4.3	0.8	0 3	65.0	0.9
		Day 56 (Unscheduled)	47.3U	43.9U	5.5U	2.4U	0.4U	0.5U	110.4U	2.1U
		Day 112	50.3	42.1	4.2	2.4	0.5	0 5	71.0	1.2
		Day 168	43.0	50.1	4.3	1.7	0.5	0.4	61.8	1.0
		Day 224	57.0	33.9	5.6	2.4	0.8	0 2	22.6	0.3

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
1	(b) (4)	Day 56	5.65	127	0.41	72.2	22.4	310	12.7	211
		Day 112	7.06	154	0.48	68.4	21.9	320	12.8	304
		Day 168	7 53	171	0.52	69.2	22.7	328	13.1	246
		Day 224	8 25	190	0.58	69.9	23.1	330	14.0	172
		Day 56	5.46	124	0.39	71.7	22.7	316	13.6	282
		Day 112	6.65	152	0.46	68.8	22.8	331	13.1	290
		Day 168	7 36	166	0.52	70.4	22.6	321	13.2	224
		Day 224	7.66	183	0.54	70.4	23.9	340	14.0	185
		Day 56	5 35	119	0.38	71.7	22.3	311	13.8	218
		Day 112	6 15	142	0.43	69.6	23.2	333	13.5	245
		Day 168	6.03	145	0.43	71.2	23.9	337	11.7	217
		Day 224	7 59	182	0.54	71.2	24.0	337	12.9	217
		Day 56	5.62	123	0.39	69.7	21.8	313	12.7	239
		Day 112	6.09	135	0.42	68.6	22.2	324	13.6	355
		Day 168	6.78	154	0.47	69.4	22.8	328	12.4	212
		Day 224	7.07	161	0.49	69.6	22.8	328	13.3	174
2		Day 56	5 91	134	0.42	71.6	22.7	317	13.2	427
		Day 112	6 59	150	0.45	68.7	22.8	331	13.1	328
		Day 168	7.00	160	0.49	70.2	22.9	326	12.9	258
		Day 224	7.49	175	0.53	70.5	23.4	331	12.7	273
		Day 56	5 97	118	0.39	65.5	19.7	301	17.0	264
		Day 112	6.40	139	0.43	67.1	21.7	323	15.0	218
		Day 168	6 94	160	0.48	68.6	23.1	337	12.7	200
		Day 224	7.09	161	0.49	69.0	22.7	329	14.1	165
		Day 56	5 36	115	0.38	70.8	21.5	304	14.8	368
		Day 112	6.45	144	0.45	70.4	22.3	317	13.2	PLT4+
		Day 168	7.63	168	0.52	68.3	22.1	323	13.1	274
		Day 224	7.73	172	0.53	67.9	22.2	327	14.1	212
		Day 56	6 21	128	0.42	67.6	20.6	305	14.4	383
		Day 112	6.66	145	0.45	67.1	21.7	324	13.4	322
		Day 168	7 15	159	0.49	68.8	22.3	324	12.4	212
		Day 224	7.79	177	0.53	68.2	22.7	333	13.4	229

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		RBC (x10^12/L)	HGB (g/L)	HCT (L/L)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW (%)	PLT (x10^9/L)
3	(b) (4)	Day 56	5.46	116	0.37	68.3	21.2	310	13.2	413
		Day 112	6.00	130	0.40	67.2	21.6	321	12.5	381
		Day 168	6 28	140	0.42	67.1	22.3	333	11.9	268
		Day 224	6.66	148	0.45	68.2	22.2	326	13.4	243
		Day 56	5.49	119	0.38	68.7	21.7	316	12.6	281
		Day 112	6 12	135	0.41	67.6	22.1	326	12.8	322
		Day 168	6.75	152	0.46	67.6	22.6	334	12.3	229
		Day 224	7.02	160	0.48	68.2	22.8	334	13.5	204
		Day 56	5 11	113	0.36	70.7	22.2	314	12.7	313
		Day 112	5.66	126	0.38	67.7	22.2	328	12.4	324
		Day 168	6.61	149	0.45	68.8	22.6	328	12.6	229
		Day 224	7 39	172	0.52	70.2	23.2	331	12.0	201
		Day 56	5.70	128	0.41	71.8	22.5	314	13.0	332
		Day 112	5 94	138	0.42	70.2	23.3	333	12.9	252
		Day 168	6.75	157	0.47	70.3	23.3	332	12.9	198
		Day 224	7 21	173	0.51	70.3	24.0	341	12.5	210
4		Day 56	5 33	114	0.38	71.0	21.4	301	13.6	322
		Day 112	6.01	129	0.40	66.2	21.5	325	12.7	300
		Day 168	7 17	158	0.48	66.9	22.0	330	12.8	278
		Day 224	7.62	174	0.52	68.0	22.8	335	13.1	223
		Day 56	5.06	113	0.36	72.1	22.4	310	13.1	423
		Day 112	5.84	133	0.41	70.0	22.8	325	13.1	350
		Day 168	6 54	152	0.46	70.7	23.3	329	12.2	253
		Day 224	6.86	163	0.49	71.2	23.8	334	12.3	222
		Day 56	5 18	115	0.37	71.6	22.2	310	13.1	456
		Day 112	5.60	126	0.39	69.0	22.5	325	13.2	389
		Day 168	6.41	148	0.45	69.7	23.2	332	12.1	286
		Day 224	6.73	154	0.47	70.5	22.9	326	13.3	272
		Day 56	5 50	108	0.37	67.3	19.7	293	16.9	393
		Day 112	5.63	116	0.36	63.7	20.7	324	13.9	316
		Day 168	6 34	136	0.41	65.3	21.5	329	12.7	249
		Day 224	7 31	157	0.48	65.8	21.5	327	13.9	230

APPENDIX NO. 56 (b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
1	(b) (4)	Day 56	11.23	6.96	3.37	0.71	0.10	0.04	0.06
		Day 112	13.30	7.05	5.17	0.73	0.23	0.07	0.05
		Day 168	10.15	5.70	3.73	0.47	0.15	0.05	0.05
		Day 224	7.24	4.07	2.47	0.38	0.23	0.06	0.02
		Day 56	8.30	4.03	3.54	0.50	0.11	0.06	0.06
		Day 112	9.35	4.01	4.43	0.63	0.20	0.05	0.04
		Day 168	8.56	3.87	3.65	0.67	0.28	0.05	0.04
		Day 224	8.09	4.03	3.09	0.51	0.33	0.10	0.04
		Day 56	8.63	3.97	3.90	0.40	0.27	0.03	0.05
		Day 112	10.41	4.33	5.12	0.48	0.40	0.05	0.04
		Day 168	8.17	3.47	3.81	0.35	0.47	0.03	0.04
		Day 224	10.64	5.00	4.37	0.73	0.37	0.11	0.06
		Day 56	9.80	5.98	2.67	0.86	0.14	0.04	0.11
		Day 112	12.40	6.93	4.33	0.58	0.47	0.05	0.05
		Day 168	9.86	5.25	3.60	0.51	0.40	0.06	0.05
		Day 224	10.47	6.05	3.25	0.72	0.28	0.10	0.07
2		Day 56	10.07	5.34	3.69	0.46	0.47	0.06	0.06
		Day 112	11.52	5.55	4.86	0.55	0.39	0.10	0.08
		Day 168	8.32	3.80	3.80	0.31	0.30	0.04	0.06
		Day 224	9.15	4.46	3.84	0.41	0.35	0.04	0.04
		Day 56	10.21	5.00	4.49	0.53	0.12	0.03	0.03
		Day 112	11.58	6.25	4.44	0.53	0.23	0.07	0.05
		Day 168	10.63	4.93	4.83	0.47	0.26	0.08	0.06
		Day 224	9.89	5.37	3.67	0.35	0.35	0.11	0.04
		Day 56	10.20	4.81	4.39	0.75	0.14	0.05	0.05
		Day 112	13.35	7.28	4.88	0.90	0.17	0.07	0.06
		Day 168	11.83	6.67	4.12	0.73	0.19	0.07	0.06
		Day 224	9.78	5.70	3.17	0.57	0.20	0.11	0.03
		Day 56	10.80	5.61	4.37	0.59	0.15	0.04	0.04
		Day 112	9.23	5.42	3.01	0.58	0.15	0.03	0.03
		Day 168	9.67	5.31	3.52	0.56	0.20	0.04	0.04
		Day 224	9.45	5.31	3.42	0.38	0.20	0.09	0.04

APPENDIX NO. 56

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		WBC (x10^9/L)	NEUT (x10^9/L)	LYMPH (x10^9/L)	MONO (x10^9/L)	EOS (x10^9/L)	BASO (x10^9/L)	LUC (x10^9/L)
3	(b) (4)	Day 56	8.49	3.66	4.07	0.46	0.23	0.02	0.05
		Day 112	9.74	4.81	4.24	0.46	0.15	0.03	0.03
		Day 168	9.29	5.00	3.53	0.50	0.15	0.06	0.04
		Day 224	6.15	3.09	2.58	0.28	0.14	0.04	0.02
		Day 56	8.49	3.72	4.07	0.45	0.17	0.04	0.05
		Day 112	10.55	5.17	4.40	0.70	0.19	0.06	0.04
		Day 168	14.39	8.64	4.32	1.11	0.18	0.08	0.07
		Day 224	8.39	4.68	3.02	0.36	0.16	0.12	0.04
		Day 56	11.92	7.31	3.49	0.72	0.31	0.03	0.06
		Day 112	8.79	5.21	2.97	0.39	0.17	0.03	0.02
		Day 168	7.98	4.25	3.00	0.44	0.23	0.03	0.03
		Day 224	8.10	4.18	3.32	0.36	0.18	0.04	0.02
		Day 56	12.83	7.15	4.73	0.57	0.29	0.03	0.05
		Day 112	13.13	8.71	3.17	0.85	0.30	0.04	0.06
		Day 168	7.68	4.31	2.66	0.45	0.19	0.04	0.02
		Day 224	7.12	4.02	2.23	0.31	0.49	0.04	0.04
4		Day 56	8.74	3.74	4.23	0.51	0.15	0.04	0.06
		Day 112	8.77	4.68	3.38	0.38	0.27	0.04	0.03
		Day 168	7.41	3.49	3.25	0.42	0.19	0.04	0.03
		Day 224	6.80	2.99	3.23	0.39	0.14	0.03	0.02
		Day 56	9.12	4.44	4.04	0.41	0.14	0.03	0.05
		Day 112	10.20	5.41	4.05	0.50	0.15	0.05	0.04
		Day 168	8.35	3.91	3.61	0.48	0.27	0.05	0.03
		Day 224	7.88	3.95	3.28	0.39	0.20	0.04	0.02
		Day 56	12.26	7.29	3.87	0.88	0.11	0.04	0.07
		Day 112	11.84	6.55	4.31	0.63	0.22	0.06	0.06
		Day 168	9.24	4.64	3.80	0.50	0.18	0.07	0.05
		Day 224	9.29	5.46	3.15	0.42	0.14	0.08	0.04
		Day 56	15.44	7.39	6.94	0.77	0.19	0.08	0.07
		Day 112	12.33	6.04	5.45	0.50	0.24	0.05	0.06
		Day 168	9.26	4.38	4.11	0.53	0.15	0.03	0.06
		Day 224	8.57	4.36	3.50	0.46	0.15	0.08	0.03

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
1	(b) (4)	Day 56	61.9	30.0	6.3	0.9	0.4	0.5	187.8	3.3
		Day 112	53.0	38.9	5.5	1.7	0.5	0.4	170.0	2.4
		Day 168	56.1	36.7	4.6	1.5	0.4	0.5	170.5	2.3
		Day 224	56.2	34.2	5.3	3.2	0.9	0.3	106.1	1.3
		Day 56	48.5	42.6	6.0	1.4	0.7	0.7	163.1	3.0
		Day 112	42.9	47.4	6.7	2.2	0.5	0.4	97.1	1.5
		Day 168	45.2	42.7	7.8	3.3	0.6	0.5	81.4	1.1
		Day 224	49.8	38.1	6.3	4.0	1.3	0.4	80.7	1.1
		Day 56	46.0	45.2	4.7	3.1	0.3	0.6	219.3	4.1
		Day 112	41.6	49.2	4.6	3.8	0.5	0.3	130.9	2.1
		Day 168	42.4	46.6	4.3	5.8	0.4	0.5	49.2	0.8
		Day 224	47.0	41.1	6.9	3.5	1.0	0.6	76.9	1.0
		Day 56	61.0	27.3	8.8	1.4	0.4	1.2	107.6	1.9
		Day 112	55.9	34.9	4.7	3.8	0.4	0.4	84.9	1.4
		Day 168	53.2	36.5	5.2	4.0	0.6	0.5	40.6	0.6
		Day 224	57.8	31.1	6.8	2.7	1.0	0.6	36.2	0.5
2		Day 56	53.0	36.7	4.6	4.6	0.6	0.6	143.0	2.4
		Day 112	48.2	42.2	4.7	3.4	0.9	0.7	90.8	1.4
		Day 168	45.7	45.7	3.7	3.6	0.5	0.7	71.0	1.0
		Day 224	48.8	42.0	4.4	3.8	0.5	0.5	49.0	0.7
		Day 56	49.0	44.0	5.2	1.2	0.3	0.3	167.8	2.8
		Day 112	54.0	38.4	4.6	2.0	0.6	0.4	91.2	1.4
		Day 168	46.4	45.4	4.4	2.4	0.7	0.6	42.1	0.6
		Day 224	54.4	37.1	3.5	3.5	1.1	0.4	38.9	0.5
		Day 56	47.2	43.0	7.4	1.4	0.5	0.5	137.1	2.6
		Day 112	54.5	36.6	6.7	1.3	0.5	0.4	130.1	2.0
		Day 168	56.4	34.8	6.1	1.6	0.6	0.5	110.4	1.4
		Day 224	58.3	32.4	5.8	2.1	1.1	0.3	98.9	1.3
		Day 56	51.9	40.5	5.5	1.4	0.4	0.3	246.8	4.0
		Day 112	58.7	32.7	6.3	1.6	0.3	0.3	95.8	1.4
		Day 168	54.9	36.4	5.7	2.0	0.4	0.4	62.2	0.9
		Day 224	56.2	36.2	4.1	2.1	1.0	0.4	68.7	0.9

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		NEUT (%)	LYMPH (%)	MONO (%)	EOS (%)	BASO (%)	LUC (%)	RETIC (x10^9/L)	RETIC (%)
3	(b) (4)	Day 56	43.1	48.0	5.4	2.7	0.3	0.5	143.4	2.6
		Day 112	49.4	43.6	4.8	1.6	0.4	0.3	89.8	1.5
		Day 168	53.9	38.0	5.4	1.7	0.6	0.5	48.0	0.8
		Day 224	50.3	41.9	4.5	2.4	0.7	0.3	70.3	1.1
		Day 56	43.8	48.0	5.3	2.0	0.5	0.5	78.1	1.4
		Day 112	48.9	41.7	6.6	1.8	0.5	0.4	61.2	1.0
		Day 168	60.0	30.0	7.7	1.2	0.5	0.5	70.1	1.0
		Day 224	55.8	36.0	4.3	1.9	1.4	0.5	27.5	0.4
		Day 56	61.3	29.3	6.0	2.6	0.3	0.5	101.2	2.0
		Day 112	59.3	33.8	4.4	1.9	0.3	0.2	52.9	0.9
		Day 168	53.3	37.5	5.5	2.9	0.4	0.4	46.6	0.7
		Day 224	51.6	41.0	4.4	2.3	0.5	0.3	42.4	0.6
		Day 56	55.8	36.8	4.5	2.3	0.3	0.4	102.3	1.8
		Day 112	66.3	24.2	6.5	2.3	0.3	0.4	80.1	1.3
		Day 168	56.1	34.7	5.9	2.5	0.5	0.3	83.2	1.2
		Day 224	56.4	31.3	4.4	6.9	0.6	0.5	38.0	0.5
4		Day 56	42.8	48.4	5.8	1.8	0.4	0.7	135.9	2.6
		Day 112	53.3	38.6	4.3	3.0	0.4	0.3	54.3	0.9
		Day 168	47.1	43.9	5.7	2.5	0.5	0.4	45.5	0.6
		Day 224	43.9	47.5	5.7	2.1	0.5	0.3	68.0	0.9
		Day 56	48.7	44.3	4.5	1.5	0.4	0.5	92.8	1.8
		Day 112	53.0	39.7	4.9	1.5	0.5	0.4	108.3	1.9
		Day 168	46.8	43.2	5.7	3.3	0.6	0.4	68.3	1.0
		Day 224	50.1	41.6	5.0	2.5	0.5	0.3	41.4	0.6
		Day 56	59.5	31.6	7.1	0.9	0.3	0.6	113.9	2.2
		Day 112	55.4	36.5	5.3	1.9	0.5	0.5	39.4	0.7
		Day 168	50.2	41.1	5.4	2.0	0.7	0.6	33.0	0.5
		Day 224	58.7	34.0	4.5	1.5	0.9	0.4	25.6	0.4
		Day 56	47.9	44.9	5.0	1.2	0.5	0.5	241.8	4.4
		Day 112	49.0	44.2	4.0	1.9	0.4	0.5	69.4	1.2
		Day 168	47.3	44.4	5.7	1.6	0.4	0.6	39.2	0.6
		Day 224	50.9	40.8	5.3	1.7	0.9	0.4	43.4	0.6

APPENDIX NO. 56 (b) (4)

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
1	(b) (4)	Anisocytosis 1+, Platelet Clumps 1+
		Anisocytosis 1+, Polychromasia 1+
		Morphology N
		Anisocytosis 1+
2		Anisocytosis 1+, Large Platelets 1+
		Anisocytosis 1+, Polychromasia 1+
		Anisocytosis 1+, Polychromasia 1+
3		Anisocytosis 1+, Platelet Clumps 1+, Polychromasia 1+
		Anisocytosis 1+, Platelet Clumps 1+
		Hypochromia 1+
		Anisocytosis 1+
4		Anisocytosis 1+, Platelet Clumps 1+

APPENDIX NO. 56

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56 (UNSCHEDULED)
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
4	(b) (4)	Anisocytosis 1+U, Hypochromia 1+U

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
2	(b) (4)	Anisocytosis 1+, Large Platelets 1+
		Anisocytosis 1+

APPENDIX NO. 56 (b) (4)

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 168
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
1	(b) (4)	Morphology N
2		Anisocytosis 1+, Large Platelets 1+
4		Anisocytosis 1+, Large Platelets 1+, Polychromasia 1+

APPENDIX NO. 56 (b) (4)

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
3	(b) (4)	Platelet Clumps 1+
		Platelet Clumps 1+

APPENDIX NO. 56 (b) (4)

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 56
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
1	(b) (4)	Anisocytosis 1+, Polychromasia 1+ Morphology N Anisocytosis 1+, Hypochromia 1+, Polychromasia 1+ Anisocytosis 1+, Platelet Clumps 1+
2		Anisocytosis 1+, Hypochromia 1+, Platelet Clumps 1+, Polychromasia 1+ Anisocytosis 1+, Polychromasia 1+ Hypochromia 1+, Platelet Clumps 2+, Polychromasia 1+
3		Anisocytosis 1+ Anisocytosis 1+, Platelet Clumps 3+
4		Anisocytosis 1+, Polychromasia 1+ Morphology N Anisocytosis 1+, Hypochromia 1+, Polychromasia 1+

APPENDIX NO. 56

(b) (4)

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 112
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
2	(b) (4)	Anisocytosis 1+, Large Platelets 1+, Platelet Clumps 3+ Anisocytosis 1+, Platelet Clumps 4+

APPENDIX NO. 56 (b) (4)

HEMATOLOGY - MORPHOLOGY - F1 GENERATION - PUPPIES - POST WEANING
DAY 224
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	
2	(b) (4)	Echinocytes 1+, Platelet Clumps 2+

APPENDIX NO. 57

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations and footnote have been used throughout the appendix and/or summary table

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

NA: Not Applicable

<: Below the lower limit of quantification or Calculated using a measurement below the lower limit of quantification

APPENDIX NO. 57

(b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		APPS	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	(b) (4)	Day 56		28	26	211	< 2.2	5.40	0.44	7.1	3.1	25
		Day 112		30	25	156	< 2.2	6.57	0.42	6.4	4.2	29
		Day 168		25	29	129	< 2.2	7.02	0.32	6.5	4.4	45
		Day 224		29	32	110	< 2.2	6.65	0.31	6.2	4.4	48
		Day 56		28	31	422	< 2.2	4.72	0.30	7.3	3.1	21
		Day 112		28	30	378	< 2.2	6.03	0.38	6.0	4.5	32
		Day 168		23	32	285	< 2.2	6.22	0.32	6.1	5.8	42
		Day 224		28	39	201	< 2.2	6.13	0.30	5.6	5.7	49
		Day 56	HE1	25	24	213	< 2.2	4.51	0.45	7.3	2.8	22
		Day 112	HE1	28	30	142	< 2.2	6.63	0.40	6.0	3.3	30
		Day 168		25	37	107	< 2.2	6.06	0.36	6.1	3.9	41
		Day 224	HE1	28	41	79	< 2.2	6.29	0.39	5.3	4.6	50
		Day 56		29	28	114	< 2.2	4.39	0.65	6.9	4.1	26
		Day 112		30	27	121	< 2.2	5.49	0.39	6.5	3.8	30
		Day 168		29	38	89	< 2.2	6.00	0.42	6.4	5.0	46
		Day 224		27	37	65	< 2.2	5.79	0.47	5.6	5.7	58
2		Day 56		34	26	203	< 2.2	4.91	0.59	6.8	4.8	37
		Day 112		26	25	182	< 2.2	6.46	0.35	6.4	4.6	33
		Day 168		26	23	152	< 2.2	6.27	0.48	5.6	4.4	43
		Day 224		28	25	111	< 2.2	5.37	0.39	5.7	5.8	53
		Day 56		29	34	275	< 2.2	5.16	0.55	5.8	4.9	29
		Day 112		28	25	227	< 2.2	7.57	0.38	5.7	4.7	37
		Day 168		28	41	162	< 2.2	7.36	0.44	5.3	4.7	51
		Day 224	HE1	30	36	115	< 2.2	7.20	0.44	5.1	5.9	59
		Day 56		31	26	200	< 2.2	4.52	0.47	5.8	4.6	31
		Day 112		32	29	173	< 2.2	5.63	0.43	5.9	5.0	32
		Day 168		33	26	140	< 2.2	6.53	0.53	5.5	4.9	45
		Day 224		33	26	89	< 2.2	6.22	0.58	5.2	5.5	50
		Day 56	HE1	33	48	161	< 2.2	5.07	0.72	6.8	4.0	24
		Day 112		27	32	139	< 2.2	6.38	0.38	6.4	4.7	29
		Day 168		28	52	108	< 2.2	6.97	0.54	6.0	4.6	40
		Day 224		28	34	78	< 2.2	6.18	0.43	5.8	4.5	49

APPENDIX NO. 57 (b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		APPS	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
3	(b) (4)	Day 56		34	29	382	< 2.2	4.80	0.64	7.0	3.4	28
		Day 112		31	24	352	< 2.2	6.40	0.43	6.6	4 1	33
		Day 168		29	30	266	< 2.2	6.03	0.48	6.1	4.7	55
		Day 224		30	26	195	< 2.2	5.93	0.41	5.8	5.0	65
		Day 56		24	35	173	< 2.2	4.02	0.37	6.2	4.4	25
		Day 112	HE1	25	37	155	< 2.2	5.61	0.38	6.1	5.0	33
		Day 168		26	53	113	< 2.2	5.88	0.43	5.4	5 9	53
		Day 224		27	55	87	< 2.2	5.33	0.44	5.0	5 2	60
		Day 56		27	28	115	< 2.2	4.98	0.60	6.9	4.0	20
		Day 112		29	28	106	< 2.2	6.08	0.46	7.0	4.0	31
		Day 168		34	45	83	< 2.2	5.83	0.50	5.9	5.0	45
		Day 224	HE1	28	44	67	< 2.2	5.45	0.56	5.5	5 9	53
		Day 56		34	27	222	< 2.2	4.59	0.45	7.0	5 9	33
		Day 112	HE1	37	24	184	< 2.2	5.14	0.30	6.9	4 9	32
		Day 168	HE1	32	24	135	< 2.2	5.98	0.29	6.2	5 3	49
		Day 224		33	24	104	< 2.2	5.52	0.31	6.2	5 5	55
4		Day 56		38	27	375	< 2.2	2.85	0.40	6.2	5 9	21
		Day 112		26	37	226	< 2.2	4.89	0.26	6.1	3.6	26
		Day 168	HE1	34	51	191	< 2.2	4.27	0.23	5.6	5.4	42
		Day 224		36	50	163	< 2.2	5.39	0.31	5.9	6.7	60
		Day 56		44	76	223	< 2.2	3.28	0.43	6.1	6.0	26
		Day 112		39	87	222	< 2.2	5.40	0.29	6.3	4 5	27
		Day 168		38	147	175	< 2.2	5.58	0.40	6.2	5 1	36
		Day 224		34	89	141	< 2.2	6.41	0.44	5.9	6 9	43
		Day 56		33	34	163	< 2.2	3.82	0.34	6.7	7.4	28
		Day 112	HE1	38	30	173	< 2.2	5.71	0.29	6.1	4.8	30
		Day 168		34	37	140	< 2.2	6.17	0.29	5.9	6.8	42
		Day 224		38	40	120	< 2.2	5.96	0.41	5.6	6.4	48
		Day 56 (Unscheduled)		37U	36U	228U	< 2.2U	3.83U	0.46U	5.9U	5.3U	25U
		Day 112	HE1	34	31	184	< 2.2	5.61	0.32	5.7	5 2	35
		Day 168		33	41	150	< 2.2	5.48	0.34	5.9	5 5	54
		Day 224		37	70	126	< 2.2	4.94	0.39	5.4	5 1	57

APPENDIX NO. 57 (b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	(b) (4)	Day 56	48.3	33.6	14.7	2.29	2.86	2.74	145	5 23	104
		Day 112	50.4	31.1	19.3	1.61	2.95	2.44	145	5 27	105
		Day 168	52.7	31.4	21.3	1.47	2.84	2.29	146	4.81	105
		Day 224	54.7	32.9	21.8	1.51	2.69	1.74	146	4.75	107
		Day 56	51.0	33.6	17.4	1.93	3.02	2.84	146	5.78	105
		Day 112	52.4	31.6	20.8	1.52	2.81	2.72	146	5.03	107
		Day 168	50.3	32.6	17.7	1.84	2.68	2.48	146	4.74	108
		Day 224	52.3	32.4	19.9	1.63	2.67	2.14	148	4.73	109
		Day 56	48.1	31.4	16.7	1.88	3.00	2.80	144	5.42	106
		Day 112	50.7	33.3	17.4	1.91	2.88	2.58	148	5.03	107
		Day 168	51.6	37.9	13.7	2.77	2.76	2.02	147	4.49	109
		Day 224	56.5	38.1	18.4	2.07	2.75	1.88	148	4.47	109
		Day 56	45.2	31.7	13.5	2.35	3.04	2.79	144	5 35	105
		Day 112	46.4	29.9	16.5	1.81	2.78	2.56	145	4 97	108
		Day 168	49.9	32.7	17.2	1.90	2.80	2.31	148	4.62	107
		Day 224	53.8	34.3	19.5	1.76	2.73	2.06	149	4.74	109
2		Day 56	48.5	33.0	15.5	2.13	2.90	2.81	144	5.75	103
		Day 112	49.1	32.2	16.9	1.91	2.82	2.32	147	5.00	106
		Day 168	52.1	33.1	19.0	1.74	2.71	2.08	146	4 90	106
		Day 224	53.1	36.9	16.2	2.28	2.71	1.97	147	4.72	108
		Day 56	46.5	33.0	13.5	2.44	2.93	2.76	148	5.46	106
		Day 112	50.6	31.2	19.4	1.61	2.88	2.68	147	4 98	110
		Day 168	52.5	33.2	19.3	1.72	2.75	2.26	148	4.67	110
		Day 224	52.2	33.1	19.1	1.73	2.68	1.98	147	4 33	109
		Day 56	46.6	32.4	14.2	2.28	2.86	2.71	145	5 33	106
		Day 112	48.1	30.8	17.3	1.78	2.82	2.50	147	5 14	109
		Day 168	52.1	30.0	22.1	1.36	2.73	2.23	145	4.84	108
		Day 224	53.5	34.0	19.5	1.74	2.75	1.96	147	4.71	108
		Day 56	49.2	32.0	17.2	1.86	3.00	2.80	143	5.03	104
		Day 112	50.8	31.6	19.2	1.65	2.85	2.47	146	5 11	107
		Day 168	52.7	37.5	15.2	2.47	2.83	2.32	147	4.78	108
		Day 224	54.1	35.5	18.6	1.91	2.76	1.89	146	4.46	109

APPENDIX NO. 57 (b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
3	(b) (4)	Day 56	48.2	34.6	13.6	2.54	3.08	2.97	148	5.44	105
		Day 112	52.0	34.9	17.1	2.04	3.00	2.57	147	4.72	107
		Day 168	52.3	34.2	18.1	1.89	2.81	2.19	148	4.42	108
		Day 224	54.5	36.5	18.0	2.03	2.72	1.74	147	4.34	108
		Day 56	43.9	30.7	13.2	2.33	2.91	2.95	145	4.84	104
		Day 112	52.0	33.0	19.0	1.74	2.93	2.63	147	4.88	109
		Day 168	56.3	34.6	21.7	1.59	2.81	2.26	147	4.34	108
		Day 224	57.3	37.5	19.8	1.89	2.78	1.98	149	4.77	108
		Day 56	46.2	31.0	15.2	2.04	2.86	2.62	145	5.56	107
		Day 112	51.2	33.6	17.6	1.91	2.87	2.42	147	4.89	109
		Day 168	51.9	32.7	19.2	1.70	2.70	2.13	147	4.73	109
		Day 224	52.3	34.2	18.1	1.89	2.63	2.14	149	4.94	113
		Day 56	49.0	34.8	14.2	2.45	2.92	2.84	147	5.48	106
		Day 112	50.9	33.5	17.4	1.93	2.82	2.45	147	4.97	108
		Day 168	52.8	33.1	19.7	1.68	2.70	2.06	147	4.55	109
		Day 224	53.0	38.0	15.0	2.53	2.68	1.89	147	4.63	111
4		Day 56	51.5	33.7	17.8	1.89	2.81	2.62	147	5.96	107
		Day 112	52.2	32.2	20.0	1.61	2.88	2.20	148	5.44	110
		Day 168	51.4	32.9	18.5	1.78	2.66	2.03	147	4.52	108
		Day 224	59.2	39.0	20.2	1.93	2.84	1.99	153	5.15	114
		Day 56	47.1	33.6	13.5	2.49	2.82	2.53	145	4.96	105
		Day 112	51.2	33.9	17.3	1.96	2.95	2.54	146	4.93	107
		Day 168	51.2	33.4	17.8	1.88	2.76	2.05	145	4.81	106
		Day 224	56.7	37.4	19.3	1.94	2.83	1.90	149	4.57	109
		Day 56	48.6	33.8	14.8	2.28	3.00	2.80	146	5.40	107
		Day 112	52.8	33.1	19.7	1.68	2.85	2.45	145	5.79	107
		Day 168	54.2	36.7	17.5	2.10	2.88	2.35	147	4.63	108
		Day 224	59.0	37.8	21.2	1.78	2.81	1.87	148	4.54	108
		Day 56 (Unscheduled)	48.4U	32.9U	15.5U	2.12U	2.90U	2.70U	144U	5.42U	105U
		Day 112	50.7	31.4	19.3	1.63	2.88	2.49	145	4.78	107
		Day 168	52.8	35.8	17.0	2.11	2.74	2.32	148	4.48	108
		Day 224	54.2	36.4	17.8	2.04	2.76	1.88	147	4.60	109

APPENDIX NO. 57

(b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		LDHI2 (U/L)	CK (U/L)	GGT (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
1	(b) (4)	Day 56	98	412	<3	3.2	351	0.79
		Day 112	48	265	<3	11.7	560	0.73
		Day 168	62	235	<3	<1.0	694	0.75
		Day 224	44	165	<3	<1.0	827	0.72
		Day 56	78	440	<3	3.0	393	0.77
		Day 112	42	281	<3	1.8	499	0.76
		Day 168	33	229	<3	1.5	576	0.73
		Day 224	46	202	<3	1.2	679	0.72
		Day 56	97	448	<3	1.3	297	0.76
		Day 112	149	342	<3	2.9	431	0.75
		Day 168	41	244	<3	<1.0	509	0.72
		Day 224	93	218	<3	2.3	589	0.71
		Day 56	60	339	<3	11.7	361	0.70
		Day 112	58	289	<3	1.7	517	0.69
		Day 168	36	203	<3	1.1	673	0.73
		Day 224	47	194	<3	<1.0	705	0.77
2		Day 56	210	667	<3	2.6	438	0.75
		Day 112	54	225	<3	1.2	656	0.67
		Day 168	55	189	<3	<1.0	885	0.71
		Day 224	53	184	<3	<1.0	849	0.70
		Day 56	93	417	<3	2.4	390	0.75
		Day 112	48	312	<3	2.6	606	0.72
		Day 168	60	242	<3	<1.0	725	0.69
		Day 224	103	223	<3	2.3	744	0.68
		Day 56	190	448	<3	3.5	352	0.77
		Day 112	73	358	<3	1.4	520	0.71
		Day 168	79	302	<3	<1.0	694	0.73
		Day 224	83	219	<3	1.0	746	0.76
		Day 56	286	588	<3	9.2	381	0.69
		Day 112	61	250	<3	1.3	548	0.69
		Day 168	62	247	<3	9.9	798	0.70
		Day 224	56	170	<3	<1.0	1049	0.71

APPENDIX NO. 57

(b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		LDHI2 (U/L)	CK (U/L)	GGT (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
3	(b) (4)	Day 56	81	311	<3	9.5	372	0.76
		Day 112	56	305	<3	1.8	542	0.72
		Day 168	41	178	<3	<1.0	758	0.71
		Day 224	54	150	<3	2.0	734	0.72
		Day 56	53	365	<3	3.3	351	0.76
		Day 112	74	335	<3	1.2	609	0.72
		Day 168	111	224	<3	<1.0	799	0.75
		Day 224	63	165	<3	<1.0	888	0.75
		Day 56	67	545	<3	4.1	393	0.75
		Day 112	52	508	<3	1.4	584	0.73
		Day 168	104	242	<3	2.8	730	0.72
		Day 224	55	145	<3	6.1	829	0.74
		Day 56	155	418	<3	6.9	418	0.77
		Day 112	141	806	<3	1.3	515	0.73
		Day 168	175	300	<3	1.3	668	0.73
		Day 224	85	385	<3	6.2	693	0.71
4		Day 56	363	684	<3	2.0	349	0.80
		Day 112	48	252	<3	<1.0	431	0.75
		Day 168	149	272	<3	1.7	543	0.76
		Day 224	80	222	<3	1.3	629	0.83
		Day 56	165	473	<3	2.9	370	0.78
		Day 112	51	264	<3	32.6	539	0.79
		Day 168	42	172	<3	<1.0	661	0.72
		Day 224	116	228	<3	2.3	737	0.75
		Day 56	87	461	<3	4.0	392	0.80
		Day 112	207	369	<3	3.6	589	0.82
		Day 168	85	249	<3	4.1	721	0.82
		Day 224	101	402	<3	2.6	807	0.80
		Day 56 (Unscheduled)	80U	465U	<3U	9.2U	304U	0.77U
		Day 112	82	321	<3	24.0	428	0.74
		Day 168	175	380	<3	<1.0	1031	0.76
		Day 224	46	196	<3	2.2	558	0.72

APPENDIX NO. 57

(b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		APPS	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
1	(b) (4)	Day 56		29	29	189	< 2.2	4.99	0.33	7.0	3.1	23
		Day 112	HE1	39	26	163	< 2.2	6.45	0.46	6.7	3.9	36
		Day 168		44	30	124	< 2.2	6.67	0.31	7.0	4.9	47
		Day 224		28	32	92	< 2.2	5.81	0.34	6.4	4.5	50
		Day 56		32	28	238	< 2.2	5.18	0.44	7.0	3.6	23
		Day 112		33	27	222	< 2.2	6.39	0.37	6.6	4.7	36
		Day 168		29	32	165	< 2.2	6.50	0.38	5.8	4.5	55
		Day 224		31	39	123	< 2.2	5.73	0.40	5.7	5.7	60
		Day 56	HE1	29	33	203	< 2.2	5.01	0.41	6.8	3.4	28
		Day 112		26	33	146	< 2.2	6.63	0.37	5.5	5.0	38
		Day 168		24	44	101	< 2.2	6.55	0.45	5.7	4.7	44
		Day 224		30	48	73	< 2.2	6.91	0.55	5.1	5.3	59
		Day 56		24	29	142	< 2.2	4.85	0.44	7.0	3.5	25
		Day 112		30	26	183	< 2.2	6.31	0.37	6.7	3.8	31
		Day 168		27	34	132	< 2.2	5.76	0.35	6.3	4.7	46
		Day 224		26	39	106	< 2.2	6.06	0.43	6.0	4.0	54
2		Day 56		31	33	176	< 2.2	4.82	0.52	6.8	3.9	31
		Day 112	HE1	30	30	141	< 2.2	6.25	0.32	6.4	3.8	36
		Day 168	HE1	31	41	109	< 2.2	5.42	0.42	5.9	4.1	48
		Day 224		29	47	85	< 2.2	5.50	0.43	5.6	6.4	61
		Day 56		37	37	325	< 2.2	5.19	0.62	5.5	5.6	38
		Day 112		33	32	249	< 2.2	7.07	0.44	5.8	5.3	36
		Day 168	HE1	34	42	167	< 2.2	7.02	0.54	5.6	5.4	54
		Day 224		29	42	116	< 2.2	7.59	0.48	5.2	5.8	61
		Day 56		42	40	162	< 2.2	3.76	0.43	6.4	4.1	27
		Day 112		35	35	120	< 2.2	5.61	0.38	6.6	4.7	35
		Day 168		35	51	93	< 2.2	4.55	0.43	5.8	4.9	46
		Day 224	HE1	35	39	57	< 2.2	4.32	0.36	5.1	5.5	53
		Day 56		37	47	125	< 2.2	3.99	0.43	6.2	3.5	18
		Day 112		28	28	97	< 2.2	6.03	0.40	5.8	3.7	27
		Day 168		28	35	75	< 2.2	5.38	0.50	5.6	3.9	42
		Day 224		31	40	61	< 2.2	5.28	0.53	5.0	4.6	49

APPENDIX NO. 57

(b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		APPS	AST (U/L)	ALT (U/L)	ALP (U/L)	BILT3 (µmol/L)	CHOL (mmol/L)	TRIG (mmol/L)	GLUC (mmol/L)	UREA (mmol/L)	CREA (µmol/L)
3	(b) (4)	Day 56		29	25	389	< 2.2	5.07	0.84	6.5	3.9	30
		Day 112		27	22	330	< 2.2	6.56	0.63	6.3	5.0	32
		Day 168		29	27	259	< 2.2	6.18	0.54	5.9	6.7	49
		Day 224		27	27	187	< 2.2	5.79	0.47	5.2	5.6	56
		Day 56		29	32	161	< 2.2	5.36	0.65	6.6	4.0	30
		Day 112		27	42	177	< 2.2	6.30	0.32	6.0	4.6	37
		Day 168		28	53	120	< 2.2	5.98	0.43	5.6	4.3	50
		Day 224		27	55	93	< 2.2	5.22	0.40	5.6	4.7	62
		Day 56		30	23	144	< 2.2	4.15	0.48	7.3	3.2	16
		Day 112		30	22	130	< 2.2	5.13	0.39	6.8	3.3	28
		Day 168		30	26	92	< 2.2	5.49	0.38	6.2	4.0	45
		Day 224		28	28	72	< 2.2	5.19	0.52	5.8	5.9	53
		Day 56		35	30	281	< 2.2	5.40	0.68	6.6	5.0	32
		Day 112		25	25	205	< 2.2	6.53	0.26	6.4	4.6	33
		Day 168		30	34	156	< 2.2	6.23	0.32	5.7	4.8	48
		Day 224		24	38	106	< 2.2	6.98	0.29	5.3	4.9	64
4		Day 56	HE1	38	30	313	< 2.2	2.93	0.41	6.2	5.8	26
		Day 112		23	25	196	< 2.2	4.70	0.25	6.3	4.6	26
		Day 168		28	40	164	< 2.2	4.43	0.34	5.7	4.3	36
		Day 224		31	39	117	< 2.2	4.47	0.36	5.2	5.0	42
		Day 56	HE1	47	64	217	< 2.2	3.89	0.40	7.2	6.4	31
		Day 112		37	76	220	< 2.2	5.82	0.31	7.2	5.4	33
		Day 168		39	109	153	< 2.2	6.13	0.42	6.2	5.1	40
		Day 224		35	70	111	< 2.2	5.91	0.43	6.1	5.8	52
		Day 56		37	36	265	< 2.2	3.43	0.40	6.3	7.1	24
		Day 112		29	29	216	< 2.2	6.05	0.31	5.9	5.5	25
		Day 168		33	40	148	< 2.2	6.83	0.30	5.9	6.1	42
		Day 224	HE1	37	41	114	< 2.2	5.62	0.47	5.5	5.3	44
		Day 56		38	53	192	< 2.2	3.80	0.42	7.4	4.9	26
		Day 112		36	45	143	< 2.2	4.84	0.23	5.9	4.3	29
		Day 168		29	56	118	< 2.2	5.93	0.38	5.9	7.0	41
		Day 224		36	102	107	< 2.2	5.21	0.36	5.4	6.5	49

APPENDIX NO. 57 (b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
1	(b) (4)	Day 56	48.4	35.2	13.2	2.67	2.84	2.69	144	5 56	102
		Day 112	54.4	35.5	18.9	1.88	3.03	2.65	147	5.67	103
		Day 168	55.3	36.7	18.6	1.97	2.74	2.17	147	4 36	107
		Day 224	55.6	37.6	18.0	2.09	2.64	1.60	146	4.46	107
		Day 56	49.5	33.1	16.4	2.02	3.00	2.72	144	5 38	103
		Day 112	51.0	33.3	17.7	1.88	2.84	2.64	145	5.02	106
		Day 168	52.8	36.4	16.4	2.22	2.76	2.14	147	4 91	109
		Day 224	56.4	37.0	19.4	1.91	2.76	1.72	148	4.63	109
		Day 56	47.4	31.6	15.8	2.00	2.93	2.51	143	4.88	106
		Day 112	51.4	33.7	17.7	1.90	2.87	2.53	148	5 21	106
		Day 168	50.9	35.8	15.1	2.37	2.67	2.24	146	4.69	108
		Day 224	54.9	35.7	19.2	1.86	2.70	1.92	146	4.86	108
		Day 56	48.4	32.0	16.4	1.95	3.08	2.65	145	5 19	105
		Day 112	51.8	33.5	18.3	1.83	2.83	2.41	146	4.77	106
		Day 168	52.8	35.5	17.3	2.05	2.81	2.11	147	4.45	108
		Day 224	56.8	34.7	22.1	1.57	2.80	1.77	148	4.66	108
2		Day 56	48.0	34.2	13.8	2.48	2.91	2.84	145	5.80	105
		Day 112	50.7	34.0	16.7	2.04	2.90	2.58	145	4.70	105
		Day 168	51.1	35.5	15.6	2.28	2.67	2.18	146	4.61	108
		Day 224	53.4	37.4	16.0	2.34	2.68	2.14	148	4.78	111
		Day 56	47.1	34.6	12.5	2.77	2.91	2.82	147	5.40	105
		Day 112	51.9	34.1	17.8	1.92	2.87	2.44	145	4.70	105
		Day 168	54.1	35.5	18.6	1.91	2.83	2.25	147	4 32	108
		Day 224	54.6	36.0	18.6	1.94	2.80	1.88	148	4 17	108
		Day 56	48.9	32.7	16.2	2.02	2.97	2.85	147	5 51	106
		Day 112	52.5	33.9	18.6	1.82	3.08	2.75	147	5.42	106
		Day 168	52.5	33.3	19.2	1.73	2.87	2.34	147	5.04	108
		Day 224	51.7	33.6	18.1	1.86	2.73	1.98	146	4 32	107
		Day 56	46.6	30.6	16.0	1.91	2.95	2.65	143	5 14	107
		Day 112	52.2	32.9	19.3	1.70	2.90	2.51	146	5 25	107
		Day 168	53.6	37.8	15.8	2.39	2.84	2.10	147	4 32	107
		Day 224	55.2	38.6	16.6	2.33	2.78	1.85	146	4.42	109

APPENDIX NO. 57 (b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		TP (g/L)	ALB (g/L)	GLOB (g/L)	A/G	CA (mmol/L)	PHOS (mmol/L)	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)
3	(b) (4)	Day 56	47.2	33.5	13.7	2.45	2.96	2.79	146	5 22	106
		Day 112	52.5	34.6	17.9	1.93	2.93	2.60	145	4 99	107
		Day 168	54.1	34.1	20.0	1.71	2.75	2.11	147	4 58	108
		Day 224	52.8	36.3	16.5	2.20	2.62	1.72	147	4.47	108
		Day 56	48.3	32.5	15.8	2.06	2.96	2.79	144	5.05	104
		Day 112	49.4	31.8	17.6	1.81	2.98	2.80	147	4.65	109
		Day 168	53.6	33.6	20.0	1.68	2.89	2.16	148	4 53	108
		Day 224	52.9	35.0	17.9	1.96	2.74	1.68	147	4 36	107
		Day 56	45.0	30.7	14.3	2.15	2.73	2.49	144	4 97	104
		Day 112	50.3	34.0	16.3	2.09	2.82	2.39	146	4 59	108
		Day 168	51.3	33.9	17.4	1.95	2.70	2.02	148	4 38	110
		Day 224	54.2	37.8	16.4	2.30	2.71	2.01	149	4.48	112
		Day 56	49.8	35.6	14.2	2.51	3.05	2.77	148	4 98	103
		Day 112	54.6	34.7	19.9	1.74	2.98	2.53	149	4 98	109
		Day 168	54.8	37.0	17.8	2.08	2.83	2.16	147	4 52	108
		Day 224	58.9	40.9	18.0	2.27	2.84	1.82	149	4 35	109
4		Day 56	48.2	33.6	14.6	2.30	2.84	2.79	145	5 55	105
		Day 112	49.2	32.0	17.2	1.86	2.83	2.32	147	4.80	109
		Day 168	50.1	33.8	16.3	2.07	2.67	1.88	147	4 37	108
		Day 224	53.3	36.4	16.9	2.15	2.65	1.74	147	4 21	109
		Day 56	49.6	33.8	15.8	2.14	2.91	2.69	146	6 11	106
		Day 112	54.6	37.3	17.3	2.16	2.95	2.44	148	5 18	108
		Day 168	54.9	35.4	19.5	1.82	2.91	2.08	147	4.74	107
		Day 224	55.9	37.7	18.2	2.07	2.74	1.80	148	4 56	108
		Day 56	48.1	34.3	13.8	2.49	2.96	2.77	144	5 38	105
		Day 112	52.5	33.7	18.8	1.79	2.92	2.65	146	5.01	108
		Day 168	53.7	36.3	17.4	2.09	2.80	2.19	147	4.48	108
		Day 224	56.1	36.8	19.3	1.91	2.75	1.79	146	4.64	109
		Day 56	47.3	33.1	14.2	2.33	3.06	2.80	145	5 36	103
		Day 112	48.8	31.6	17.2	1.84	2.85	2.44	146	4.69	108
		Day 168	51.8	35.5	16.3	2.18	2.80	1.97	146	4 39	107
		Day 224	54.1	36.1	18.0	2.01	2.76	1.66	148	4.40	109

APPENDIX NO. 57 (b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		LDHI2 (U/L)	CK (U/L)	GGT (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
	(b) (4)							
1		Day 56	78	414	<3	1.4	372	0.79
		Day 112	170	346	<3	6.6	550	0.79
		Day 168	107	1266	<3	<1.0	628	0.74
		Day 224	39	152	<3	<1.0	547	0.71
		Day 56	61	420	<3	10.1	386	0.79
		Day 112	129	324	<3	4.9	558	0.80
		Day 168	31	196	<3	<1.0	725	0.75
		Day 224	44	173	<3	1.6	746	0.75
		Day 56	73	477	<3	2.6	377	0.71
		Day 112	46	275	<3	29.9	555	0.78
		Day 168	29	183	<3	6.9	643	0.74
		Day 224	54	186	<3	4.9	830	0.78
		Day 56	59	335	<3	5.9	377	0.71
		Day 112	62	306	<3	1.1	470	0.67
		Day 168	46	195	<3	2.8	529	0.70
		Day 224	45	139	<3	1.1	701	0.73
2		Day 56	64	379	<3	3.3	365	0.78
		Day 112	59	278	<3	47.8	534	0.71
		Day 168	113	237	<3	2.6	532	0.74
		Day 224	78	171	<3	7.2	639	0.77
		Day 56	122	461	<3	23.5	446	0.77
		Day 112	58	297	<3	<1.0	609	0.72
		Day 168	78	260	<3	7.1	691	0.72
		Day 224	50	162	<3	7.2	749	0.72
		Day 56	113	1183	<3	7.3	431	0.77
		Day 112	58	305	<3	2.9	667	0.80
		Day 168	76	265	<3	3.3	838	0.75
		Day 224	127	236	<3	2.2	820	0.78
		Day 56	82	537	<3	2.1	373	0.74
		Day 112	78	312	<3	1.4	529	0.71
		Day 168	71	231	<3	10.5	653	0.71
		Day 224	91	234	<3	1.5	626	0.75

APPENDIX NO. 57

(b) (4)

CLINICAL CHEMISTRY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		LDHI2 (U/L)	CK (U/L)	GGT (U/L)	TBA (µmol/L)	AMYL (U/L)	MG (mmol/L)
3	(b) (4)	Day 56	59	327	<3	10.6	330	0.72
		Day 112	49	295	<3	7.3	564	0.71
		Day 168	52	205	<3	<1.0	641	0.70
		Day 224	63	157	<3	1.3	729	0.69
		Day 56	47	497	<3	7.1	284	0.74
		Day 112	44	235	<3	25.3	505	0.80
		Day 168	44	173	<3	5.0	708	0.76
		Day 224	53	141	<3	3.1	523	0.75
3		Day 56	56	351	<3	4.6	364	0.71
		Day 112	46	281	<3	1.5	494	0.68
		Day 168	42	178	<3	1.0	584	0.68
		Day 224	43	146	<3	6.3	575	0.74
		Day 56	122	395	<3	23.3	342	0.83
		Day 112	64	248	<3	<1.0	508	0.80
		Day 168	52	212	<3	1.2	551	0.76
		Day 224	48	128	<3	<1.0	537	0.79
4		Day 56	206	487	<3	2.1	435	0.77
		Day 112	48	215	<3	2.0	551	0.73
		Day 168	56	180	<3	1.7	646	0.77
		Day 224	92	171	<3	4.6	646	0.81
		Day 56	204	451	<3	2.1	435	0.83
		Day 112	65	315	<3	3.5	614	0.80
		Day 168	44	213	<3	3.9	741	0.77
		Day 224	58	182	<3	4.8	829	0.78
		Day 56	74	402	<3	16.0	360	0.79
		Day 112	50	243	<3	18.0	535	0.82
		Day 168	102	242	<3	8.2	542	0.81
		Day 224	170	255	<3	2.4	542	0.76
		Day 56	78	424	<3	13.2	353	0.82
		Day 112	55	322	<3	28.2	477	0.79
		Day 168	42	210	<3	1.0	476	0.77
		Day 224	49	174	<3	<1.0	519	0.76

APPENDIX NO. 58 (b) (4)

COAGULATION - F1 GENERATION - PUPPIES - POST WEANING

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum

MIN: Minimum

APPENDIX NO. 58

(b) (4)

COAGULATION - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		PT (Sec)	APTT (Sec)	FIB (g/L)
	(b) (4)				
1		Week 13	7.6	29.2	2.1
		Week 34	8.1	21.7	2.0
		Week 13	7.5	27.6	2.7
		Week 34	7.6	24.1	2.6
		Week 13	8.0	27.9	2.5
		Week 34	8.2	23.9	1.5
		Week 13	8.0	24.5	2.2
		Week 34	7.7	19.4	2.0
2		Week 13	7.7	22.9	2.2
		Week 34	8.4	18.2	1.6
		Week 13	8.0	27.6	2.3
		Week 34	8.2	27.5	2.1
		Week 13	7.6	26.9	2.1
		Week 34	7.9	25.1	2.0
		Week 13	7.6	24.0	2.3
		Week 34	7.6	20.7	1.6
3		Week 13	7.9	25.3	2.2
		Week 34	8.1	22.8	2.4
		Week 13	8.0	23.7	2.0
		Week 34	8.4	21.4	1.6
		Week 13	7.5	25.8	2.4
		Week 34	7.8	23.9	2.4
		Week 13	7.5	22.6	2.0
		Week 34	8.5	17.8	1.7
4		Week 13	7.5	27.9	2.1
		Week 34	8.6	20.3	1.5
		Week 13	8.1	27.2	2.1
		Week 34	8.2	25.1	1.7
		Week 13	7.9	23.6	2.4
		Week 34	8.4	20.7	1.6
		Week 13	7.6	24.8	1.9
		Week 34	7.8	18.8	1.6

APPENDIX NO. 58

(b) (4)

COAGULATION - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		APPP	PT (Sec)	APTT (Sec)	FIB (g/L)
1	(b) (4)	Week 13		8.1	28.7	2.0
		Week 34		8.2	19.6	1.8
		Week 13		7.7	23.6	2.1
		Week 34		7.7	19.4	2.9
		Week 13		7.9	28.1	2.2
		Week 34		7.9	24.7	1.8
		Week 13		7.8	26.0	1.9
		Week 34		7.7	22.8	1.6
2		Week 13		8.3	23.1	2.7
		Week 34		8.7	20.4	1.3
		Week 13		7.6	27.9	1.9
		Week 34		8.4	31.2	1.6
		Week 13	HE1	7.5	22.7	2.2
		Week 34		7.9	22.1	1.8
		Week 13		7.7	23.7	2.1
		Week 34		8.1	20.6	1.6
3		Week 13		7.8	25.3	1.9
		Week 34		8.7	24.3	1.3
		Week 13		7.4	22.1	1.8
		Week 34		8.5	20.7	1.2
3		Week 13		7.5	25.4	2.0
		Week 34		8.3	22.4	1.3
		Week 13		7.5	23.1	2.2
		Week 34		8.6	21.5	1.6
4		Week 13		7.6	23.2	1.8
		Week 34		8.7	24.1	1.3
		Week 13		8.3	26.4	1.9
		Week 34		8.0	23.5	1.7
		Week 13	HE1	8.2	19.5	1.8
		Week 34		8.0	21.4	2.1
		Week 13		7.6	25.4	2.1
		Week 34		7.5	19.6	2.1

APPENDIX NO. 59 (b) (4)

BUCCAL MUCOSAL BLEEDING TIME
F1 GENERATION - PUPPIES - POST WEANING

The following abbreviation and footnotes have been used throughout the appendix

min: Minute

Ω: Maximum bleeding time.

^: Buccal mucosa bleeding stain was blank.

APPENDIX NO. 59 [redacted] (b) (4)

BUCCAL MUCOSAL BLEEDING TIME
MEASUREMENT TIME (min)
F1 GENERATION - PUPPIES - POST WEANING - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		WEEK 34	
1	[redacted] (b) (4)			
	MEAN	>	27.25	
	SD		5.50	
	MIN		19.0	
	MAX		30.0	Ω
	N		4	
2	[redacted] (b) (4)			
	MEAN		22.13	
	SD		8.89	
	MIN		9.5	
	MAX		30.0	
	N		4	
3	[redacted] (b) (4)			
	MEAN	>	17.38	
	SD		10.13	
	MIN		8.0	
	MAX		30.0	Ω
	N		4	
4	[redacted] (b) (4)			
	MEAN		15.75	
	SD		8.65	
	MIN		6.5	
	MAX		27.0	
	N		4	

APPENDIX NO. 59 (b) (4)

BUCCAL MUCOSAL BLEEDING TIME
MEASUREMENT TIME (min)
F1 GENERATION - PUPPIES - POST WEANING - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		WEEK 34	
1	(b) (4)			
	MEAN	>	24.00	
	SD		7.12	
	MIN		16.0	
	MAX		30.0	Ω
	N		4	
2	(b) (4)			
	MEAN		16.75	
	SD		4.27	
	MIN		11.0	
	MAX		20.0	
	N		4	
3	(b) (4)			
	MEAN	>	14.88	
	SD		10.73	
	MIN		7.0	
	MAX		30.0	Ω
	N		4	
4	(b) (4)			
	MEAN	>	15.00	
	SD		10.11	
	MIN		8.5	
	MAX		30.0	Ω
	N		4	

URINALYSIS - F1 GENERATION - PUPPIES - POST WEANING

Universal mathematical symbols are not defined in the legend page but should be interpreted as such when applicable in the tables and appendices.

The following abbreviations and footnotes have been used throughout the appendix and/or summary table.

SD: Standard Deviation

N: Number of animals

MAX: Maximum

MIN: Minimum

SNR: Sample not received

APPENDIX NO. 60

(b) (4)

URINALYSIS - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		VOL (mL)	COL	CLA	SG	pH	GLU (mmol/L)	BIL	KET (mmol/L)	BLD (Ery/µL)	PRO (g/L)	UBG (µmol/L)	NIT	LEU (Leu/µL)
1		Week 13	38.0	Yellow	Cloudy	1.035	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	22.0	Yellow	Clear	1.046	6.0	Negative	Small	Negative	Negative	Trace	3.2	Negative	Negative
		Week 13	140.0	Yellow	Clear	1.016	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Approx 70
		Week 34	24.0	Yellow	Clear	1.029	6.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	62.0	Yellow	Clear	1.028	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	38.0	Yellow	Clear	1.039	6.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	50.0	Yellow	Cloudy	1.032	6.0	Negative	Negative	Negative	Tr-Lysed	Negative	3.2	Negative	Negative
		Week 34	71.0	Yellow	Cloudy	1.047	6.0	Negative	Small	Negative	Negative	Trace	3.2	Negative	Negative
2		Week 13	5.8	Yellow	Cloudy	1.068	5.5	Negative	Small	Negative	Negative	0 3	16	Negative	Negative
		Week 34	SNR	SNR	SNR	SNR	SNR	SNR	SNR	SNR	SNR	SNR	SNR	SNR	SNR
		Week 13	67.0	Yellow	Clear	1.022	5.5	Negative	Negative	Negative	Tr-Intact	Negative	3.2	Negative	Approx 15
		Week 34	58.0	Yellow	Clear	1.042	5.5	Negative	Small	Negative	Negative	Trace	3.2	Negative	Negative
		Week 13	27.0	Yellow	Clear	1.041	5.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	44.0	Yellow	Cloudy	1.060	5.5	Negative	Small	Negative	Negative	0 3	3.2	Negative	Negative
	(b) (4)	Week 13	20.0	Yellow	Clear	1.042	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	62.0	Yellow	Cloudy	1.037	6.0	Negative	Small	Negative	Negative	Trace	3.2	Negative	Negative

APPENDIX NO. 60

[redacted] (b) (4)

URINALYSIS - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		VOL (mL)	COL	CLA	SG	pH	GLU (mmol/L)	BIL	KET (mmol/L)	BLD (Ery/µL)	PRO (g/L)	UBG (µmol/L)	NIT	LEU (Leu/µL)
3	[redacted] (b) (4)	Week 13	34.0	Yellow	Cloudy	1.026	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	280.0	Yellow	Cloudy	1.020	6.0	Negative	Negative	Negative	Approx 25	Negative	3.2	Negative	Approx 15
		Week 13	37.0	Yellow	Clear	1.034	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	46.0	Yellow	Clear	1.048	5.5	Negative	Small	Negative	Negative	0.3	3.2	Negative	Negative
		Week 13	33.0	Yellow	Cloudy	1.031	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	18.0	Yellow	Cloudy	1.070	5.5	Negative	Small	Negative	Negative	0.3	16	Negative	Negative
		Week 13	21.0	Yellow	Cloudy	1.045	5.5	Negative	Small	Negative	Negative	Negative	3.2	Positive	Negative
		Week 34	71.0	Yellow	Clear	1.046	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
4		Week 13	73.0	Yellow	Cloudy	1.020	6.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Approx 15
		Week 34	58.0	Yellow	Clear	1.046	5.5	Negative	Negative	Negative	Negative	Negative	16	Negative	Negative
		Week 13	32.0	Yellow	Cloudy	1.047	5.5	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
		Week 34	58.0	Yellow	Cloudy	1.050	5.5	Negative	Small	Negative	Negative	Trace	16	Negative	Negative
		Week 13	38.0	Yellow	Cloudy	1.043	5.5	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
		Week 34	23.0	Yellow	Cloudy	1.050	6.5	Negative	Small	Negative	Negative	0.3	3.2	Negative	Negative
		Week 13	42.0	Yellow	Cloudy	1.039	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	98.0	Yellow	Clear	1.034	6.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative

APPENDIX NO. 60

[redacted] (b) (4)

URINALYSIS - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		VOL (mL)	COL	CLA	SG	pH	GLU (mmol/L)	BIL	KET (mmol/L)	BLD (Ery/µL)	PRO (g/L)	UBG (µmol/L)	NIT	LEU (Leu/µL)
1	[redacted] (b) (4)	Week 13	26.0	Yellow	Clear	1.042	5.0	Negative	Small	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	40.0	Yellow	Cloudy	1.045	6.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	50.0	Yellow	Cloudy	1.031	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Approx 15
		Week 34	36.0	Yellow	Clear	1.038	6.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	59.0	Yellow	Clear	1.026	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	61.0	Yellow	Clear	1.044	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	62.0	Yellow	Cloudy	1.020	5.5	Negative	Negative	Negative	Approx 200	Negative	3.2	Negative	Negative
		Week 34	50.0	Yellow	Clear	1.050	6.0	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
2		Week 13	13.0	Yellow	Cloudy	1.048	5.5	Negative	Small	Negative	Negative	0.3	3.2	Positive	Negative
		Week 34	52.0	Yellow	Cloudy	1.033	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	26.0	Yellow	Clear	1.038	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	63.0	Yellow	Cloudy	1.044	5.5	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
		Week 13	37.0	Yellow	Cloudy	1.043	5.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	26.0	Yellow	Clear	1.048	5.5	Negative	Small	Negative	Negative	Trace	3.2	Negative	Negative
		Week 13	25.0	Yellow	Clear	1.050	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	32.0	Yellow	Clear	1.048	6.0	Negative	Small	Negative	Negative	Negative	3.2	Negative	Negative

APPENDIX NO. 60

[redacted] (b) (4)

URINALYSIS - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.		VOL (mL)	COL	CLA	SG	pH	GLU (mmol/L)	BIL	KET (mmol/L)	BLD (Ery/µL)	PRO (g/L)	UBG (µmol/L)	NIT	LEU (Leu/µL)
3	[redacted]	Week 13	22.0	Yellow	Clear	1.033	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	49.0	Yellow	Clear	1.044	5.5	Negative	Small	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	32.0	Yellow	Clear	1.033	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	30.0	Yellow	Clear	1.038	5.5	Negative	Small	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	28.0	Yellow	Cloudy	1.036	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	9.0	Yellow	Clear	1.047	5.0	Negative	Small	Negative	Negative	Trace	3.2	Negative	Negative
		Week 13	21.0	Yellow	Cloudy	1.042	5.5	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
		Week 34	120.0	Yellow	Clear	1.037	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
4		Week 13	30.0	Yellow	Cloudy	1.049	5.5	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
		Week 34	60.0	Yellow	Clear	1.060	5.0	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 13	14.0	Yellow	Cloudy	1.068	5.5	Negative	Small	Negative	Negative	0.3	3.2	Negative	Negative
		Week 34	45.0	Yellow	Cloudy	1.060	5.5	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
		Week 13	58.0	Yellow	Clear	1.024	5.5	Negative	Negative	Trace	Negative	Negative	3.2	Negative	Negative
		Week 34	55.0	Yellow	Cloudy	1.062	6.0	Negative	Negative	Negative	Negative	Trace	3.2	Negative	Negative
	[redacted] (b) (4)	Week 13	28.0	Yellow	Clear	1.048	5.5	Negative	Negative	Negative	Negative	Negative	3.2	Negative	Negative
		Week 34	56.0	Yellow	Clear	1.050	6.0	Negative	Small	Negative	Negative	Negative	3.2	Negative	Negative

APPENDIX NO. 60

[redacted] (b) (4)

URINE MICROSCOPY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (/HPF)	WBC (/HPF)	EPITH (/HPF)	GC (/LPF)	HC (/LPF)	RBCC (/LPF)	WBCC (/LPF)	CRY (/HPF)	AP (/HPF)	AU (/HPF)	BILI (/HPF)	CO (/HPF)	TP (/HPF)	Yeast (/HPF)	SP (/HPF)	Other (/HPF)	Mucus (/HPF)	BACT (/HPF)
1	[redacted]																		
2																			

(b) (4)

APPENDIX NO. 60

[redacted] (b) (4)

URINE MICROSCOPY - F1 GENERATION - PUPPIES - POST WEANING
MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (/HPF)	WBC (/HPF)	EPITH (/HPF)	WBCC (/LPF)	AU (/HPF)	BILI (/HPF)	TP (/HPF)	BACT (/HPF)
3	[redacted]								
4									

[redacted] (b) (4)

APPENDIX NO. 60

[redacted] (b) (4)

URINE MICROSCOPY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (/HPF)	WBC (/HPF)	EPITH (/HPF)	AU (/HPF)	BACT (/HPF)
1	[redacted] (b) (4)					
2						

APPENDIX NO. 60

[redacted]

URINE MICROSCOPY - F1 GENERATION - PUPPIES - POST WEANING
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL NO.	RBC (/HPF)	WBC (/HPF)	EPITH (/HPF)	WBCC (/LPF)	AU (/HPF)	BACT (/HPF)
3	[redacted]						
4							

(b) (4)

APPENDIX NO. 61
CLINICAL PATHOLOGY REPORT



CONFIDENTIAL

CLINICAL PATHOLOGY REPORT

Algal Oil containing EPA and DHA (AOCED):
A Gestation, Lactation and Growth
Dietary Safety Study
in Dogs/Puppies



Sponsor:

DSM Nutritional Products AG
6480 Dobbin Road
Columbia, MD USA 21045

Issue Date: September 24, 2018

This document is confidential and should not be disseminated to entities or individuals, without the written approval of the Sponsor.

1 OBJECTIVE

The objective of this study was to evaluate safety and bioavailability of Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to Beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old).

2 EXPERIMENTAL DESIGN

The test and reference items were administered as a diet as shown below:

Text Table 1: Study Design

Treatment Group	Dose Level (X of Targeted Dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F_0 Generation (dams)@	F_1 Generation (puppies)[a]	
					F	M(Spare)	F(Spare)
1. Control Diet*	0	0	0.11%	0.12%	5	4 (1)	4 (1)
2. AOCED	1/2X	0.75%	0.41%**	0.44%	5	4 (1)	4 (1)
3. AOCED	1X	1.5%	0.77%**	0.83%	5	4 (1)	4 (1)
4. AOCED	2X	3.0%	1.55%**	1.69%	5	4 (1)	4 (1)

* Group 1 animals received the control diet, which were formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA level (0.11%) is achieved by using the chicken by-product meal as one of the ingredients.
** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content was the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA) and from the chicken by-product meal (0.11%). Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.
*** Calculated based on dry matter basis (adjusted for moisture content).
[a] Two puppies per litter (1 male and 1 female), randomly selected, the spare was randomly selected from any litter within each group.
[b] Since this study design include blinding to treatment groups, designations for individual animals were not revealed during the conduct of the study and were only available following the end of the data collection period and interpretation by the Study Director.
@ Six (6) females per group were mated, as an attempt to have at least 5 females per group confirmed pregnant at GD 28. Only confirmed pregnant females (up to a maximum of 5/group, randomly selected) were shipped to (b) (4)
M: male; F: female.

Clinical Pathology data was collected from F_0 generation females at predose and during gestation and at lactation (Day 56) and consisted of hematology and clinical chemistry clinical pathology data. Interpretation of clinical pathology data involved comparing the lactation timepoint (Day 56) with the predose timepoint with consideration was given to control data. The predose timepoint for gestational and lactating females was performed at a different site (b) (4) and; therefore, inherent variability would be considered during interpretation of data. For the F_1 generation puppies, clinical pathology included hematology, clinical chemistry, coagulation, and urinalysis data. No predose data was

available so interpretation of clinical pathology parameter data involved comparing the AOCED fed animals with the control F_1 animals.

3 RESULTS AND DISCUSSION

Hematology (Gestation and Lactation F_0)
No changes were noted in hematology related to the addition of Algal Oil containing EPA and DHA (AOCED) at any dose to the diet of the pregnant and lactating females during this study.

Differences in hematology between AOCED-fed animals and control animals were considered incidental because many differences were noted in control animals and were consistent with normal biological and/or analytical variability and potentially associated with a different location of analysis.

Hematology and Coagulation (Generation F_1)
No changes were noted in hematology related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the offspring (Generation F_1) at any dose during this study. Some parameters varied during the study in AOCED-dosed animals but similar variability was also noted within the control group and therefore considered incidental.

No changes were noted in coagulation parameters.

Differences were noted in many hematology parameters over the different timepoints during the study. However, between AOCED-fed animals and control there was no notable difference. Therefore; this variability in parameters was consistent with normal biological (growth) and/or analytical variability and were considered incidental.

Clinical Chemistry (Gestation and Lactation F_0)
No changes were noted in clinical chemistry related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the pregnant and lactating females during this study.

Differences in clinical chemistry between AOCED-fed animals and control animals were not notable and any changes during the study that occurred in were also noted in control animals and were consistent with normal biological and/or analytical variability and were considered incidental.

Clinical Chemistry (Generation F_1)
No changes were noted in clinical chemistry related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the offspring (Generation F_1 males and females) during this study.

Urea concentrations were higher on Day 56 in the high dose males and females when compared with control but this did not correspond with any increases in creatinine. Therefore, this was considered prerenal in cause and not associated with the administration of AOCED. Creatinine values were higher in all animals with primary increases by Day 168 and peaking at Day 224. This was an expected result due to increased muscle mass during the growth period and was noted in all groups, including control.

Differences in clinical chemistry between AOCED-fed animals and control animals were not notable and any variability that occurred during the study were also noted in control animals

(b) (4)

and were consistent with normal biological (growth) and/or analytical variability and were considered incidental.

Urinalysis (Generation F_1)

No changes were noted in urinalysis parameters related to the addition of Algal Oil containing EPA and DHA (AOCED) to the diet of the offspring (Generation F_1) during this study.

4 SUMMARY/CONCLUSION

Administration of Algal Oil containing EPA and DHA (AOCED) to gestational and lactating females did not result in any changes in hematology or clinical chemistry parameters at any dose during this study. Differences were considered normal biological variability.

Administration of Algal Oil containing EPA and DHA (AOCED) to offspring (Generation F_1 males and females) of females (F_0) did not result in any changes in hematology, coagulation, clinical chemistry, or urinalysis parameters during this study. Differences were considered normal biological variability (growth period) and noted in control.

5 SIGNATURE PAGE

This clinical pathology report was written by:

(b) (4), (b) (6)

24-SEP-2018

Date

(b) (4)

APPENDIX NO. 62
BIOANALYTICAL REPORT

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies:

BIOANALYSIS REPORT

SPONSOR

DSM Nutritional Products
6480 Dobbin Rd.
Columbia MD 20853 USA
PI: (b) (4), (b) (6)

STUDY FACILITY

(b) (4)

(b) (4)

BIOANALYSIS FACILITY

(b) (4)

September 24, 2018

Contents

1. INTRODUCTION 3
1.1.1. Study Number 3
1.1.2. Study Title 3
1.1.3. Bioanalytical Study Design 3
1.1.4. Compliance 3
Fatty acid analysis was performed by (b) (4), a certified lab using internal SOPs. The analytical method met established system suitability criteria. The complete statistical analysis for this study was performed by (b) (4), (b) (6), DSM, Kaiseraugst, Switzerland, and (b) (4), (b) (6), DSM, Columbia, USA. The full statistical report is included as an appendix to this report. 3
1.1.5. Test Site 3
1.1.6. Personnel 4
2. ANALYTE 5
Identification of Analytes 5
3. STUDY DESIGN 5
3.1.1. Dose Levels 5
4. SAMPLE COLLECTION AND ANALYSIS 6
4.1.1. Sample Collection 6
4.1.2. Sample Receipt and Handling 6
4.1.3. Sample Analysis 7
4.1.4. Data Review 8
4.1.5. Statistics 8
4.1.6. Statistical Software 8
5. RESULTS 9
5.1.1. F0 generation: plasma DHA, EPA and ARA concentrations 9
5.1.2. F1 Generation: plasma DHA, EPA and ARA concentrations 14
6. SUMMARY 22
7. DATA RETENTION 22
8. APPENDIX 23
9. INDIVIDUAL DATA 32
10. SIGNATURES 37
Responsible Scientist Approval 37

1. INTRODUCTION

1.1.1. Study Number

(b) (4)

1.1.2. Study Title

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies: Bioanalysis Results.

1.1.3. Bioanalytical Study Design

The objective of this study is to evaluate safety and bioavailability of Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to Beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks of age). Plasma samples were collected from F0 Generation during the pre-treatment period at baseline, after 4-5 weeks of treatment and at weaning. Plasma samples were collected from the puppies at weaning and at Weeks 13 and 34 of age. All samples were analyzed for DHA (docosahexaenoic acid), EPA (eicosapentaenoic acid), and ARA (arachidonic acid) concentrations. Results were ex ressed as µg of DHA/EPA/ARA per m of plasma. Anal sis was conducted at (b) (4) aboratory using methods detailed in SOP (b) (4). Whole Plasma Fatty Acid Concentrations and data were submitted to DSM Analytics. Statistical data anal sis was erformed by DSM. The report was prepared by DSM and submitted to (b) (4) a for inclusion in the main study report.

1.1.4. Compliance

Fatty acid analysis was performed by (b) (4) certified lab using internal SOPs. The analytical method met established system suitability criteria. The complete statistical analysis for this stud was erformed by (b) (4), (b) (6) DSM, Kaiseraugst, Switzerland, and (b) (4), (b) (6) DSM, Columbia, USA. The full statistical report is included as an appendix to this report.

1.1.5. Test Site

(b) (4)

1.1.6. Personnel

1.1.6.1. Test Site Personnel:

Principal Investigator

(b) (4), (b) (6)

(b) (4), (b) (6)

1.1.6.2. Data Analysis Personnel:

Statistical Analysis:

(b) (4), (b) (6)

Data Reporting:

(b) (4), (b) (6)

2. ANALYTE

Identification of Analytes

Analytes Name: Docosahexaenoic Acid (DHA)
Eicosapentaenoic Acid (EPA)
Arachidonic Acid (ARA)

3. STUDY DESIGN

3.1.1. Dose Levels

Study Design

Treatment Group	Dosage Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F0 Generation (dams)	F1 Generation (puppies)	
					F	M(Spare)	F(Spare)
1. Control diet*	0	0	0.11%	0.12%	5	4(1)	4(1)
2. AOCED	½ X	0.75%	0.41%**	0.44%	5	4(1)	4(1)
3. AOCED	1X	1.5%	0.77%**	0.83%	5	4(1)	4(1)
4. AOCED	2X	3.0%	1.55%**	1.69%	5	4(1)	4(1)

* Group 1 animals received the control diet, which was formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA total content (0.11%) was achieved by using the chicken by-product meal as one of the ingredients.

** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content was the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA) and from the chicken by-product meal (0.11%).
Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.

*** Calculated based on dry matter basis (adjusted for moisture content).

M: male; F: female

4. SAMPLE COLLECTION AND ANALYSIS

4.1.1. Sample Collection

Blood samples were collected from the F0 Generation during the retreatment eriod at (b) (4) baseline after 4 to 5 weeks of treatment at (b) (4) and at weaning a (b) (4). Blood samples were collected from all selected weaned puppies (F1) at weaning at Week 13 and Week 34.

Blood samples were collected by jugular venipuncture into tubes containing K_2-EDTA as anticoagulant and kept on wet ice until centrifugation. Samples were centrifuged at 1500 g RCF for 10 minutes at +4°C (b) (4)) or room temperature (b) (4) (b) (4).

Plasma was transferred into 2 separate tubes, placed on dry ice until storage in a -70°C freezer until shipment. One set of samples was shipped overnight on dry ice to (b) (4) for fatty acid evaluation. The other set of samples was held until after the study was completed and shipped to the study sponsor (DSM, Columbia, MD) for retention.

4.1.2. Sample Receipt and Handling

Samples were shipped on dry ice to (b) (4) Once the sam les arrived at (b) (4) the sample log was signed and e-mailed to (b) (4) rica as verification of receipt of the samples. Samples were stored at -60°C to -90°C conditions until analysis was complete. If there is no need for re-analysis, the remaining samples will be stored frozen (nominally -60°C to -90°C) prior to final disposition. All remaining tissue samples will be discarded at the Study Director's discretion upon completion of the study (final report issue date).

Sample Type	Samples Received at (b) (4)	Samples Analyzed at (b) (4)
Plasma F0 Pre-treatment	8/22/17	9/27/17
Plasma F0 Gestation Day 28 (GD28)	7/21/2017	9/27/2017
Plasma F0 Postpartum Day 56	11/28/17	12/27/17
Plasma F1 Postpartum Day 56	11/28/17	12/27/17
Plasma F1 Week 13 of age	1/9/2018	1/11/2018
Plasma F1 Week 34 of age	05/24/2018	05/24/2018

4.1.3. Sample Analysis

This study was conducted in accordance with (b) (4) validated assay:

(b) (4): Whole Plasma Fatty Acid Concentrations

Plasma fatty acid concentrations was analyzed by (b) (4) using gas chromatography (GC) with flame ionization detection. Plasma was transferred to a screw-cap glass vial which contained (b) (4) , GC was carried out using a GC-2010 Gas Chromatograph (Shimadzu Corporation, Columbia, MD) equipped with a SP-2560, 100-m fused silica capillary column (0.25 mm internal diameter, 0.2 um film thickness; Supelco, Bellefonte, PA).

Fatt acids were identified b comparison with a standard mixture of fatty acids (b) (4)) which was also used to determine individual fatty acid calibration curves. The (b) (4) was used to calculate recovery efficiency of the assay and applied to all fatty acids. The following 24 fatty acids (by class) were identified: saturated (14:0, 16:0, 18:0, 20:0, 22:0 24:0); *cis* monounsaturated (16:1, 18:1, 20:1, 24:1); trans [16:1, 18:1*, 18:2* - see below for more details); *cis* n-6 polyunsaturated (18:2, 18:3, 20:2, 20:3, 20:4, 22:4, 22:5); *cis* n-3 polyunsaturated (18:3, 20:5, 22:5, 22:6). Fatty acid composition was expressed as a percent of total identified fatty acids and concentrations as µg/mL of plasma. The chromatographic conditions used in this study were sufficient to isolate the C16:1*trans* isomers and the C18:2 Δ 9t-12c, 9t-12t, and 9c-12t isomers, which is reported as C18:2n6t. However, each individual C18:1 *trans* molecular species (i.e., C18:1 Δ6 thru Δ13) could not be segregated but appeared as two blended peaks that eluted just before oleic acid. The areas of these two peaks were summed and referred to a C18:1 *trans*.

4.1.4. Data Review

DHA, EPA and ARA concentrations (µg/mL) were calculated by (b) (4). (b) (4) reviewed the raw data for accuracy.

4.1.5. Statistics

The raw data was tabulated by (b) (4). Group means and standard deviations for DHA, EPA, and ARA concentrations were calculated by sex and group by DSM. For each dietary group, male and female means were compared using a two sample T-test to determine if gender differences existed. If no differences existed, the male and female groups were combined. Dose groups comparisons at each timepoint for DHA, EPA and ARA were calculated using R statistical software version 3.4.3. Pairwise comparison adjusted (Tukey, single-step) P-values were calculated using linear models that included treatment as a categorical explanatory variable. P-Values to determine DHA, EPA and ARA changes over time by dosage in the F0 and F1 generations were calculated using linear mixed models with random intercept by animal and dose-time interaction terms.

4.1.6. Statistical Software

Descriptive statistics (means, standard deviations, T-tests) were generated using Minitab™ statistical software. Dose group and pairwise comparisons were generated using R statistical software version 3.4.3.

5. RESULTS

5.1.1. F0 generation: plasma DHA, EPA and ARA concentrations

5.1.1.1. Pretreatment F0: DHA, EPA and ARA

Table 1. *DHA, EPA and ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from F0 Generation at Pre-treatment (Figs 7-9 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group.*

	Description	DHA (n=4)	EPA (n=4)	ARA (n=4)
Group 1	Control	61.14 (8.63)[a]	20.62 (3.37)[a]	851.2 (79.1)[a]
Group 2	Low dose	83.78 (9.25)[a]	23.79 (5.67)[a]	1071.3 (102.6)[a]
Group 3	Mid dose	75.14 (17.74)[a]	27.91 (1.76)[a]	1156.0 (264.2)[a]
Group 4	High dose	73.96 (17.87)[a]	24.39 (2.69)[a]	1032.0 (207.0)[a]

[a,b] signify between group differences for each analyte ($p<0.05$)

At Pretreatment, there were no differences in DHA, EPA and ARA levels between the groups (Figs 7-9).

5.1.1.2. Gestation Day 28 F0: DHA, EPA and ARA

Table 2. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Gestation Day 28 (Figs 10-12 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group.*

	Description	DHA (n=4)	EPA (n=4)	ARA (n=4)
Group 1	Control	90.34 (6.85)[a]	15.47 (4.11)[a]	949.5 (57.9)[a]
Group 2	Low dose	223.5 (45.4)[b]	36.15 (5.16)[a,b]	965.0 (56.6)[a]
Group 3	Mid dose	313.9 (116.2)[b]	94.20 (49.8)[b,c]	1027.0 (277)[a]
Group 4	High dose	318.7 (32.3)[b]	116.1 (42.5)[c]	865.0 (235)[a]

[a,b,c] signify between group differences for each analyte ($p<0.05$)

At Gestation Day 28, DHA levels in the low, mid and high dose groups were all significantly higher than that in the control group (Fig 10). There were no statistical differences between the low, mid and high dose DHA levels at this time point.
At Gestation Day 28, dose-dependent differences were observed in EPA levels (Fig 11). The mid and high dose group EPA levels were significantly higher than the control group level. The low dose group EPA levels did not differ from the control group levels. The mid dose group EPA levels did not differ from the low and high dose group levels. The high dose group levels were significantly higher than that of the low dose group.

At Gestation Day 28, there were no differences in ARA levels between the control, low, mid and high dose groups (Fig 12).

5.1.1.3. Postpartum Day 56 F0: DHA, EPA and ARA

Table 3. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Day 56 Postpartum F0 Generation (Figs 13-15 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group.*

	Description	DHA (n=4)	EPA (n=4)	ARA (n=4)
Group 1	Control	75.29 (11.43)[a]	27.66 (4.41)[a]	1000.4 (136.1)[a]
Group 2	Low dose	319.7 (36.6)[b]	79.53 (19.80)[a]	964.2 (131.3)[a]
Group 3	Mid dose	359.6 (92.4)[b]	173.6 (44.4)[b]	809.1 (185.7)[a,b]
Group 4	High dose	391.03 (14.40)[b]	267.2 (57.9)[c]	641.0 (94.4)[b]

[a,b,c] *signify between group differences for each analyte ($p<0.05$)*

At Postpartum Day 56, DHA levels in the low, mid and high dose groups were all significantly higher than that in the control group (Fig 13). There were no statistical differences between the low, mid and high dose group DHA levels at this time point.

At Postpartum Day 56, dose-dependent increases were observed in EPA levels in the AOCED-treated groups (Fig 14). Although the low dose group EPA levels increased more than two-fold compared to the control, the difference did not reach statistical significance. The mid and high dose group EPA levels were significantly higher than that of the control and the low dose groups, and differences between the high and the mid dose groups were statistically significant.

At Postpartum Day 56, the low and mid dose group ARA levels were statistically the same as in the control group (Fig 15). The high dose group ARA levels were significantly lower than the control and low dose group levels but were the same as the mid dose ARA levels at this timepoint.

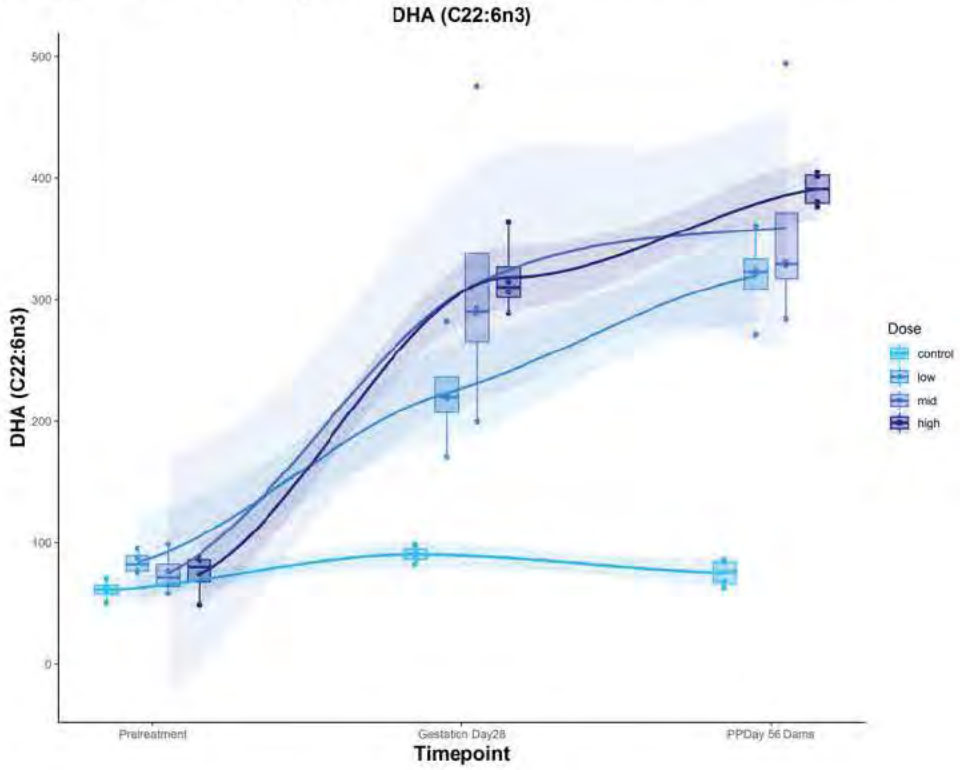
5.1.1.4. F0: DHA changes over time

Table 4. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids of F0 Generation. At each timepoint Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group.*

DHA	Description	Pretreat F0	GD28 F0	PPD56 F0
Group 1	Control	61.14 (8.63)	90.34 (6.85)	75.29 (11.43)
Group 2	Low dose	83.78 (9.25)	223.5 (45.4)	319.7 (36.6)
Group 3	Mid dose	75.14 (17.74)	313.9 (116.2)	359.6 (92.4)
Group 4	High dose	73.96 (17.87)	318.7 (32.3)	391.03 (14.40)

A linear mixed model which included a random intercept by subject was employed to model simultaneously the effect of dose, time and dose-time interaction. F-tests were used to test the impact of each variable on DHA. These tests revealed overall significant effects of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p<0.001$). Individual interaction terms indicated whether treatment groups evolved differently over time. All treatment groups increased significantly more than the control group at all timepoints (all $p<0.001$ and increase >200 *µg/mL* versus the control group, except low dose group at Gestation Day 28 with $p=0.004$, where the increase over time versus the control group was 110.48 *µg/mL*). (Fig 1)

Figure 1. *F0 Generation DHA Levels from Fatty Acid Analysis of Plasma Total Lipids at each timepoint for control and each dose group. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group*



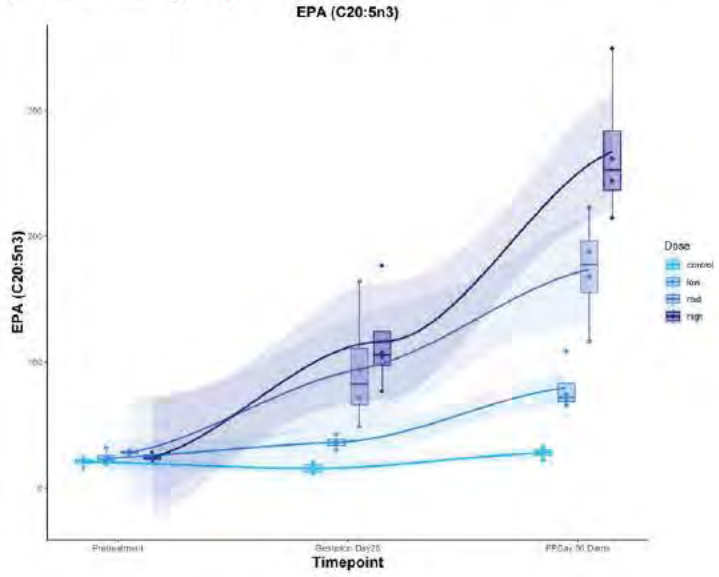
5.1.1.5. F0: EPA changes over time

Table 5. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids of F0 Generation. At each timepoint Values are given as Mean (SD) and expressed as µg/mL n=4 in each group.*

EPA	Description	Pretreat F0	GD28 F0	PPD56 F0
Group 1	Control	20.62 (3.37)	15.47 (4.11)	27.66 (4.41)
Group 2	Low dose	23.79 (5.67)	36.15 (5.16)	79.53 (19.80)
Group 3	Mid dose	27.91 (1.76)	94.20 (49.8)	173.6 (44.4)
Group 4	High dose	24.39 (2.69)	116.1 (42.5)	267.2 (57.9)

A linear mixed model which included a random intercept by subject was employed to model simultaneously the effect of dose, time and dose-time interaction. F-tests were used to test the impact of each variable on EPA. These tests revealed overall significant effects of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p<0.001$). Individual interaction terms indicated whether treatment groups evolved differently versus control over time. For the low dose group, the changes from pretreatment to Gestation Day 28 and to Postpartum Day 56 were not significantly different versus the control group (17.510 *µg/mL*, $p = 0.521$ for Gestation Day 28 and 48.698 *µg/mL*, $p = 0.083$ for Postpartum Day 56). For the mid dose group, the increase from pretreatment to Gestation Day 28 was significant (71.469 *µg/mL*, $p=0.014$) versus the control group. From Pretreatment to Postpartum Day 56 the increase versus the control group was even higher (138.62 *µg/mL*, $p<0.001$). For the high dose group, the increase from pretreatment to Gestation Day 28 was significant (96.903 *µg/mL*, $p=0.001$) versus the control group. From Pretreatment to Postpartum Day 56 the increase versus the control group was even higher (235.76 *µg/mL*, $p<0.001$). (Fig 2).

Figure 2. *F0 Generation EPA Levels from Fatty Acid Analysis of Plasma Total Lipids at each timepoint for control and each dose group. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group*



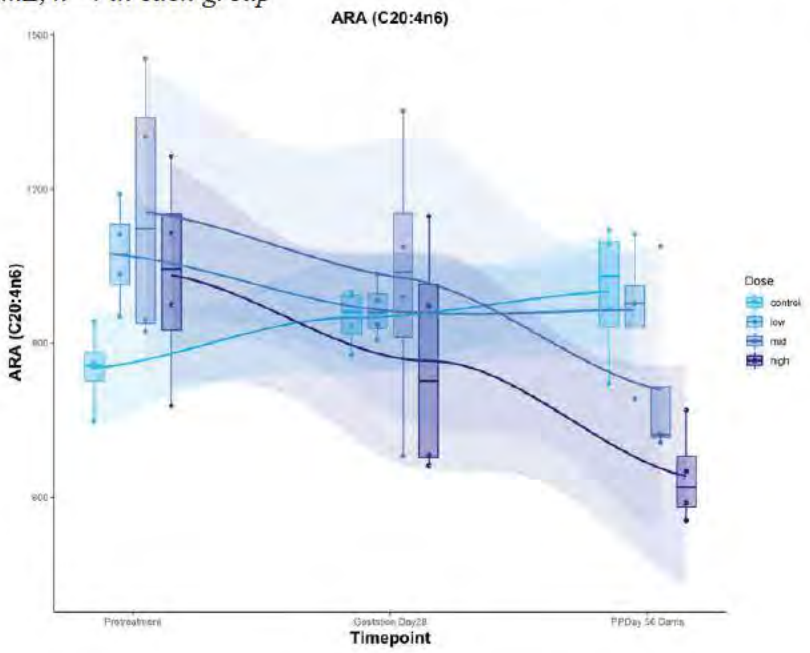
5.1.1.6. F0: ARA changes over time

Table 6. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids of F0 Generation. At each timepoint Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group.*

ARA	Description	Pretreat F0	GD28 F0	PPD56 F0
Group 1	Control	851.2 (79.1)	949.5 (57.9)	1000.4 (136.1)
Group 2	Low dose	1071.3 (102.6)	965.0 (56.6)	964.2 (131.3)
Group 3	Mid dose	1156.0 (264)	1027.0 (277)	809.1 (185.7)
Group 4	High dose	1032 (207)	865.0 (235)	641.0 (94.4)

A linear mixed model which included a random intercept by subject was employed to model simultaneously the effect of dose, time and dose-time interaction. F-tests were used to test the impact of each variable on ARA. For ARA, there was a significant effect of time ($p<0.001$), no significant effect of dose ($p<0.443$) but significant dose-time interaction ($p<0.001$). For the low dose group (½X), the changes from Pretreatment to GD 28 were not significantly different versus the control group (-204.562 *µg/mL*, $p = 0.061$) but were significantly different from Pretreatment to PPD 56 (-256.381 *µg/ml*, $p=0.022$). For the mid dose group (1X), the decrease from pretreatment to GD 28 was significant (-226.306 *µg/ml*, $p=0.04$) versus the control group. From Pretreatment to PPD 56 the decrease versus the control group was even higher (-495.068 *µg/ml*, $p<0.001$). For the high dose group (2X), the decrease from pretreatment to GD 28 was significant (-265.004 *µg/ml*, $p=0.018$) versus the control group. From Pretreatment to PPD 56 the decrease versus the control group was even higher (-540.477 *µg/ml*, $p<0.001$). (Fig 3)

Figure 3. *F0 Generation ARA Levels from Fatty Acid Analysis of Plasma Total Lipids at each timepoint for control and each dose group. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group*



5.1.2. F1 Generation: plasma DHA, EPA and ARA concentrations

5.1.2.1. Postpartum Day 56: F1 DHA

Table 7. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56 F1 Generation (Fig 16 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

DHA	Description	PPD56 F1 Females n=4	PPD56 F1 Males n=4	PPD56 F1 Combined n=8
Group 1	Control	138.33 (3.70)	138.89 (17.98)	138.61 (12.02)[a]
Group 2	Low dose	289.3 (24.7)	301.8 (24.3)	295.52 (23.68)[b]
Group 3	Mid dose	365.1 (51.4)	341.7 (35.9)	353.40 (42.9)[c]
Group 4	High dose	340.30 (34.7)	339.01 (13.43)	339.65 (24.37)[c]

At Postpartum Day 56, there were no significant differences between male and female DHA plasma levels in any of the dose groups, therefore genders were combined
[a,b,c] signify between group differences ($p<0.05$)

At Postpartum Day 56, the low, mid and high dose group DHA levels were all significantly higher than in the control group. Differences between groups were statistically significant between the low and mid dose groups but not between the mid and high dose groups.

5.1.2.2. Postpartum Day 56 F1: EPA

Table 8. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56 F1 Generation (Fig 17 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

EPA	Description	PPD56 F1 Females n=4	PPD56 F1 Males n=4	PPD56 F1 Combined n=8
Group 1	Control	14.43 (3.21)	14.24 (1.84)	14.33 (2.42)[a]
Group 2	Low dose	49.88 (13.56)	48.29 (5.94)	49.08 (9.73)[b]
Group 3	Mid dose	107.59 (14.94)	94.6 (21.4)	101.11 (18.42)[c]
Group 4	High dose	147.3 (30.4)	142.8 (31.7)	145.0 (28.9)[d]

At Postpartum Day 56, there were no significant differences between male and female EPA plasma levels in any of the dose groups, therefore genders were combined
[a,b,c,d] signify between group differences ($p<0.05$)

At Postpartum Day 56, the low, mid and high dose group EPA levels were all significantly higher than that in the control group. There was a dose dependent increase in EPA concentrations across the three doses.

5.1.2.3. Postpartum Day 56 F1: ARA

Table 9. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56 F1 Generation (Fig 18 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

ARA	Description	PPD56 F1 Females n=4	PPD56 F1 Males n=4	PPD56 F1 Combined n=8
Group 1	Control	855.3 (59.3)	851.8 (68.2)	853.0 (59.2)[a]
Group 2	Low dose	784.7 (100.9)	764.9 (64.4)	774.8 (79.1)[a]
Group 3	Mid dose	803.5 (136.2)	703.6 (84.2)	753.5 (117.6)[a]
Group 4	High dose	479.2 (69.2)	478.7 (85.0)	479.0 (71.8)[b]

At Postpartum Day 56, there were no significant differences between male and female ARA plasma levels in any of the dose groups, therefore genders were combined
[a,b,] signify between group differences ($p<0.05$)

At Postpartum Day 56, the low and mid dose group ARA levels did not differ from control group levels and were equivalent to each other. The high dose group ARA level was significantly lower than those in other dose groups and the control at this timepoint.

5.1.2.4. Week 13 F1: DHA

Table 10. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 13 F1 Generation (Fig 19 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

DHA	Description	Week 13 F1 Females n=4	Week 13 F1 Males n=4	Week 13 F1 Combined n=8
Group 1	Control	152.76 (11.3)	147.85 (18.11)	150.31 (14.22)[a]
Group 2	Low dose	268.1 (23.2)	297.1 (20.7)	282.6 (25.6)[b]
Group 3	Mid dose	349.0 (42.9)	326.8 (16.3)	337.9 (32.3)[c]
Group 4	High dose	380.6 (37.8)	347.0 (25.7)	363.8 (34.9)[c]

At Week 13, there were no significant differences between male and female DHA plasma levels in any of the dose groups, therefore genders were combined.
[a,b,c] signify between group differences ($p<0.05$)

At Week 13, the low, mid and high dose group DHA levels were all significantly higher than that in the control group. DHA levels increased significantly between the low and mid dose group but not between the mid and high dose group.

5.1.2.5. Week 13 F1: EPA

Table 11. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 13 F1 Generation (Fig 20 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

EPA	Description	Week 13 F1 Males n=4	Week 13 F1 Males n=4	Week 13 F1 Combined n=8
Group 1	Control	17.34 (2.09)	17.75 (2.08)	17.55 (1.94)[a]
Group 2	Low dose	57.13 (8.57)	58.84 (6.11)	57.98 (6.95)[b]
Group 3	Mid dose	120.44 (10.00)	109.61 (11.21)	115.03 (11.41)[c]
Group 4	High dose	181.7 0 (34.9)	183.5 (10.45)	182.58 (23.89)[d]

At Week 13, there were no significant differences between male and female EPA plasma levels in any of the dose groups, therefore genders were combined.
[a,b,c,d] signify between group differences (p<0.05)

At Week 13, the low, mid and high dose group EPA levels were significantly higher than that in the control group. There was a dose dependent increase in EPA levels across all three dose levels.

5.1.2.6. Week 13 F1: ARA

Table 12. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 13 F1 Generation (Fig 21 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

ARA	Description	Week 13 F1 Males n=4	Week 13 F1 Males n=4	Week 13 F1 Combined n=8
Group 1	Control	979.33 (16.55)	989.0 (99.3)	984.2 (66.1)[a]
Group 2	Low dose	858.8 (88.6)	885.1 (44.7)	872.0 (66.5)[b]
Group 3	Mid dose	795.5 (110.8)	740.1 (92.0)	767.8 (98.8)[c]
Group 4	High dose	639.3 (66.1)	590.7 (47.5)	615.0 (59.3)[d]

At Week 13, there were no significant differences between male and female ARA plasma levels in any of the dose groups, therefore genders were combined.
[a,b,c,d] signify between group differences (p<0.05)

At Week 13, the low, mid and high dose group ARA levels were all significantly lower than that in the control group. There was a dose dependent decrease in ARA levels across all three dose levels.

5.1.2.7. Week 34 F1: DHA

Table 13. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 34 F1 Generation (Fig 22 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

DHA	Description	Week 34 F1 Females n=4	Week 34 F1 Males n=4	Week 34 F1 Combined n=8
Group 1	Control	98.44 (18.54)	100.12 (8.34)	99.28 (13.34)[a]
Group 2	Low dose	219.9 (28.0)	254.83 (13.06)	237.35 (27.52)[b]
Group 3	Mid dose	287.1 (25.6)	250.1 (32.8)	268.6 (33.70)[b]
Group 4	High dose	365.0 (40.3)	312.0 (50.8)	338.5 (51.0)[c]

At Week 34, there were no significant differences between male and female DHA plasma levels in any of the dose groups, therefore genders were combined.
[a,b,c] signify between group differences ($p<0.05$)

At Week 34, the low, mid and high dose group DHA levels were significantly higher than that in the control group. DHA levels did not differ significantly between the low and mid dose groups but were different between the mid and high dose levels.

5.1.2.8. Week 34 F1: EPA

Table 14. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 34 F1 Generation (Fig 23 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

EPA	Description	Week 34 F1 Females n=4	Week 34 F1 Males n=4	Week 34 F1 Combined n=8
Group 1	Control	17.32 (2.41)	15.19 (1.03)	16.26 (2.06)[a]
Group 2	Low dose	61.6 (24.1)	57.39 (9.51)	59.50 (17.09)[b]
Group 3	Mid dose	118.40 (18.43)	100.78 (12.89)	109.59 (17.47)[c]
Group 4	High dose	198.0 (21.8)	213.8 (42.7)	205.9 (32.5)[d]

At Week 34, there were no significant differences between male and female EPA plasma levels in any of the dose groups, therefore genders were combined.
[a,b,c,d] signify between group differences ($p<0.05$)

At Week 34, the low, mid and high dose group EPA levels were all significantly higher than that in the control group. There was a dose dependent increase in EPA levels across all three dose levels.

5.1.2.9. Week 34 F1: ARA

Table 15. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 34 F1 Generation (Fig 24 in APPENDIX). Values are given as Mean (SD) and expressed as µg/mL.*

ARA	Description	Week 34 F1 Females n=4	Week 34 F1 Males n=4	Week 34 F1 Combined n=8
Group 1	Control	1077.7 (151.5)	1105.0 (81.8)	1091.4 (113.7)[a]
Group 2	Low dose	919.9 (164.3)	989.0 (94.7)	954.4 (129.5)[a,b]
Group 3	Mid dose	809.3 (73.8)	810.8 (89.3)	810.0 (75.8)[b,c]
Group 4	High dose	786.5 (106.3)	704.4 (108.6)	745.4 (108.8)[c]

At Week 34, there were no significant differences between male and female ARA plasma levels in any of the dose groups, therefore genders were combined.
[a,b,c] signify between group differences ($p<0.05$)

At Week 34, the mid and high dose group ARA levels were significantly lower than the control group level. The low dose group ARA levels did not differ from that in the control. The mid dose group ARA level did not differ from the low and high dose group levels. The high dose group level was significantly lower than that in the low dose.

5.1.2.10. F1: DHA changes over time

Table 16. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids of F1 Generation. At each timepoint Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*

DHA	Description	PPD 56 F1	Week 13 F1	Week 34 F1
Group 1	Control	138.61 (12.02)	150.31 (14.22)	99.28 (13.34)
Group 2	Low dose	295.52 (23.68)	282.6 (25.58)	237.35 (27.52)
Group 3	Mid dose	353.40 (42.9)	337.9 (32.3)	268.6 (33.70)
Group 4	High dose	339.65 (24.37)	363.8 (34.9)	338.5 (51.0)

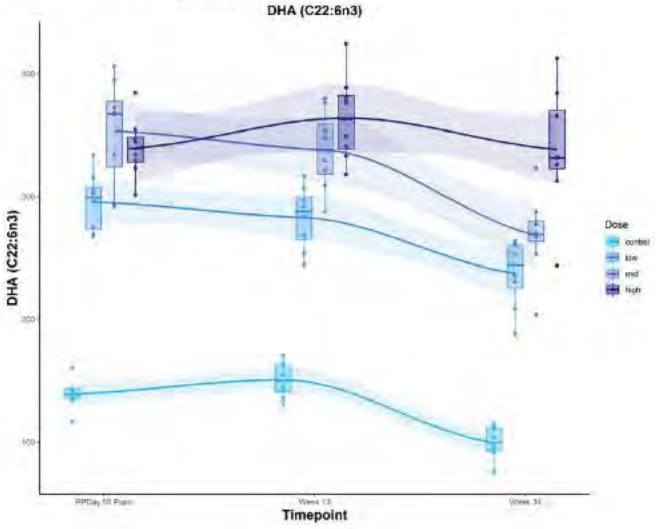
A linear mixed model which included a random intercept by subject was employed to model simultaneously the effect of dose, time and dose-time interaction. F-tests were used to test the impact of each variable on DHA. These tests revealed overall significant effects of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p<0.001$). Individual interaction terms indicated whether treatment groups evolved differently over time.

For the low dose group, the changes from Postpartum Day 56 to Week 13 and Week 34 were not significantly different versus the control group (-24.62 *µg/mL*, $p = 0.101$ for week 13 and -18.841 *µg/mL*, $p = 0.207$ for week 34).

For the mid dose group, the change from Postpartum Day 56 to Week 13 was not significant (-27.191 *µg/mL*, $p=0.071$) versus the control group. From Postpartum Day 56 to Week 34 the decrease was significantly different versus the control group (additional decrease by 45.432 *µg/mL*, $p=0.003$).

For the high dose group, the change from Postpartum Day 56 to Week 13 was not significant (12.455 *µg/mL*, $p=0.402$) versus the control group. From Postpartum Day 56 to Week 34 the change was significantly different versus the control group (38.14 *µg/mL*, $p=0.012$). (Figure 4)

Figure 4. *F1 Generation DHA Levels from Fatty Acid Analysis of Plasma Total Lipids at each timepoint for control and each dose group. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



5.1.2.11. F1: EPA changes over time

Table 17. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids of F1 Generation. At each timepoint Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*

EPA	Description	PPD 56 F1	Week 13 F1	Week 34 F1
Group 1	Control	14.33 (2.42)	17.55 (1.94)	16.26 (2.06)
Group 2	Low dose	49.08 (9.73)	57.98 (6.95)	59.50 (17.09)
Group 3	Mid dose	101.11(18.42)	115.03 (11.41)	109.59 (17.47)
Group 4	High dose	145.0 (28.9)	182.58 (23.89)	205.9 (32.5)

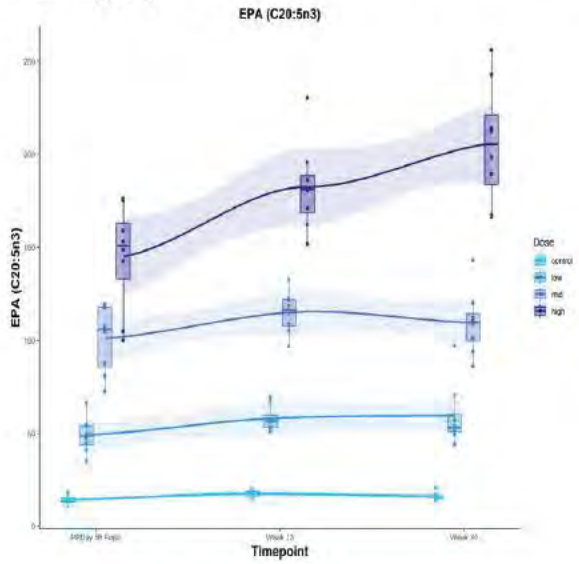
A linear mixed model which included a random intercept by subject was employed to model simultaneously the effect of dose, time and dose-time interaction. F-tests were used to test the impact of each variable on EPA. These tests revealed overall significant effects of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p<0.001$). Individual interaction terms indicated whether treatment groups evolved differently over time.

For the low dose group, the increases from Postpartum Day 56 to Week 13 and Week 34 were not significantly different versus the control group (5.687 *µg/mL*, $p = 0.578$ for Week 13 and 8.498 *µg/mL*, $p = 0.407$ for Week 34).

For the mid dose group, the increases from Postpartum Day 56 to Week 13 and Week 34 were not significantly different versus the control group (10.709 *µg/mL*, $p = 0.297$ for Week 13 and 6.592 *µg/mL*, $p = 0.521$ for Week 34).

For the high dose group, the increases from Postpartum Day 56 to Week 13 and Week 34 were significantly different versus the control group (34.327 *µg/mL*, $p = 0.001$ for Week 13 and 58.959 *µg/mL*, $p<0.001$ for Week 34). (Figure 5)

Figure 5. *F1 Generation EPA Levels from Fatty Acid Analysis of Plasma Total Lipids at each timepoint for control and each dose group. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



5.1.2.12. F1: ARA changes over time

Table 18. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids of F1 Generation. At each timepoint Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group.*

ARA	Description	PPD56 F1	Week 13 F1	Week 34 F1
Group 1	Control	853.0 (59.2)	984.2 (66.1)	1091.4 (113.7)
Group 2	Low dose	774.8 (79.1)	872.0 (66.5)	954.4 (129.5)
Group 3	Mid dose	753.5 (117.6)	767.8 (98.8)	810.0 (75.8)
Group 4	High dose	479.0 (71.8)	615.0 (59.3)	745.4 (108.8)

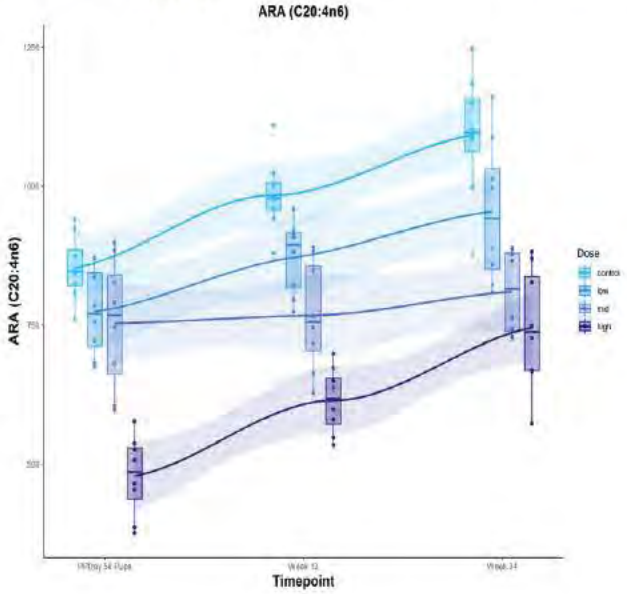
A linear mixed model which included a random intercept by subject was employed to model simultaneously the effect of dose, time and dose-time interaction. F-tests were used to test the impact of each variable on ARA. These tests revealed overall significant effects of time ($p<0.001$), dose ($p<0.001$) and dose-time interaction ($p=0.004$). Individual interaction terms indicated whether treatment groups evolved differently over time.

For the low dose group, the changes from Postpartum Day 56 to Week 13 and Week 34 were not significantly different versus the control group (-33.96 *µg/mL*, $p = 0.489$ for Week 13 and -58.669 *µg/mL*, $p = 0.234$ for Week 34).

For the mid dose group, the changes from Postpartum Day 56 to Week 13 and Week 34 were significantly different versus the control group (-116.878 *µg/mL*, $p = 0.02$ for Week 13 and -181.825 *µg/mL*, $p<0.001$ for Week 34).

For the high dose group, the changes from Postpartum Day 56 to Week 13 and Week 34 were not significantly different versus the control group (4.837 *µg/mL*, $p = 0.921$ for Week 13 and -28.138 *µg/mL*, $p = 0.566$ for Week 34). (Figure 6)

Figure 6. *F1 Generation ARA Levels from Fatty Acid Analysis of Plasma Total Lipids at each timepoint for control and each dose group. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



6. SUMMARY

Algal Oil containing EPA and DHA (AOCED) was administered via the diet at three dose levels to female dogs (F0 generation) starting at mating and throughout gestation and lactation. Plasma fatty acid profiles were assessed at Pretreatment, Gestation Day 28 and Postpartum Day 56. The offspring of treated females received their dams corresponding diets for 26 weeks after weaning. Plasma fatty acids of puppies (F1 generation) were assessed at weaning (Postpartum Day 56), and at Weeks 13 and 34 of age.

AOCED as a source of EPA and DHA was bioavailable to both generations as demonstrated by the increases in plasma levels of these fatty acids compared to the control and baseline (pretreatment) levels.

In the F0 generation, DHA and EPA levels in the mid and high dose groups were significantly higher than control levels and baseline at each timepoint. In the low dose AOCED group, DHA levels also substantially increased compared to the control and baseline while EPA increases did not reach statistical significance compared to the control.

In the F1 generation, DHA and EPA levels were significantly higher than those in the control at each timepoint and at all three dose levels. EPA increases were dose-dependent at each timepoint while those of DHA, although were generally dose-dependent, did not reach statistical significance at every timepoint. This could be related to substantially higher amounts of DHA in AOCED compare to EPA leading to earlier saturation of DHA in plasma.

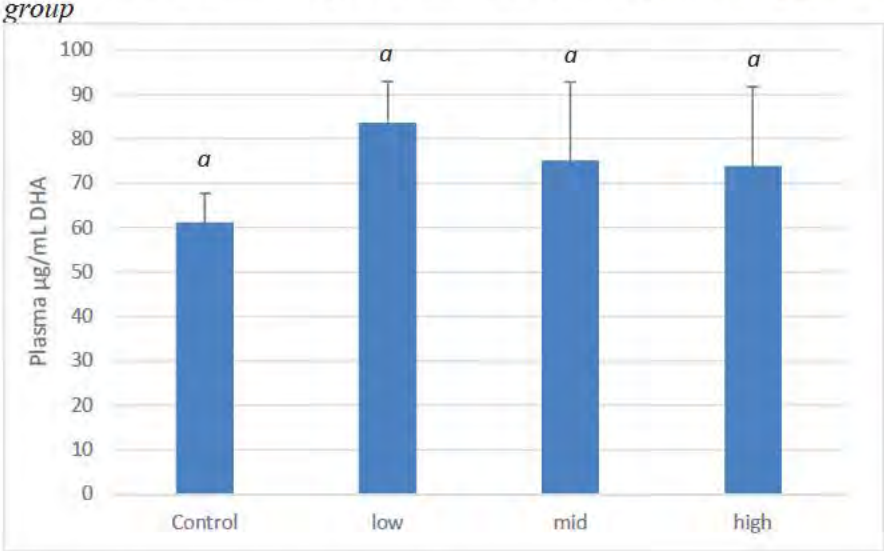
Since arachidonic acid (ARA) is known to compete with DHA and EPA for inclusion in membrane phospholipids, we analyzed ARA levels in the study as well. ARA levels indeed decreased in the F0 generation but not in the F1 generation. This may be due to the presence ARA in the diets, sufficient to maintain and even increase ARA levels after weaning of puppies. At earlier stages of the development, during lactation, their dams provided ARA via milk could have depleted their own ARA deposits.

7. DATA RETENTION

All raw data, documentation, records, study plan and the final report generated as a result of this study will be retained at DSM, or an approved archive facility contracted by DSM for a period of 5 years following completion of the study (final report issue date).

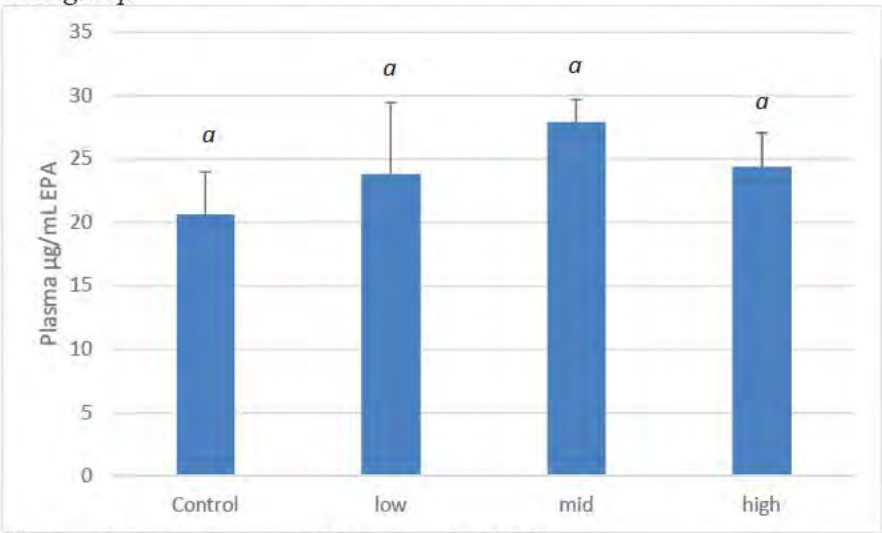
8. APPENDIX

Figure 7. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Pretreated*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



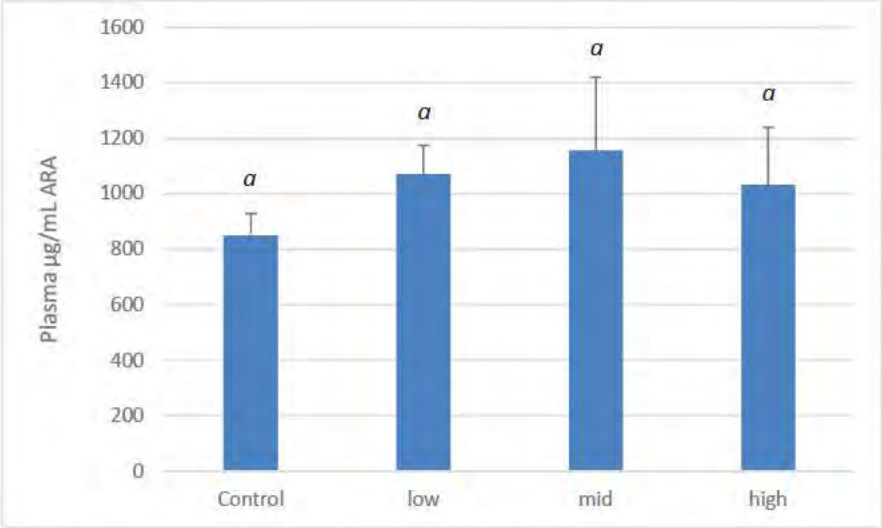
[a] *signify between group differences (p<0.05)*

Figure 8. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Pretreated*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



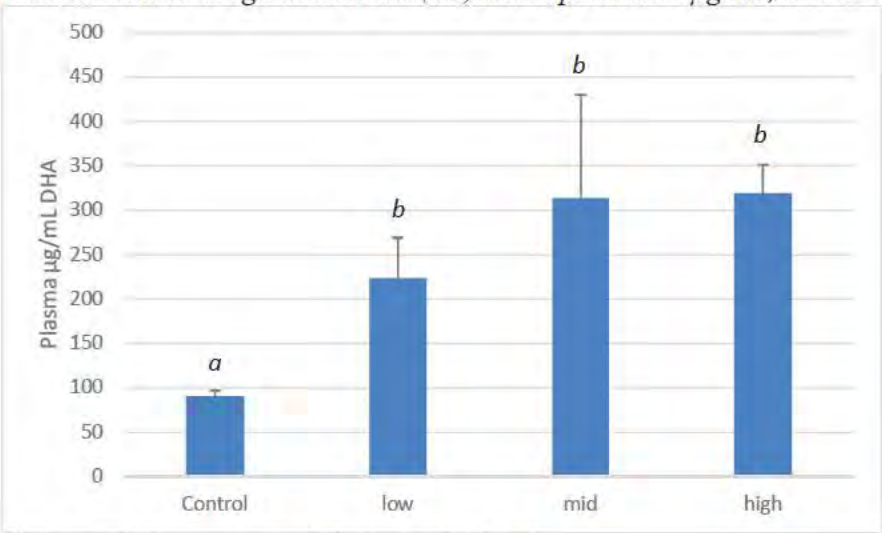
[a,b] *signify between group differences (p<0.05)*

Figure 9. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Pretreated*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



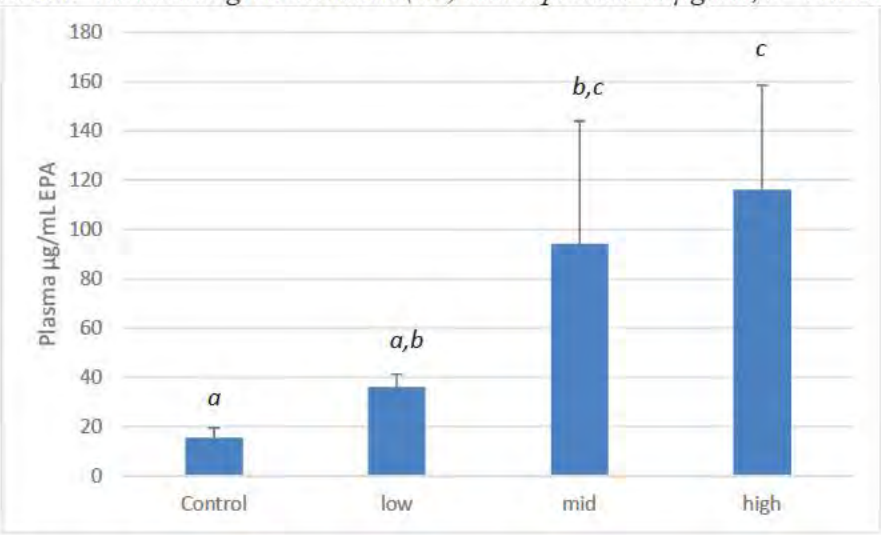
[a] *signify between group differences (p<0.05)*

Figure 10. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Gestation Day 28*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



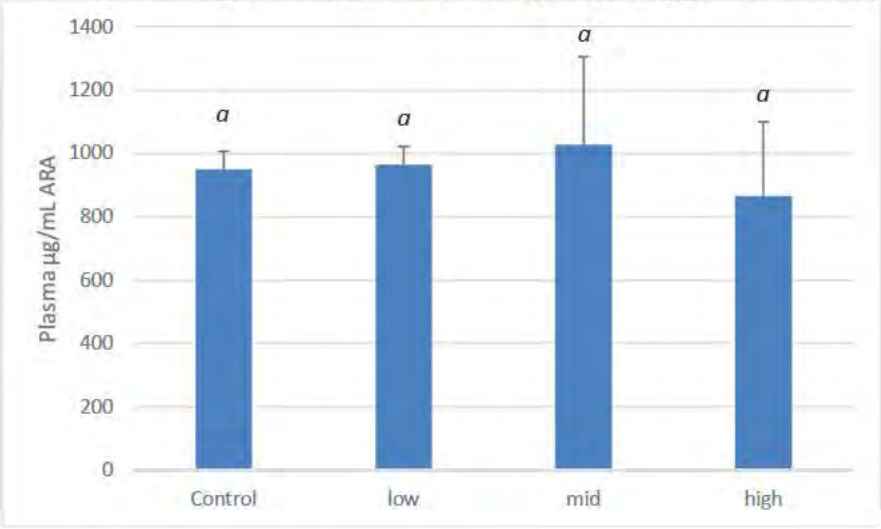
[a,b] *signify between group differences (p<0.05)*

Figure 11. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Gestation Day 28*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



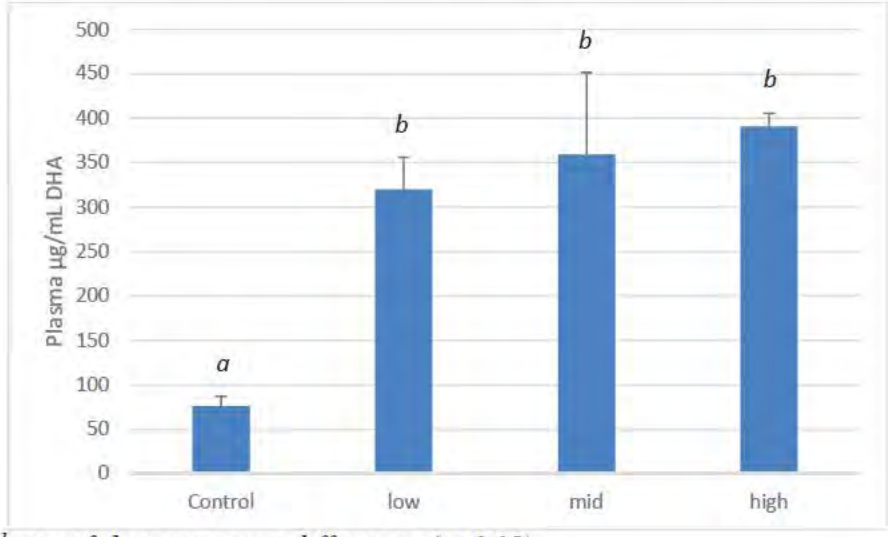
[a,b,c,d] signify between group differences (p<0.05)

Figure 12. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Gestation Day 28*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



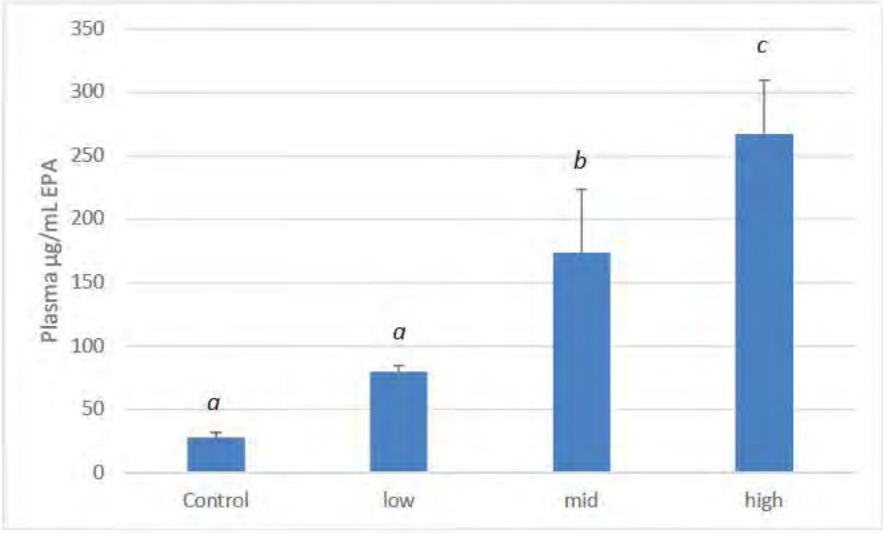
[a,b] signify between group differences (p<0.05)

Figure 13. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



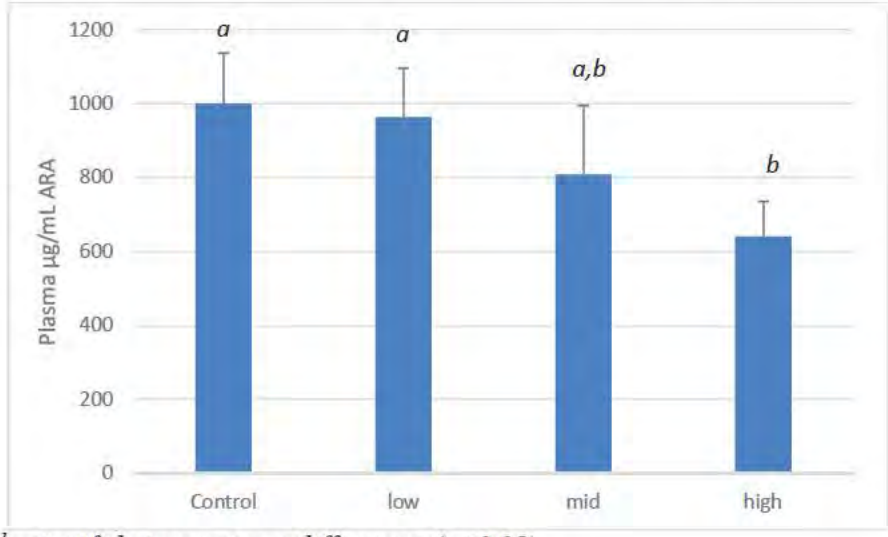
[a,b] *signify between group differences (p<0.05)*

Figure 14. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



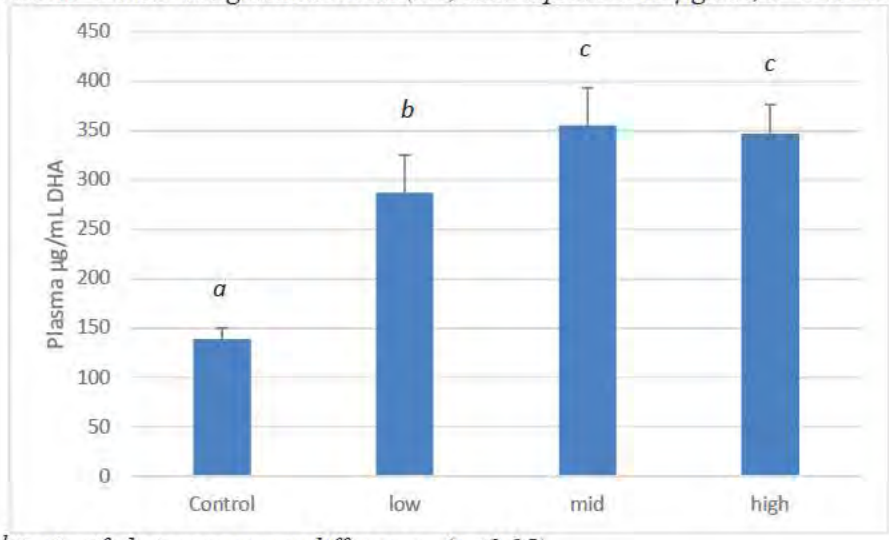
[a,b,c] *signify between group differences (p<0.05)*

Figure 15. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56*
F0 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=4 in each group



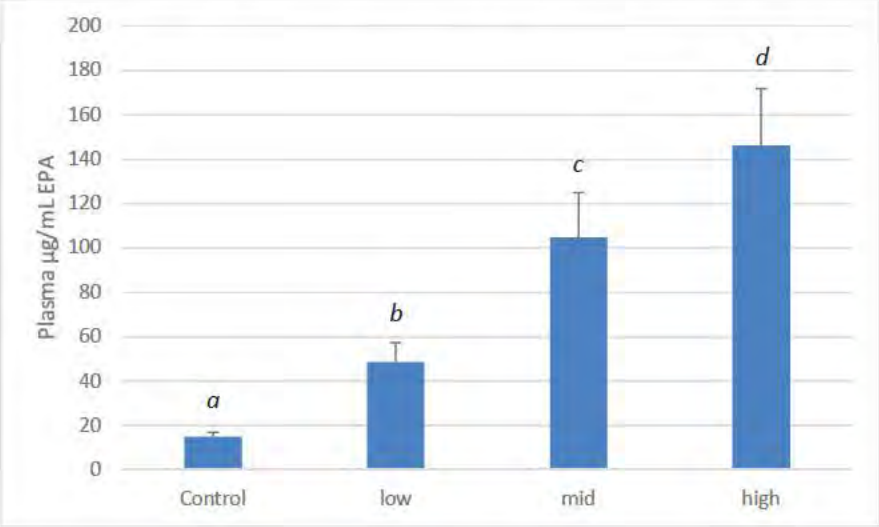
a,b, signify between group differences (p<0.05)

Figure 16. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56*
F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group



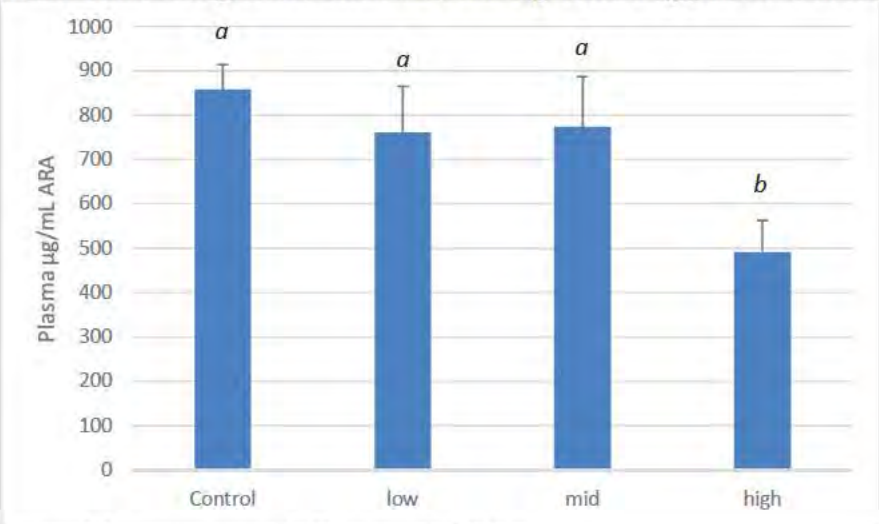
a,b,c signify between group differences (p<0.05)

Figure 17. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56*
F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group



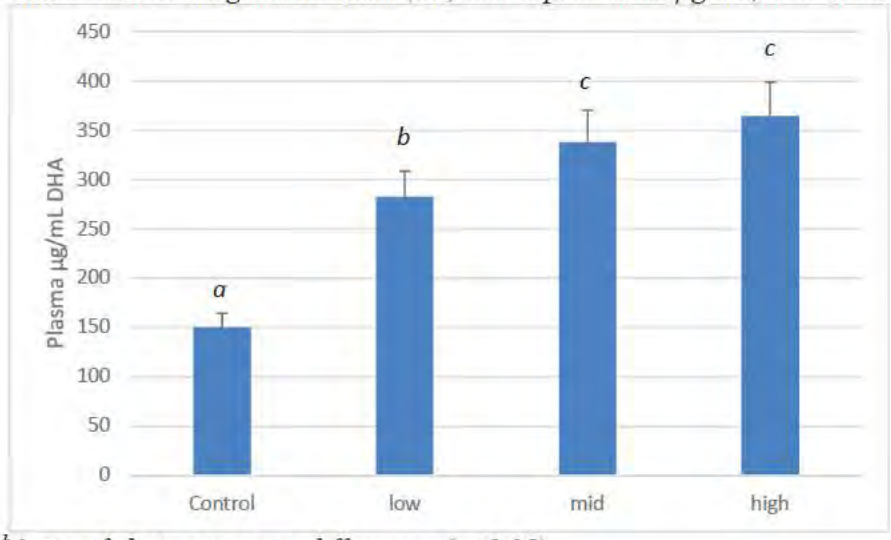
a,b,c,d signify between group differences (p<0.05)

Figure 18. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Postpartum Day 56*
F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group



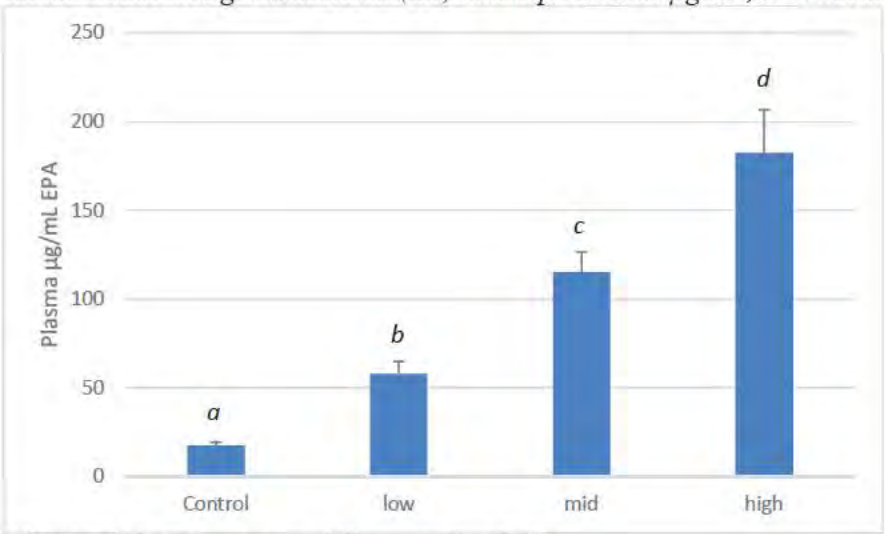
a,b signify between group differences (p<0.05)

Figure 19. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 13 F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



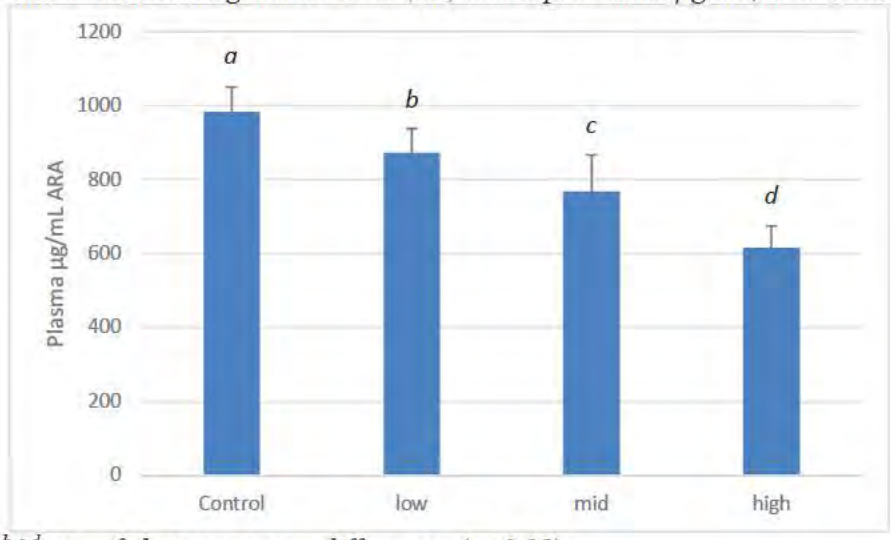
a,b,c signify between group differences (p<0.05)

Figure 20. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 13 F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



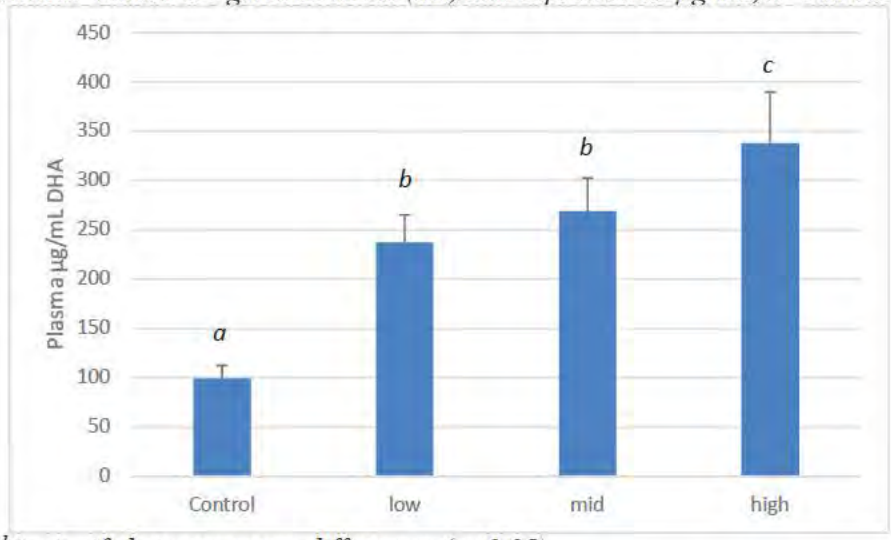
a,b,c,d signify between group differences (p<0.05)

Figure 21. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 13 F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



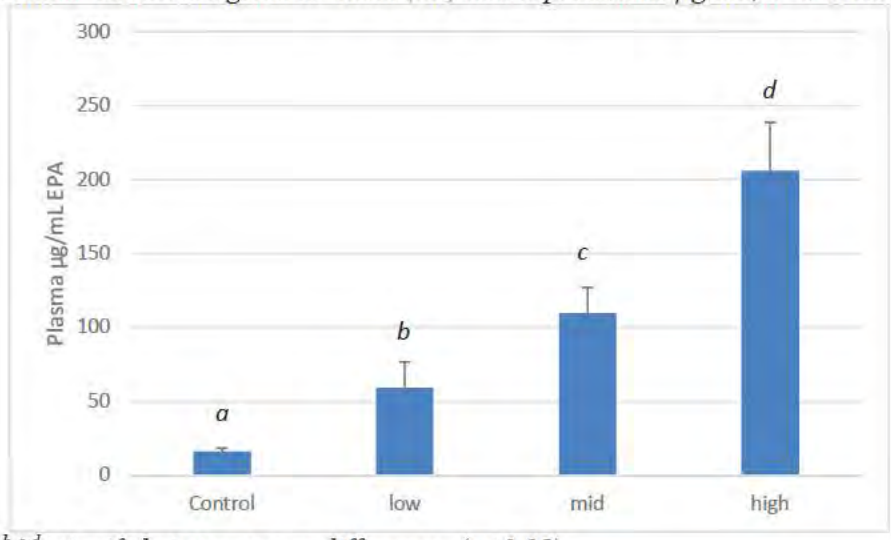
^{a,b,c,d} *signify between group differences ($p<0.05$)*

Figure 22. *DHA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 34 F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



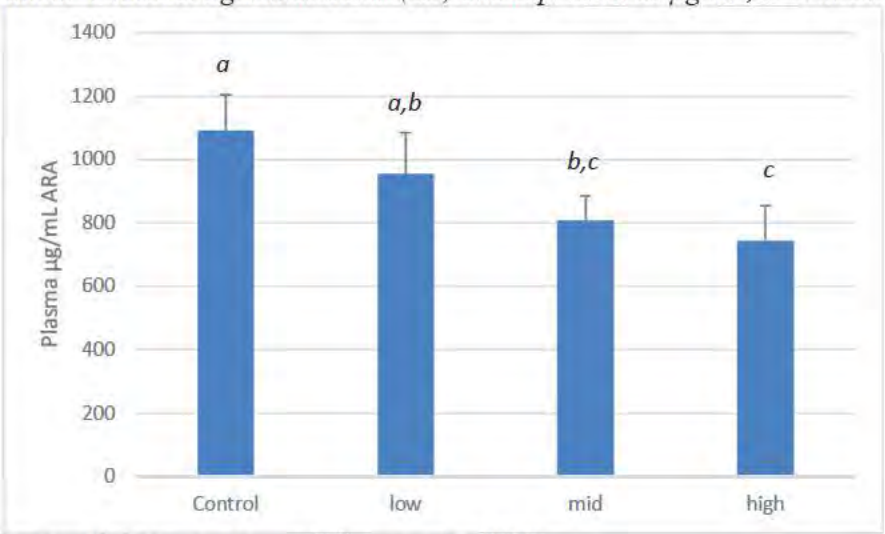
^{a,b,c} *signify between group differences ($p<0.05$)*

Figure 23. *EPA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 34 F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



a,b,c,d signify between group differences (p<0.05)

Figure 24. *ARA Levels from Fatty Acid Analysis of Plasma Total Lipids from Week 34 F1 Generation. Values are given as Mean (SD) and expressed as µg/mL, n=8 in each group*



a,b,c signify between group differences (p<0.05)

9. INDIVIDUAL DATA

F0 ID	Dose	Gender	Pretreat DHA	GD28 DHA	PPD56 DHA
(b) (4)					

F0 ID	Dose	Gender	Pretreat EPA	GD28 EPA	PPD56 EPA
(b) (4)					

F0 ID	Dose	Gender	Pretreat ARA	GD28 ARA	PPD56 ARA
					(b) (4)

F1 ID	Dose	Gender	PPD56 DHA	Week13 DHA	Week 34 DHA
(b) (4)					

F1 ID	Dose	Gender	PPD56 EPA	Week13 EPA	Week 34 EPA
(b) (4)					

F1 ID	Dose	Gender	PPD56 ARA	Week13 ARA	Week 34 ARA
(b) (4)					

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10. SIGNATURES

Responsible Scientist Approval

(b) (4), (b) (6)

09/28/18
Date

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F0 AND F1 GENERATIONS

The following abbreviations have been used throughout the appendix and/or summary table.

SD: Standard Deviation

MIN: Minimum

MAX: Maximum

N: Number of Animals

On Summary Table No. 49, data for F_0 and F_1 generations are presented.

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F0 GENERATION – GESTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	DAM No.	Days 0 to 6	Days 7 to 13	Days 14 to 20	Days 21 to 27	Days 28 to 34
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	5	5	5	5	5
2	(b) (4)					
	MEAN	156.781	191.567	138.738	88.373	83.959
	SD	15.340	16.837	26.080	25.218	20.153
	MIN	130.61	175.31	112.50	47.60	65.77
	MAX	170.23	219.76	178.71	110.82	112.72
	N	5	5	5	5	5
3	(b) (4)					
	MEAN	229.058	324.745	234.625	167 194	202.772
	SD	48.987	58.048	52.310	40.033	87.221
	MIN	176.52	252.00	184.48	115.79	108 53
	MAX	281.63	386.99	309.34	216.71	301 30
	N	5	5	5	5	5
4	(b) (4)					
	MEAN	464.138	749.502	495.416	313 187	289 247
	SD	172.881	108.786	170.823	59.410	189.859
	MIN	282.60	581.51	241.94	240.35	105.08
	MAX	697.74	883.93	636.13	382.74	547.67
	N	5	5	5	5	5

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F0 GENERATION – GESTATION PERIOD
FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	DAM No.	Days 35 to 41	Days 42 to 48	Days 49 to 55	Days 56 to 62
1	(b) (4)				
	MEAN	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00
	N	5	5	5	5
2	(b) (4)				
	SD	13.628	40.612	31.611	22.794
	MIN	135.27	116.43	95.96	97.12
	MAX	171.07	205.32	179.88	159.28
	N	5	5	5	5
3	(b) (4)				
	MEAN	304.340	283.671	266.331	224.257
	SD	78.196	31.412	36.873	80.591
	MIN	229.31	230.51	211.00	137.39
	MAX	434.16	307.21	301.56	333.54
	N	5	5	5	5
4	(b) (4)				
	MEAN	562.529	654.179	435.021	310.954
	SD	253.955	138.191	172.989	55.531
	MIN	211.19	538.94	128.88	226.91
	MAX	838.37	880.71	545.57	381.52
	N	5	5	5	5

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F0 GENERATION – LACTATION - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	DAM No.	Days 0 to 6	Days 7 to 13	Days 14 to 20	Days 21 to 27	Days 28 to 34
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	5	5	5	5	5
2	(b) (4)					
	MEAN	209.852	352.321	371.503	414.998	419.622
	SD	126.354	44.586	54.795	42.125	56.387
	MIN	0.37	300.54	296.39	360.85	336.82
	MAX	303.13	408.04	427.91	459.15	458.64
	N	5	4	4	4	4
3	(b) (4)					
	MEAN	378.339	625.242	801.247	838.068	915.333
	SD	216.054	83.673	145.328	94.972	90.384
	MIN	113.84	542.71	695.77	743.76	794 18
	MAX	701.76	740.32	1014.99	952.75	1005.17
	N	5	4	4	4	4
4	(b) (4)					
	MEAN	799.752	1162.251	1417.365	1610.404	1680.543
	SD	332.730	176.368	73.593	134.744	151.637
	MIN	474.49	956.68	1316.93	1489.46	1492.14
	MAX	1125.00	1379.32	1481.74	1803.26	1810.49
	N	4	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	DAM No.	Days 35 to 41	Days 42 to 48	Days 49 to 55
1	(b) (4)			
	MEAN	0.000	0.000	0.000
	SD	0.000	0.000	0.000
	MIN	0.00	0.00	0.00
	MAX	0.00	0.00	0.00
	N	5	5	5
2	(b) (4)			
	MEAN	257.611	267.978	259.996
	SD	10.861	10.047	23.477
	MIN	248.97	257.42	237.60
	MAX	273.28	280.91	282.53
	N	4	4	4
3	(b) (4)			
	MEAN	525.130	532.654	494.379
	SD	21.690	41.951	8.135
	MIN	509.53	482.47	488.62
	MAX	557.21	584.89	505.93
	N	4	4	4
4	(b) (4)			
	MEAN	1136.630	1122.582	1021.185
	SD	51.833	108.235	61.445
	MIN	1076.95	994.06	946.83
	MAX	1201.61	1236.89	1083.76
	N	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES – CAGES (MALES AND FEMALES)
WEEKS 1 AND 2

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	CAGE No.	Week 1	Week 2
1	(b) (4)		
	MEAN	0.000	0.000
	SD	0.000	0.000
	MIN	0.00	0.00
	MAX	0.00	0.00
	N	4	4
2	(b) (4)		
	MEAN	281.390	347.176
	SD	19.819	20.070
	MIN	252.83	323.05
	MAX	297.57	366.36
	N	4	4
3	(b) (4)		
	MEAN	485.575	651.098
	SD	49.763	75.187
	MIN	414.48	545.43
	MAX	530.04	718.77
	N	4	4
4	(b) (4)		
	MEAN	1250.880	1368 947
	SD	155.916	76.231
	MIN	1130.63	1285.03
	MAX	1478.78	1443.09
	N	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 3	Week 4	Week 5	Week 6	Week 7
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	288.896	294.453	313.527	314.073	300.542
	SD	40.093	38.981	35.955	28.162	38.115
	MIN	258.30	258.45	271.59	277.89	271.00
	MAX	345.62	348.73	354.46	346.66	356.42
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	559.604	555 574	569.005	580.449	546.737
	SD	53.912	49.874	34.212	50.409	28.770
	MIN	493.54	510.39	524.66	518.24	516.16
	MAX	620.01	616.22	607.63	641.20	573.69
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	1215.318	1265.177	1269.571	1297.113	1285.422
	SD	81.498	124 178	65.596	38.776	84.012
	MIN	1138.24	1153.40	1186.16	1250.48	1162.65
	MAX	1302.80	1436 90	1344.87	1344.77	1353.10
	N	4	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 8	Week 9	Week 10	Week 11	Week 12
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	295.527	283 592	279.121	259.498	235.966
	SD	26.815	26.045	26.706	21.227	20.280
	MIN	265.11	245.80	249.19	237.48	207.76
	MAX	318.88	302.60	305.92	283.58	254.39
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	548.787	501 979	503.037	469.000	474.922
	SD	29.290	23.057	16.720	17.367	32.546
	MIN	506.19	477.52	479.94	449.68	438.52
	MAX	572.67	533.13	516.58	491.39	508.53
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	1161.030	1130.303	1119.001	1049.563	1062.712
	SD	67.219	60.385	149.899	25.489	49.641
	MIN	1089.18	1058.42	903.97	1030.26	1004.23
	MAX	1240.96	1202.04	1252.45	1086.65	1109.52
	N	4	4	4	4	4

APPENDIX NO. 63 (b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 13	Week 14	Week 15	Week 16	Week 17
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	227.327	221.865	231 320	208.599	216.091
	SD	26.198	23.188	15.600	26.743	22.307
	MIN	204.69	206.45	214 51	183.50	189.46
	MAX	258.88	256.03	251.82	245.15	237.02
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	464.237	419.720	427 206	389.857	394.814
	SD	40.209	16.437	32.736	34.604	4.572
	MIN	408.89	405.23	398.85	352.87	388.29
	MAX	501.13	435.15	470.80	425.38	398.99
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	1012.483	933.838	917.744	878.538	857.388
	SD	73.853	94.045	75.406	47.661	107.707
	MIN	923.27	819.50	815.83	808.86	759.51
	MAX	1076.80	1012.37	994 31	910.29	1000.74
	N	4	4	4	4	4

APPENDIX NO. 63 (b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 18	Week 19	Week 20	Week 21	Week 22
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	198.609	195.881	182.514	182.690	175 236
	SD	16.514	23.950	18.525	10.590	21.995
	MIN	182.14	161.48	162.93	169.91	157.89
	MAX	214.86	217.12	200.89	195.49	207.44
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	361.277	394.288	364.268	333.895	334.664
	SD	15.647	21.398	10.761	17.503	20.896
	MIN	340.63	374.03	355.11	316.62	315 14
	MAX	378.47	424.33	379.73	357.76	361 26
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	853.302	825.075	762.457	762 395	740.668
	SD	50.647	102.866	61.550	94.199	95.232
	MIN	799.55	718.83	703.74	675.86	630.43
	MAX	899.52	958.07	847.40	888.23	862.65
	N	4	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - MALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 23	Week 24	Week 25	Week 26
1	(b) (4)				
	MEAN	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00
	N	4	4	4	4
2	(b) (4)				
	MEAN	168.121	172.784	162.435	150.158
	SD	24.901	18.874	17.256	20.325
	MIN	134.38	147.21	148.36	122.66
	MAX	194.27	192.76	187.54	171.29
	N	4	4	4	4
3	(b) (4)				
	MEAN	321.346	350.154	299.671	286.726
	SD	19.689	23.965	21.964	18.078
	MIN	292.51	331.73	278.57	267.31
	MAX	336.93	384.22	328.29	310.61
	N	4	4	4	4
4	(b) (4)				
	MEAN	693.243	686.801	635.881	612.730
	SD	72.844	72.113	89.499	99.788
	MIN	616.52	613.19	564.16	504.20
	MAX	789.24	755.95	764.89	746.06
	N	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 3	Week 4	Week 5	Week 6	Week 7
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	288.241	315 909	324.965	321.696	299.814
	SD	32.597	42.157	38.246	25.350	21.804
	MIN	245.24	274.38	285.80	300.32	268.07
	MAX	322.90	367.65	377.44	355.11	315.90
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	488.582	534.654	545.401	570.296	555.610
	SD	97.948	37.017	36.881	22.288	18.335
	MIN	394.71	489.96	497.87	539.91	542.79
	MAX	597.84	578.71	583.71	589.03	582.82
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	1189.028	1326.716	1308.831	1326.911	1287.713
	SD	105.452	126.819	45.009	95.154	62.263
	MIN	1056.22	1184 95	1243.11	1238.57	1204.43
	MAX	1301.11	1444.74	1344.72	1461.80	1355.29
	N	4	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 8	Week 9	Week 10	Week 11	Week 12
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	294.872	289 387	281.098	261.387	248.061
	SD	20.097	25.944	24.480	24.214	17.275
	MIN	273.13	261.95	257.14	226.85	225.32
	MAX	314.67	315.54	315.17	282.39	267.14
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	528.051	514 119	512.340	479.611	456.515
	SD	18.190	46.881	33.444	14.883	19.848
	MIN	506.34	476.53	462.56	458.44	435.48
	MAX	550.36	580.27	534.01	490.95	473.82
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	1248.706	1201.184	1148.091	1124.851	1073.085
	SD	73.821	98.197	54.901	28.573	39.563
	MIN	1178.57	1069 37	1068.81	1086.08	1025.04
	MAX	1335.30	1298 53	1190.05	1152.66	1114.69
	N	4	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 13	Week 14	Week 15	Week 16	Week 17
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	231.603	224.863	217.270	207.612	220 105
	SD	12.423	20.692	6.287	7.758	6.102
	MIN	214.43	207.85	211.07	200.31	214 14
	MAX	243.54	254.80	223.55	217.22	228 57
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	468.502	430.585	426.741	440.633	420 197
	SD	12.772	29.597	23.514	50.868	29.056
	MIN	450.22	393.67	391.50	383.26	393 31
	MAX	479.94	463.19	439.61	505.20	461 50
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	999.056	910.333	938.321	924.094	861.704
	SD	85.315	49.149	43.083	103.493	90.882
	MIN	917.43	853.57	902.41	855.52	768.04
	MAX	1103.90	957.49	1000.00	1076.08	971 98
	N	4	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 18	Week 19	Week 20	Week 21	Week 22
1	(b) (4)					
	MEAN	0.000	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00	0.00
	N	4	4	4	4	4
2	(b) (4)					
	MEAN	206.997	200.027	186.893	182.877	171.811
	SD	23.996	12.094	21.480	16.718	21.992
	MIN	173.34	183.89	164.55	166.35	142.82
	MAX	228.59	213.16	214.04	199.62	189.04
	N	4	4	4	4	4
3	(b) (4)					
	MEAN	394.522	398.976	356.651	370.483	362.084
	SD	28.202	33.562	9.506	26.377	12.352
	MIN	367.68	371.39	346.33	350.91	349.72
	MAX	434.19	446.14	368.64	407.73	375.00
	N	4	4	4	4	4
4	(b) (4)					
	MEAN	808.927	858.216	758.173	730.045	713.647
	SD	52.022	32.983	11.608	89.550	76.775
	MIN	755.72	810.98	741.98	662.92	617 31
	MAX	876.41	881.82	769.58	855.56	796 22
	N	4	4	4	4	4

APPENDIX NO. 63

(b) (4)

ACHIEVED AOCED INTAKE
AVERAGE DAILY DOSE (mg/kg)
F1 GENERATION – PUPPIES - FEMALES

See Appendix No. 3 Experimental Design for group definition

GROUP NO.	ANIMAL No.	Week 23	Week 24	Week 25	Week 26
1	(b) (4)				
	MEAN	0.000	0.000	0.000	0.000
	SD	0.000	0.000	0.000	0.000
	MIN	0.00	0.00	0.00	0.00
	MAX	0.00	0.00	0.00	0.00
	N	4	4	4	4
2	(b) (4)				
	MEAN	182.022	175.729	180.481	162.548
	SD	15.011	6.086	11.934	16.699
	MIN	173.24	166.63	162.71	149.87
	MAX	204.50	179.39	188.45	186.59
	N	4	4	4	4
3	(b) (4)				
	SD	31.853	32.101	49.302	14.729
	MIN	297.10	295.86	257.87	293.18
	MAX	363.33	367.60	368.44	324.81
	N	4	4	4	4
4	(b) (4)				
	MEAN	680.930	722.768	670.552	606.842
	SD	57.001	82.857	60.600	60.356
	MIN	603.30	602.48	593.26	516.78
	MAX	728.19	792.30	727.67	641.88
	N	4	4	4	4

(b) (4)

APPENDIX NO. 64
STATISTICAL REPORT



CONFIDENTIAL

STATISTICAL REPORT
Numerical Data

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies





Sponsor:
DSM Nutritional Products AG
6480 Dobbin Road
Columbia, MD
USA 21045

Issue Date: October 09, 2018

This document is confidential and should not be disseminated to entities or individuals, without the written approval of the Sponsor.

1 EXPERIMENTAL DESIGN

The statistical analysis was based on the following study design. The test and reference items were administered as a diet as shown below:

Treatment Group	Target Dosage Level (% of AOCED in the diet on DM basis)	Number of Animals		
		F_0 Generation (dams) [1]	F_1 Generation (puppies) [2]	
		Females	Males	Females
1. Control diet	0	5	4	4
2. AOCED	0.75%	5	4	4
3. AOCED	1.5%	5	4	4
4. AOCED	3.0%	5	4	4

[1] – Confirmed pregnant females

[2] - Two puppies per litter (1 male and 1 female) when possible, randomly selected

The following values were excluded from the statistical analysis:

- body weight of animal (b) (4) at gestation day 70 and body weight change between gestation days 63 and 70 since for these occasions, only one observation was present and the LSMeans could not be estimated
- body temperature, heart rate and respiratory rate for animal (b) (4) at PPD 2 and animal (b) (4) at PPD 5 since for these occasions, only one observation was present and the LSMeans could not be estimated
- occasions after gestation day 63 were removed from the F_0 food consumption during gestation since the data was not representative (not enough observations remaining) and LSMeans could not be estimated

2 DATA ANALYSIS

The statistical analysis was performed according to the study plan including amendments no. 1 to 11 and the following statistical method.

Statistical analysis was performed independently for the three study periods gestation, pre and post weaning.

A one-way ANOVA was performed on the following datasets:

- average of pre-treatment individual results of body weights F_0
- average of pre-treatment individual results of food consumption F_0
- average of pre-treatment individual results for body temperature F_0
- average of pre-treatment individual results for heart rate F_0
- average of pre-treatment individual results for respiratory rate F_0
- percentage live pups by litter, percentage malformed pups per litter at PPD0

- clinical pathology parameters of F_0 during pre-treatment and, for parameters without baseline values, at weaning

A one-way analysis of covariance (ANCOVA) was performed for the following datasets:

- clinical pathology parameters of F0 at weaning

A two-way analysis of variance (ANOVA) was performed for the following datasets:

- body weights for F_1 at PPD0

A two-way repeated measures ANOVA was performed on the following datasets:

- body weight for F_0 during lactation;
- body weight changes for F_0 during gestation and lactation
- body temperature for F_0 during lactation
- heart rate for F_0 during lactation
- respiratory rate for F_0 during lactation phase
- food consumption for F_0 and F_1 combined (by cage) during lactation (PPD0 to weaning)
- food consumption F_1 during the first 2 weeks post weaning

A two-way repeated measures ANCOVA was performed for the following datasets:

- post-start of treatment results of body weights F_0 during gestation
- post-start of treatment results of food consumption F_0 during gestation
- post-start of treatment results of body temperature F_0 during gestation;
- post-start of treatment results of heart rate F_0 during gestation;
- post-start of treatment results of respiratory rate F_0 during gestation

A three-way repeated measures ANOVA was performed for the following datasets:

- body weight and body weight change for F_1 post-weaning
- food consumption for F_1 after the first 2 weeks post-weaning
- numerical clinical pathology data for F_1
- body temperature for F_1 post-weaning;
- heart rate for F_1 post-weaning;
- respiratory rate for F_1 post-weaning;
- height and height changes for F_1 post-weaning;
- head circumference and head circumference changes for F_1 post-weaning

A three-way nested repeated measures ANOVA was performed for the following datasets (pups nested within litter) including only the animals selected at culling:

- body weight and body weight changes for F_1 pre-weaning
- height and height changes for F_1 pre-weaning;
- head circumference and head circumference changes for F_1 pre-weaning

The Log-rank test was performed for the following data set:

- buccal mucosal bleeding time for F_1

Statistical Methods

Log-rank test

The statistical analyses for bleeding time were performed on sexes combined due to the low number of animals. All animals still bleeding at the end of the observation period (30 min) were censored at 30 min. Inter-group differences of the time to event curve estimates were tested using the Log-Rank test. The log rank test was applied to all groups in order to assess the significance of the overall group effect.

One-Way ANOVA/ANCOVA

The following statistical group comparison did not include groups with less than three observations or with zero variance.

For each data set, a one-way ANOVA/ANCOVA was performed with group as fixed effect. In addition, for the ANCOVA models, the pre-treatment average was used as covariate. When significant differences among the group means were indicated by the model's overall *F*-test ($p \leq 0.10$), a *t*-test was used to perform the group mean comparisons between the control diet group and each test item treated group.

Two-Way ANOVA

The fixed effects in the model were the group, the sex, their interaction and litter nested within group.

When the model indicated that the group-by-sex interaction was significant ($p \leq 0.10$), the group effect was assessed within each sex using *F*-test on least-squares (LS) means. When there was no significant group-by-sex interaction, then the group effect was assessed for each sex using the *F*-test from the model.

When the group effect was significant ($p \leq 0.10$), *t*-test on least-squares means was performed to compare control diet group with each of the test item treated groups.

Two-Way Repeated Measures ANOVA/ANCOVA

The average of pre-treatment results was used as covariate in the analysis of the F0 generation gestation period.

The fixed effects in the model were the group, the time and their interaction with the animal as subject and, when applicable, the pre-treatment as covariate. For the pre-weaning period, subject

was the pup nested within litter. The repeated measures analysis of variance was performed using each of the following four covariance structures: the first-order autoregressive (AR(1)), the heterogeneous first-order autoregressive (ARH(1)), the compound symmetry (CS) and the heterogeneous compound symmetry (CSH) in order to determine which one would best express the pattern of measurement correlations across time. A common covariance matrix for all groups was used. The Kenward and Roger's method was used when computing the denominator degrees of freedom for the tests involving the fixed effects. When the final Hessian was not positive definite or computational limitation/convergence problems were encountered while fitting a model, the model was not considered in the following steps. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) was selected.

When the retained two-way repeated measures ANOVA/ANCOVA model indicated that the group-by-time interaction was significant ($p \leq 0.10$), the group effect was assessed within each time point using *F*-test on least-squares means. When there was no significant group-by-time interaction, then the group effect was assessed across pooled time points using the F-test from the retained model.

When the group effect was significant ($p \leq 0.10$), *t*-test on least-squares means was performed to compare control diet group with each of the test item treated groups.

Three-Way Repeated Measures ANOVA

The fixed effects in the model were the group, the sex, the time and their two-way and three-way interactions with the animal as subject. For the pre-weaning period, subject was the pup nested within litter. The repeated measures analysis of variance was performed using each of the following six covariance structures: the spatial power (SP(POW)), the spatial anisotropic power (SP(POWA)), the first-order autoregressive (AR(1)), the heterogeneous first-order autoregressive (ARH(1)), the compound symmetry (CS) and the heterogeneous compound symmetry (CSH) in order to determine which one would best express the pattern of measurement correlations across time. A common covariance matrix for all group-sex levels was used. The Kenward and Roger's method was used when computing the denominator degrees of freedom for the tests involving the fixed effects. When the final Hessian was not positive definite or computational limitation/convergence problems were encountered while fitting a model, the model was not considered. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) was selected.

When the retained model indicated significant ($p \leq 0.05$) group-by-sex-by-time interaction, the group effect was assessed within each sex-time combination using *F*-test on least-squares means. When there was no significant group-by-sex-by-time interaction, then the group-by-sex and the group-by-time interactions were assessed using the *F*-test from the retained model.

When the group-by-sex interaction was significant ($p \leq 0.10$), the group effect was assessed within each sex using F-test on least-squares means. When the group-by-time interaction was significant ($p \leq 0.10$), the group effect was assessed within each time using *F*-test on least-

squares means. When both group-by-sex and group-by-time interactions were not significant, then the group effect was assessed on pooled sexes and pooled time points using the *F*-test i.e. the main group effect from the retained model.

When the group effect was significant ($p \leq 0.10$), *t*-test on least-squares means was performed to compare control diet group with each of the test item treated groups.

For all analyses, the pairwise group comparisons were assessed at an alpha level of 0.10. Significant differences from group mean comparisons were reported as $p \leq 0.10$, $p \leq 0.05$, $p \leq 0.01$, where *p* represented the *t*-test probability. Least-square means related to the pairwise group comparisons were presented with *p*-values.

3 SUMMARY RESULTS

F_0 generation

Results from the analysis of clinical chemistry and hematology parameters for F_0 generation are presented in Part A of the following result section. Analysis on pre-treatment data and on post-treatment RETIC and %RETIC was performed using a one-way ANOVA model with treatment as fixed effect. Analysis on the post-treatment data was performed using 1-way ANCOVA model with treatment as fixed effect and the pre-treatment as covariate.

No malformed puppies were present at PPD0. Results from the analysis of percentage live pups per litter using one-way ANOVA model are presented in the table below:

Generation	Period	Parameter	Overall Treatment Difference *p*-Value
F1	PPD 0	Percentage live pups	0.4826

Significant overall treatment differences: ¶ - $p \leq 0.1$

Results from the analysis on the average of pre-treatment data using a one-way ANOVA model are presented in the table below. No significant group differences were revealed.

Parameter	Body Temperature	Body Weight	Food Consumption	Heart Rate	Respiratory Rate
Overall Treatment Difference *p*-Value	0.7374	0.8587	0.9098	0.4332	0.3935

Significant overall treatment differences: ¶ - $p \leq 0.1$

Data from the gestation period (excluding body weight changes) was analysed using a two-way repeated measures ANCOVA model with time and group and their interaction as fixed effects and the average of pre-treatment data as covariate. For food consumption, due to no data for group 4 at week 10, the LS mean for group 4 could not be estimated. Statistical comparisons were repeated including data from weeks 1 to 9. Results from the selection of the covariance structure using the AICC criteria are presented in the table below:

	AICC Value and selected model					
Covariance Structure	Body Temperature	Body Weight	Food Consumption Weeks 1 to 10	Food Consumption Weeks 1 to 9	Heart Rate	Respiratory Rate
AR1	69.0 <=	191.9	1629.1 <=	15459.4 <=	798.9	635.5
ARH1	74.4	169.2 <=	1629.6	1546.0	806.8	622.6 <=
CS	69.7	264.2	1634.9	1551.3	791.2 <=	637.1
CSH	76.9	240.7	1638.6	1555.3	798.7	631.1

<= - Selected model

The summary results from the selected model including the group LS means are presented in the table below. No interaction effect was detected for any of the parameters and thus, the group effect was assessed on all days pooled together. No significant group differences were revealed.

Parameter	Main Effect *p*-Value (Pr > F)				LS Mean			
	Group*Day	Pre-dose	Day	Group	Group 1	Group 2	Group 3	Group 4
Body temperature	0.6931	0.0205	<.0001 #	0.9828	38.4	38.3	38.3	38.3
Body weight	0.1024	<.0001	<.0001 #	0.2745	11.0	11.2	11.0	11.5
Food, weeks 1 to 10	0.2080	<.0004	<.0001 #	0.7106	178	187	176	--
Food, weeks 1 to 9	0.1486	0.0006	<.0001 #	0.5374	179	194	180	180
Heart rate	0.1590	0.1278	0.0096 #	0.5967	108	106	102	112
Respiratory rate	0.6979	0.028	0.1612	0.4311	25	25	27	29

Significant interaction effect: X - $p \leq 0.1$ (*F*-Test)
Significant group effect: * - $p \leq 0.1$ (*F*-Test)
Significant day effect: # - $p \leq 0.1$ (*F*-Test)

Data from the lactation period and the body weight changes from gestation period were analysed using a two-way repeated measures ANOVA model with time and group and their interactions as fixed effects. Results from the selection of the covariance structure using AICC criteria are presented in the table below:

Covariance Structure	AICC Value and selected model						
	Body Temperature	Body Weight	Bodyweight Change, Gestation	Bodyweight Change, Lactation	Food Consumption	Heart Rate	Respiratory Rate
AR1	72.4	140.7	182.3	87.6 <=	1200.0	373.9	302.3
ARH1	71.0 <=	153.4	165.6	100.1	1201.9	369.3 <=	300.7
CS	73.7	150.5	181.8	92.4	1225.4 <=	373.9	301.2
CSH	71.5	164	162.3 <=	105.8	1221.5	369.5	298.8 <=

<= - Selected model

The summary of the results from the selected model are presented in the table below together with the group's LS means. No interaction effect was present for any of the parameters and the group effect was assessed on all days pooled together. No significant group differences were revealed for any of the parameters.

Parameter	Main Effect *p*-Value (Pr > F)			LS Mean			
	Group*Day	Day	Group	Group 1	Group 2	Group 3	Group 4
Body temperature	0.5056	0.3180	0.3654	38.2	38.5	38.2	38.4
Body weight	0.7669	<.0001 #	0.8480	10.0	10.0	10.2	10.4
Bodyweight change, gestation	0.3364	<.0001 #	0.4827	0.3	0.4	0.3	0.4
Bodyweight change, lactation	0.7129	<.0001 #	0.1430	0.1	0.0	0.0	0.1
Food consumption	0.8362	<.0001 #	0.9272	514	501	519	540
Heart rate	0.8219	0.0020 #	0.1370	109	112	98	113
Respiratory rate	0.3696	0.0036 #	0.5900	33	35	34	30

Significant interaction effect: X - $p \leq 0.1$ (*F*-Test)
Significant group effect: * - $p \leq 0.1$ (*F*-Test)
Significant day effect: # - $p \leq 0.1$ (*F*-Test)

F_1 generation before weaning

The group comparisons of puppies' bodyweights at PPD 0 were performed using a two-way nested ANOVA model with fixed effects group, sex, their interaction and the litter nested within group. Summary of the results, including the group LS means are presented in the table below. There was no significant sex by group interaction and therefore the group effect was assessed on pooled sexes. There was a significant difference between the control and groups 2 and 3.

				Group 1	Group 2		Group 3		Group 4	
Parameter	Source of Effect	Main Effect (Pr > F)	Sex	LSMean	*p*-Value	LSMean	*p*-Value	LSMean	*p*-Value	LSMean
Body weights	Group	<.0001 *	Pooled	219	**0.0133 E**	236	**<.0001 F**	262	0.4730	224
	Sex	0.0002 #	--	--	--	--	--	--	--	--
	Group*Sex	0.9519	--	--	--	--	--	--	--	--
	Litter(Group)	<.0001	--	--	--	--	--	--	--	--

Significant interaction effect: X - $p \leq 0.1$ (*F*-Test)
Significant group effect: * - $p \leq 0.1$ (*F*-Test)
Significant sex effect: # - $p \leq 0.1$ (*F*-Test)
Significant differences against group 1 across sexes: D - $p \leq 0.1$, E - $p \leq 0.05$, F - $p \leq 0.01$ (*t*-test)

The group comparisons of puppies' data before weaning were performed using a three-way nested repeated measures ANOVA model with fixed effects group, sex, day and all their interactions. Only puppies selected after the culling (on PPD 4) were included in the analysis. Results from the selection of the covariance structure using AICC criteria are presented in the table below:

	AICC Value					
Covariance Structure	Height	Height Change	Head Circumference	Head Circumference Change	Body Weight	Bodyweight Change
SP(POW)(Occasion)	1524.2	1404.4	1336.5	1190.3	12040.5	11188.3
SP(POWA)(Occasion)	1524.2	1404.4	1336.5	1190.3	12040.5	11188.3
AR(1)	1524.2	1385.6	1336.5	1169.7	12013.0 <=	11188.2
ARH(1)	1523.2 <=	1353	1296.7 <=	1134.6	#	10834.6
CS	1592	1372.9	1408.6	1139.5	13643.4	11168.9 <=
CSH	1594.6	1346.5 <=	1379	1108.5 <=	#	10798.2

<= - Selected model
- Did not converge or stopped because of infinite likelihood

The *p*-values of the main effects of the selected models are presented in the table below. For all parameters, a significant group by day interaction was present so the group effect was assessed on each day separately.

	Effect (Pr > F)					
Effect	**Height**	**Height Change**	**Head Circumference**	**Head Circumference Change**	**Body Weight**	**Bodyweight Change**
Group*sex*day	0.4232	0.3051	0.5709	0.4613	0.9911	0.9928
Group*sex	0.8041	0.5371	0.9353	0.9927	0.8201	0.4842
Group*day	**0.0340** C	**0.0077** C	**<.0001** C	**<.0001** C	**0.0003** C	**<.0001** C
Group	-- E	-- E	-- E	-- E	-- E	-- E

C - Significant Group*Day interaction ($p \leq 0.1$), group mean comparisons are assessed for each day
E - *p*-Values are discarded since a significant higher interaction is present

The *p*-values for the overall group effect at each day on pooled sexes are presented in the tables below:

GROUP EFFECT (Pr > F)					
Day	**Height**	**Head**	**DAY**	**Height**	**Head Circumference**
Day 7	0.9897	**<.0001** B	Day 7 to 14	**0.0640** B	**0.0934** B
Day 14	**0.0545** B	**<.0001** B	Day 14 to 21	**0.0010** B	**<.0001** B
Day 21	0.1719	**0.0720** B	Day 21 to 28	0.7637	**0.0713** B
Day 28	0.452	0.1793	Day 28 to 35	0.4463	**0.0049** B
Day 35	**0.0440** B	**<.0001** B	Day 35 to 42	0.1343	0.2684
Day 42	0.5608	**<.0001** B	Day 42 to 49	0.2151	**0.0151** B
Day 49	**0.0819** B	**0.0435** B	Day 49 to 56	0.456	0.7699
Day 56	**0.0519** B	**0.0040** B			

GROUP EFFECT (Pr > F)							
Day	**Body Weight**	**Day**	**Body Weight**	**Day**	**Bodyweight Change**	**Day**	**Bodyweight Change**
Day 0	0.9153	Day 30	**0.0036** B	Day 0 to 4	**0.0100** B	Day 30 to 33	**0.0505** B
Day 4	0.6507	Day 33	**0.0008** B	Day 4 to 7	**<.0001** B	Day 33 to 37	0.9334
Day 7	0.2244	Day 37	**0.0005** B	Day 7 to 10	**0.0082** B	Day 37 to 40	0.5886
Day 10	0.1014	Day 40	**0.0006** B	Day 10 to 14	**0.0751** B	Day 40 to 43	0.4588
Day 14	**0.0417** B	Day 43	**0.0008** B	Day 14 to 17	0.6664	Day 43 to 47	**0.0327** B
Day 17	**0.0419** B	Day 47	**0.0089** B	Day 17 to 21	0.1466	Day 47 to 50	0.1746
Day 21	**0.0327** B	Day 50	**0.0110** B	Day 21 to 24	0.3358	Day 50 to 53	0.1737
Day 24	**0.0148** B	Day 53	**0.0339** B	Day 24 to 27	0.1132	Day 53 to 56	0.3394
Day 27	**0.0074** B	Day 56	**0.0345** B	Day 27 to 30	**0.0563** B		

B (*p*-values in bold) - significant overall group effect ($p \leq 0.1$) on pooled sexes

When a significant overall group difference was revealed for a specific occasion, the pairwise group comparisons were performed on pooled sexes (since no group by sex interaction was present) using two-sided *t*-test on the LS means. Summary of the results is presented in the table below:

Pairwise group comparisons when the overall group difference was significant, combined sexes:

Parameter	Day	Group 1	Group 2		Group 3		Group 4	
		LS Mean	LS Mean	*p*-Value *	LS Mean	*p*-Value *	LS Mean	*p*-Value *
HEIGHT	Day 14	15.0142	15.1071	0.8619	15.9206	**0.0936** A	14.3571	0.2216
	Day 35	21.3608	22.2381	**0.0297** B	22.1825	**0.0412** B	21.4048	0.9118
	Day 49	24.7557	24.6706	0.8224	25.3254	0.1351	24.3056	0.2366
	Day 56	25.7386	25.6468	0.8298	26.131	0.3595	24.9048	**0.0536** A
HEIGHT CHANGES	Day 7 to 14	2.6165	2.7032	0.8815	3.6151	**0.0675** A	2.1032	0.3424
	Day 14 to 21	2.0795	2.9246	**0.0195** B	1.4286	**0.0697** A	2.5119	0.2250
HEAD CIRCUMFERENCE	Day 7	15.6165	17.3492	**<.0001** C	17.0119	**0.0007** C	15.4127	0.6027
	Day 14	18.3665	19.7183	**0.0037** C	20.2183	**0.0001** C	17.6944	0.1398
	Day 21	20.7895	21.1111	0.4333	21.5833	**0.0559** A	20.5159	0.5048
	Day 35	22.9318	24.8889	**<.0001** C	23.6786	**0.0702** A	22.9008	0.9394
	Day 42	24.0142	25.496	**<.0001** C	24.5714	0.1140	23.8413	0.6213
	Day 49	24.9943	25.6865	**0.0222** B	25.2778	0.3427	24.8651	0.6646
	Day 56	25.7955	26.6151	**0.0051** C	26.0278	0.4155	25.5399	0.3767
HEAD CIRCUMFERENCE CHANGE	Day 7 to 14	2.75	2.369	0.3262	3.2063	0.2403	2.2817	0.2284
	Day 14 to 21	2.4717	1.3929	**0.0010** C	1.3651	**0.0007** C	2.8214	0.2672
	Day 21 to 28	0.8763	1.7738	**0.0374** B	0.9324	0.9047	1.7103	**0.0526** A
	Day 28 to 35	1.2784	2.004	**0.0421** B	1.5892	0.4284	0.6746	**0.0894** A
	Day 42 to 49	0.9801	0.1905	**0.0051** C	0.7063	0.3194	1.0238	0.8733
BODY WEIGHTS	Day 14	760.3	913.67	**0.0561** A	924.36	**0.0413** B	743.48	0.8323
	Day 17	897.07	1050.67	**0.0558** A	1072.13	**0.0298** B	892.93	0.9584
	Day 21	1105.72	1242.48	**0.0878** A	1277.29	**0.0332** B	1072.62	0.6770
	Day 24	1235.95	1385.7	**0.0621** A	1427.48	**0.0177** B	1202	0.6692
	Day 27	1339.77	1514.4	**0.0302** B	1559.56	**0.0068** C	1330.52	0.9074
	Day 30	1452.47	1623.16	**0.0340** B	1700.22	**0.0024** C	1447.76	0.9527
	Day 33	1554.77	1740.13	**0.0216** B	1834.1	**0.0007** C	1548.56	0.9377
	Day 37	1706.48	1896.05	**0.0189** B	1996.39	**0.0004** C	1703.48	0.9699
	Day 40	1839.19	2042.85	**0.0119** B	2133.96	**0.0004** C	1856.83	0.8243
	Day 43	1998.35	2180.16	**0.0242** B	2282.21	**0.0006** C	1993.88	0.9552
	Day 47	2220.15	2374.08	**0.0553** A	2452.69	**0.0043** C	2220.76	0.9939
	Day 50	2406.69	2542.94	**0.0890** A	2610.89	**0.0117** B	2367.4	0.6211
	Day 53	2590.44	2732.67	**0.0761** A	2740.54	**0.0615** A	2542.35	0.5453
	Day 56	2698	2760.25	0.4340	2809.03	0.1646	2575.34	0.1252
BODY WEIGHT CHANGES	Day 0 to 4	89.3864	137.77	**0.0042** C	113.45	0.1447	86.5	0.8600
	Day 4 to 7	120.08	171.8	**<.0001** C	162.53	**0.0007** C	119.67	0.9731
	Day 7 to 10	139.37	161.14	**0.0284** B	156.65	**0.0797** A	129.89	0.3322
	Day 10 to 14	188.11	196.25	0.5601	216.11	**0.0484** B	179.06	0.5174
	Day 27 to 30	112.7	108.76	0.7440	140.67	**0.0234** B	117.24	0.7073
	Day 30 to 33	102.3	116.98	0.2572	133.87	**0.0168** B	100.8	0.9073
	Day 43 to 47	221.81	193.92	0.1788	170.48	**0.0150** B	226.88	0.8054

Significant differences when compared to group 1 (pooled sexes): **A** - $p \leq 0.1$, **B** - $p \leq 0.05$, **C** - $p \leq 0.01$ (*t*-test)

(b) (4)

F_1 generation after weaning

Results from the analysis of clinical pathology parameters for F_1 generation after weaning are presented in Parts B to E of the following result section. Analysis was a three-way repeated measures ANOVA model with fixed effects group, sex, day and all their interactions. Part B presents the selection of the covariance structure. Part C presents the *p*-values of the main effects of the selected model. Part D presents the group effect by sex or by day depending on the significant interactions. Part E presents the pairwise comparisons and the group LS Means used in these comparisons when the overall group effect was significant.

Cage food consumption for the first 2 weeks of weaning (puppies were grouped housed) was analysed using a two-way repeated measures ANOVA model with time and group and their interactions as fixed effects. Results from the selection of the covariance structure using AICC criteria are presented in the table below:

	Covariance Structures			
	AR1	ARH1	CS	CSH
AICC Value	215.3 <==	217.9	215.3	217.9

<= - Selected model

The summary of the results from the selected model are presented in the table below together with the group's LS means. Significant group by day interaction effect was present and the group effect was assessed for each week. Significant overall group effect was revealed for week 1 with significant group differences between groups 1 and 3.

			Group 1	Group 2		Group 3		Group 4	
Source of Effect	Main Effect (Pr > F)	Day	LSMean	*p*-Value	LSMean	*p*-Value	LSMean	*p*-Value	LSMean
Group	0.2432 Dis	Pooled	249	--	247	--	223	--	251
Day	<.0001 Dis	--	--	--	--	--	--	--	--
Group*Day	0.0262 X	--	--	--	--	--	--	--	--
Group*Day	0.0638 *	Week 1	212	0.6576	206	0.0358 B	177	0.6188	220
Group*Day	0.6410	Week 2	286	--	288	--	270	--	283

Significant interaction effect: X - $p \leq 0.1$ (*F*-Test)

Significant group effect: * - $p \leq 0.1$ (*F*-Test)

Significant sex effect: # - $p \leq 0.1$ (*F*-Test)

Significant differences against group 1 across sexes: A- $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)

Results from group comparisons of puppies' data after weaning (for food consumption, after the first 2 weeks post weaning) were performed using a three-way repeated measures ANOVA model with fixed effects group, sex, day and all their interactions. Results from the selection of the covariance structure using AICC criteria are presented in the table below:

	AICC Value					
Covariance Structure	**SP(POW) (Occasion)**	**SP(POWA) (Occasion)**	**AR(1)**	**ARH(1)**	**CS**	**CSH**
Body weight	99.8	99.8	99.8	66.0 <=	1022.1	475.3
Body weight change	35.1	35.1	-20.0	-70.9 <=	35.0	-43.1
Food consumption	4900.3 <=	4900.3	4900.3	4911.2	4951.5	4964.2
Body temperature	157.8	157.8	142.7 <=	126.7	142.9	125.8 <=
Heart rate	1743.9	1743.9	1743.8	1746.6	1731.4 <=	1733.6
Respiratory rate	1516.9	1516.9	1507.7	1498.5 <=	1510.6	1501.0
Height	2616.9	2616.9	2616.9	2384.6 <=	2631.6	2579.8
Height change	2650.7	2650.7	2541.0	2165.0 <=	2597.8	#
Head circumference	1709.0	1709.0	1709.0	1538.2 <=	1829.8	1795.6
Head circumference change	1708.6	1708.6	1586.8	1355.9 <=	1669.3	#

<= - Selected model

- Did not converge or stopped because of infinite likelihood

The *p*-values of the main effects of the selected models are presented in the table below. When a significant group by day interaction was present (body weight, height, head circumference and their changes and food consumption), the group effect was assessed on each day separately. When a group by sex interaction was present (heart rate and respiratory rate), the group effect was assessed for each sex.

	Effect (Pr > F)			
	GROUP*SEX*DAY	**GROUP*SEX**	**GROUP*DAY**	**GROUP**
Body weight	1.0000	0.9149	**0.0006** [C]	-- [E]
Body weight change	1.0000	0.6596	**<.0001** [C]	-- [E]
Food consumption	0.9708	0.4111	**<.0001** [C]	-- [E]
Body temperature	0.8861	0.5622	0.5504	0.9161
Heart rate	0.7085	**0.0827** [B]	0.1932	-- [E]
Respiratory rate	0.7085	**0.0827** [B]	0.1932	-- [E]
Height	1.0000	0.9445	**0.0166** [C]	-- [E]
Height change	1.0000	0.9979	**0.0095** [C]	-- [E]
Head circumference	0.9996	0.8762	**0.0014** [C]	-- [E]
Head circumference change	0.9994	0.9442	**<.0001** [C]	-- [E]

B - Significant Group*Sex interaction ($p \leq 0.1$), group mean comparisons are assessed for each sex

C - Significant Group*Day interaction ($p \leq 0.1$), group mean comparisons are assessed for each day

E - *p*-Values are discarded since a significant higher interaction is present

(b) (4)

The *p*-values for the overall group effect at each sex on pooled days are presented in the table below:

	Evaluation of GROUP Effect (Pr > F)	
Parameter	**MALES**	**FEMALES**
Heart rate	**0.0101** [A]	**0.0613** [A]
Respiratory rate	0.4457	**0.0455** [A]

A (*p*-values in bold) - significant overall group effect ($p \leq 0.1$) on pooled days

The *p*-values for the overall group effect at each occasion (week for food consumption and day for the others) on pooled sexes are presented in the tables below:

GROUP EFFECT (Pr > F)							
DAY	**Body Weight**	**DAY**	**Body Weight**	**DAY**	**Bodyweight Change**	**DAY**	**Bodyweight Change**
Day 56	0.9719	Day 154	0.3002	Day 56 to 63	0.5797	Day 147 to 154	0.5166
Day 63	0.9525	Day 161	0.2624	Day 63 to 70	**0.0453** [B]	Day 154 to 161	**0.0340** [B]
Day 70	0.6825	Day 168	0.2823	Day 70 to 77	0.9224	Day 161 to 168	0.2054
Day 77	0.7531	Day 175	0.2454	Day 77 to 84	0.6426	Day 168 to 175	**0.0042** [B]
Day 84	0.8102	Day 182	**0.0826** [B]	Day 84 to 91	**0.0328** [B]	Day 175 to 182	**0.0744** [B]
Day 91	0.8514	Day 189	**0.0654** [B]	Day 91 to 98	0.3547	Day 182 to 189	0.1775
Day 98	0.7876	Day 196	**0.0900** [B]	Day 98 to 105	0.2703	Day 189 to 196	0.2522
Day 105	0.8218	Day 203	**0.0398** [B]	Day 105 to 112	0.3256	Day 196 to 203	**0.0055** [B]
Day 112	0.8914	Day 210	**0.0440** [B]	Day 112 to 119	0.1118	Day 203 to 210	**0.0275** [B]
Day 119	0.7040	Day 217	**0.0318** [B]	Day 119 to 126	0.2855	Day 210 to 217	0.7422
Day 126	0.5108	Day 224	**0.0224** [B]	Day 126 to 133	**0.0218** [B]	Day 217 to 224	0.2860
Day 133	0.4504	Day 231	**0.0106** [B]	Day 133 to 140	0.1147	Day 224 to 231	0.1375
Day 140	0.3008	Day 238	**0.0325** [B]	Day 140 to 147	0.9741	Day 231 to 238	0.2179
Day 147	0.3752						

B (*p*-values in bold) - significant overall group effect ($p \leq 0.1$) on pooled sexes

FOOD CONSUMPTION: GROUP EFFECT (Pr > F)							
Week 3	0.6734	Week 9	**0.0479** [B]	Week 15	**0.0722** [B]	Week 21	**0.0834** [B]
Week 4	0.3789	Week 10	**0.0371** [B]	Week 16	**0.0595** [B]	Week 22	**0.0665** [B]
Week 5	0.1730	Week 11	**0.0349** [B]	Week 17	**0.0297** [B]	Week 23	**0.0372** [B]
Week 6	0.1455	Week 12	**0.0352** [B]	Week 18	**0.0319** [B]	Week 24	**0.0235** [B]
Week 7	**0.0625** [B]	Week 13	0.2595	Week 19	**0.0312** [B]	Week 25	**0.0340** [B]
Week 8	0.1773	Week 14	**0.0232** [B]	Week 20	**0.0837** [B]		

B (*p*-values in bold) - significant overall group effect ($p \leq 0.1$) on pooled sexes

GROUP EFFECT (Pr > F)					
DAY	Height	Head Circumference	DAY	Height Change	Head Circumference Change
Day 56	0.8002	0.7113	Day 56 to 63	0.3065	**0.0981** B
Day 63	0.7205	0.5297	Day 63 to 70	0.3569	**0.0027** B
Day 70	0.9331	0.5723	Day 70 to 77	0.7124	0.2679
Day 77	0.4409	0.7214	Day 77 to 84	0.3350	**0.0019** B
Day 84	0.6214	0.8371	Day 84 to 91	0.5284	0.3706
Day 91	0.2847	0.2690	Day 91 to 98	0.2162	0.1416
Day 98	0.7035	**0.0303** B	Day 98 to 105	0.2873	0.1941
Day 105	0.7168	**0.0937** B	Day 105 to 112	0.4333	0.1735
Day 112	0.4092	0.6753	Day 112 to 119	0.4897	0.6161
Day 119	0.8732	0.9646	Day 119 to 126	**0.0405** B	0.1295
Day 126	0.2534	0.6477	Day 126 to 133	0.4674	0.1858
Day 133	0.1349	0.7015	Day 133 to 140	**0.0947** B	**0.0731** B
Day 140	**0.0444** B	0.9729	Day 140 to 147	0.2078	0.5422
Day 147	0.1660	0.9366	Day 147 to 154	**0.0332** B	0.1400
Day 154	0.8618	0.6863	Day 154 to 161	**0.0253** B	**0.0253** B
Day 161	0.2861	0.8842	Day 161 to 168	**0.0153** B	0.3925
Day 168	0.8861	0.7893	Day 168 to 175	0.4679	0.9614
Day 175	0.6758	0.8717	Day 175 to 182	0.4675	0.2989
Day 182	0.6744	0.5284	Day 182 to 189	**0.0696** B	0.3868
Day 189	0.3463	0.3050	Day 189 to 196	0.1795	0.4084
Day 196	0.6532	0.5229	Day 196 to 203	0.4802	0.8087
Day 203	0.8578	0.5782	Day 203 to 210	**0.0859** B	0.1746
Day 210	0.7810	0.6098	Day 210 to 217	0.3548	**0.0728** B
Day 217	0.9783	0.5783	Day 217 to 224	0.7144	**0.0607** B
Day 224	0.9541	0.1314	Day 224 to 231	0.2786	**0.0019** B
Day 231	0.6927	**0.0072** B	Day 231 to 238	**0.0457** B	0.3778
Day 238	0.3481	**0.0028** B			

B (*p*-values in bold) - significant overall group effect ($p \leq 0.1$) on pooled sexes

When a significant overall group difference was revealed, the pairwise group comparisons were performed using two-sided *t*-test on the LSMeans (pooled days). Summary of the results is presented in the table below:

Pairwise group comparisons when the overall group difference was significant, combined days:

Parameter	Sex	Group 1	Group 2		Group 3		Group 4	
		LS Mean	LS Mean	*p*-Value *	LS Mean	*p*-Value *	LS Mean	*p*-Value *
Heart Rate	Males	152.50	163.12	0.1415	143.37	0.2040	138.88	**0.0630** A
	Females	153.75	147.12	0.3525	134.12	**0.0097** C	147.88	0.4088
Respiratory rate	Females	43.7500	45.2500	0.6186	42.5000	0.6781	50.6250	**0.0256** B

Significant differences when compared to group 1 (pooled sexes): **A** - $p \leq 0.1$, **B** - $p \leq 0.05$, **C** - $p \leq 0.01$ (*t*-test)

Pairwise group comparisons when the overall group difference was significant, combined sexes:

Parameter	DAY	Group 1	Group 2		Group 3		Group 4	
		LS Mean	LS Mean	*p*-Value *	LS Mean	*p*-Value *	LS Mean	*p*-Value *
HEAD CIRCUMFERENCE	Day 98	27.9375	29.0625	**0.0066** C	28.7500	**0.0440** B	28.2500	0.4265
	Day 105	28.3750	29.2500	**0.0298** B	28.7500	0.3373	28.3750	1.0000
	Day 231	34.0625	34.9375	**0.0599** A	33.5000	0.2221	33.5000	0.2221
	Day 238	34.4375	35.1250	0.1424	33.5625	**0.0637** A	33.5625	**0.0637** A
HEAD CIRCUMFERENCE CHANGE	Day 56 to 63	1.1875	-0.1250	**0.0241** B	0.1875	**0.0792** A	0.0195	**0.0499** B
	Day 63 to 70	-0.2500	0.2500	0.4557	1.8125	**0.0041** C	2.0625	**0.0015** C
	Day 77 to 84	0.4375	1.1875	**0.0054** C	0.3125	0.6160	0.1875	0.3195
	Day 133 to 140	0.5000	-0.4375	**0.0466** B	-0.2500	0.1073	0.5625	0.8909
	Day 154 to 161	0.0625	0.0625	1.0000	0.4375	**0.0081** C	0.1875	0.3463
	Day 210 to 217	-0.4375	0.3750	**0.0321** B	0.3750	**0.0321** B	-0.1875	0.4930
	Day 217 to 224	0.3125	0.1250	0.4543	-0.3750	**0.0097** C	0.0625	0.3204
	Day 224 to 231	0.0000	0.6250	**0.0008** C	0.1250	0.4533	0.0000	1.0000
HEIGHT	Day 140	36.5000	37.7500	0.1479	37.6250	0.1916	35.5625	0.2747
HEIGHT CHANGE	Day 119 to 126	1.3125	2.1875	0.3489	0.4375	0.3489	-0.5000	**0.0585** A
	Day 133 to 140	0.5000	-0.7500	**0.0278** B	0.2500	0.6459	0.4375	0.9084
	Day 147 to 154	2.7500	0.1250	**0.0166** B	-0.1250	**0.0094** C	1.5000	0.2340
	Day 154 to 161	-2.0000	0.2500	**0.1000** A	2.3125	**0.0029** C	-0.2500	0.1967
	Day 161 to 168	1.3750	0.8125	0.5500	-1.4375	**0.0054** C	1.3750	1.0000
	Day 182 to 189	0.6250	0.2500	**0.0857** A	0.0625	**0.0128** B	0.1875	**0.0472** B
	Day 203 to 210	1.3125	0.1250	**0.0273** B	0.1875	**0.0357** B	0.8125	0.3346
	Day 231 to 238	1.0000	0.1875	**0.0229** B	0.0625	**0.0098** C	0.3750	**0.0739** A
FOOD CONSUMPRION	Week 7	214.04	212.68	0.9247	180.48	**0.0207** B	210.45	0.8026
	Week 9	225.86	228.00	0.8813	192.16	**0.0202** B	221.25	0.7481
	Week 10	231.68	244.00	0.3913	202.88	**0.0465** B	228.88	0.8451
	Week 11	237.00	247.46	0.4664	206.89	**0.0376** B	236.13	0.9514
	Week 12	242.79	235.48	0.6110	207.73	**0.0158** B	245.98	0.8238
	Week 14	247.64	235.38	0.3934	204.27	**0.0030** C	232.82	0.3028
	Week 15	230.07	250.32	0.1600	216.24	0.3361	246.21	0.2619
	Week 16	243.88	236.79	0.6215	213.18	**0.0341** B	250.09	0.6652
	Week 17	227.07	257.43	**0.0361** B	219.41	0.5937	248.37	0.1395
	Week 18	241.84	249.68	0.5852	211.66	**0.0371** B	247.39	0.6989
	Week 19	223.20	253.23	**0.0380** B	225.14	0.8921	256.16	**0.0230** B
	Week 20	235.55	240.98	0.7054	209.04	**0.0665** A	240.86	0.7118
	Week 21	225.54	238.32	0.3738	207.55	0.2117	241.00	0.2824
	Week 22	223.02	233.88	0.4499	206.89	0.2625	243.95	0.1465
	Week 23	220.38	236.23	0.2704	198.50	0.1293	233.77	0.3516
	Week 24	213.52	241.42	**0.0537** A	202.33	0.4362	235.29	0.1311
	Week 25	202.84	227.82	**0.0836** A	188.16	0.3075	218.55	0.2747

Parameter	DAY	Group 1 LS Mean	Group 2 LS Mean	Group 2 *p*-Value *	Group 3 LS Mean	Group 3 *p*-Value *	Group 4 LS Mean	Group 4 *p*-Value *
BODY WEIGHTS	Day 182	8.8500	9.5875	**0.0869** A	8.5075	0.4186	9.1725	0.4461
	Day 189	9.0600	9.7675	**0.0966** A	8.6975	0.3875	9.5125	0.2822
	Day 196	9.2125	9.8000	0.1594	8.8550	0.3876	9.7075	0.2339
	Day 203	9.6575	10.0850	0.3282	8.9500	0.1097	10.0825	0.3310
	Day 210	9.5500	10.1800	0.1495	9.1350	0.3384	10.2150	0.1287
	Day 217	9.6075	10.3550	**0.0907** A	9.2550	0.4179	10.3475	**0.0938** A
	Day 224	9.7675	10.6100	**0.0703** A	9.4150	0.4406	10.6100	**0.0703** A
	Day 231	9.9125	10.9075	**0.0464** B	9.4775	0.3738	10.8525	**0.0592** A
	Day 238	9.6575	10.4700	**0.0954** A	9.2925	0.4473	10.5100	**0.0808** A
BODY WEIGHT CHANGES	Day 63 to 70	0.3075	0.4575	**0.0158** B	0.4225	**0.0579** A	0.3300	0.7001
	Day 84 to 91	0.5600	0.4750	0.2288	0.3600	**0.0080** C	0.3875	**0.0198** B
	Day 126 to 133	0.3400	0.2225	0.1769	0.1225	**0.0163** B	0.3800	0.6405
	Day 154 to 161	0.4475	0.2025	**0.0358** B	0.1462	**0.0115** B	0.3838	0.5686
	Day 168 to 175	-0.0025	0.3950	**0.0013** C	0.3550	**0.0032** C	0.1575	0.1584
	Day 175 to 182	0.2050	0.3400	0.1988	0.0700	0.1988	0.2800	0.4705
	Day 196 to 203	0.4450	0.2850	**0.0963** A	0.0950	**0.0009** C	0.3750	0.4565
	Day 203 to 210	-0.1075	0.0950	**0.0442** B	0.1850	**0.0051** C	0.1325	**0.0188** B

Significant differences when compared to group 1 (pooled sexes): **A** - $p \leq 0.1$, **B** - $p \leq 0.05$, **C** - $p \leq 0.01$ (*t*-test)

The statistical analyses for buccal mucosal bleeding time were performed on sexes combined using the log-rank test and the results are summarised in the table below. No statistically significant difference among the groups was detected.

Sex	End of measurement	Considered Groups	Raw *p*-Value
Pooled	30 min	1, 2, 3, 4	0.0891

Significant overall group effect: * - $p \leq 0.05$

4 SOFTWARE USED

The statistical analysis of this study was performed according to the study documentation using the software SAS® System for Windows™ (Release 9.3), SAS Institute, Cary, NC.

5 SIGNATURE

The statistical report constitutes a true and faithful record of the procedures undertaken and the results obtained during the execution of the statistical analyses.

(b) (4), (b) (6)

09-Oct-2018

Date

(b) (4)

PART A:

Analysis on Clinical Chemistry and Hematology Parameters on F_0 Generation

(b) (4)

SUMMARY OF STATISTICAL COMPARISONS USING 1-WAY ANOVA\ANCOVA
GENERATION F0 FEMALES

Parameter	PRETREATMENT				LACTATION PERIOD AT PPD 56				
	Overall Treatment Difference *p*-Value	Group Comparisons *p*-Value			Overall Treatment Difference *p*-Value	Covariate Effect (Predose) *p*-Value	Group Comparisons *p*-Value		
		1 vs 2	1 vs 3	1 vs 4			1 vs 2	1 vs 3	1 vs 4
CLINICAL CHEMISTRY									
AST (U/L)	0.4612	--	--	--	0.1557	0.8625	--	--	--
ALT (U/L)	0.4682	--	--	--	0.5564	0.4966	--	--	--
ALP (U/L)	0.5234	--	--	--	0.5771	0.0024	--	--	--
BILT3 (µmol/L)	0.2286	--	--	--	--	--	--	--	--
CHOL (mmol/L)	0.0841 ¶	0.0698 A	0.0146 B	0.1582	0.0325	0.0011	0.0756 A	0.0332 B	0.0051 C
TRIG (mmol/L)	0.6729	--	--	--	0.1145	0.1859	--	--	--
GLUC (mmol/L)	0.1229	--	--	--	0.0065	0.0210	0.0712 A	0.0359 B	0.9049
UREA (mmol/L)	0.9087	--	--	--	--	--	--	--	--
CREA (µmol/L)	0.3021	--	--	--	--	--	--	--	--
TP (g/L)	0.5592	--	--	--	0.8796	0.6316	--	--	--
ALB (g/L)	0.0929 ¶	0.5244	0.0297 B	1.0000	0.7087	0.7928	--	--	--
GLOB (g/L)	0.3909	--	--	--	0.2441	0.8951	--	--	--
A/G	0.0985 ¶	0.0959 A	0.0959 A	0.7719	0.1926	0.9910	--	--	--
CA (mmol/L)	0.4149	--	--	--	0.9038	0.4779	--	--	--
PHOS (mmol/L)	0.6698	--	--	--	0.4788	0.1753	--	--	--
Na (mmol/L)	0.3920	--	--	--	0.3780	0.3602	--	--	--
K (mmol/L)	0.2646	--	--	--	0.9817	0.2507	--	--	--
Cl (mmol/L)	0.6067	--	--	--	0.5934	0.1989	--	--	--
LDHI2 (U/L)	0.7930	--	--	--	0.2946	0.2884	--	--	--
CK (U/L)	0.4241	--	--	--	0.1226	0.2348	--	--	--
GGT (U/L)	0.6860	--	--	--	--	--	--	--	--
AMYL (U/L)	0.4153	--	--	--	0.1505	0.1119	--	--	--
MG (mmol/L)	0.6695	--	--	--	0.7683	0.8978	--	--	--
HEMATOLOGY									
RBC (x10^12/L)	0.1627	--	--	--	0.7223	0.8063	--	--	--
HGB (g/L)	0.3171	--	--	--	0.4355	0.8240	--	--	--
HCT (L/L)	0.3459	--	--	--	0.3876	0.6428	--	--	--
MCV (fL)	0.3160	--	--	--	0.6541	0.2538	--	--	--
MCH (pg)	0.1651	--	--	--	0.7121	0.0031	--	--	--
MCHC (g/L)	0.4293	--	--	--	0.1242	0.3494	--	--	--
RDW (%)	0.5534	--	--	--	0.6038	0.5983	--	--	--
PLT (x10^9/L)	0.0279 ¶	0.9549	0.3435	0.0342 B	0.9739	0.4457	--	--	--
WBC (x10^9/L)	0.1837	--	--	--	0.4347	0.0052	--	--	--
NEUT (x10^9/L)	0.1603	--	--	--	0.0440	0.0006	0.0386 B	0.0089 C	0.0955 A
LYMPH (x10^9/L)	0.0231 ¶	0.0761 A	0.4291	0.1444	0.7425	0.0528	--	--	--
MONO (x10^9/L)	0.3294	--	--	--	0.3743	0.0457	--	--	--
EOS (x10^9/L)	0.7484	--	--	--	0.5858	0.1348	--	--	--
BASO (x10^9/L)	0.2640	--	--	--	0.1572	0.1481	--	--	--
LUC (x10^9/L)	0.6716	--	--	--	0.1520	0.1500	--	--	--
NEUT (%)	0.1123	--	--	--	0.1379	0.0061	--	--	--
LYMPH (%)	0.0975 ¶	0.1938	0.0489 B	0.8389	0.5372	0.0897	--	--	--
MONO (%)	0.6182	--	--	--	0.4896	0.0055	--	--	--
EOS (%)	0.2719	--	--	--	0.5035	0.2624	--	--	--
BASO (%)	0.7597	--	--	--	0.1929	0.1941	--	--	--
LUC (%)	0.4389	--	--	--	0.3916	0.5761	--	--	--
RETIC (x10^9/L)	--	--	--	--	0.9377	--	--	--	--
RETIC (%)	--	--	--	--	0.7857	--	--	--	--

Significant overall treatment differences: ¶ - $p \leq 0.1$
Significant pairwise differences: A - $p \leq 0.1$, B - $p \leq 0.05$, C - $p \leq 0.01$ (*t*-test)
-- - Not applicable or not performed

(b) (4)

PART B:

Analysis on Clinical Pathology Parameters on F_1 Generation after Weaning
Selection of the Covariance Structure

SUMMARY RESULTS OF REPEATED TIME, THREE-WAY ANALYSIS OF VARIANCE
MODEL COVARIANCE STRUCTURE SELECTION - REML ESTIMATION METHOD
AKAIKE'S INFORMATION CRITERION (AICC, SMALLER IS BETTER) OBTAINED FROM THE FITTED COVARIANCE STRUCTURES
GENERATION F1 POST-WEANING

Covariance Structure	AICC Value					
	SP(POW) (Occasion)	SP(POWA) (Occasion)	AR(1)	ARH(1)	CS	CSH
CLINICAL CHEMISTRY						
AST (U/L)	557.1	557 1	557.1	553.7	556	550.9 <=
ALT (U/L)	798.3	798 3	798.3	759.7 <=	794	762.4
ALP (U/L)	993.9	993 9	993.9	925.9 <=	1023.6	934.2
CHOL (mmol/L)	178.4	178.4	178.4	178.1	176.8	172.4 <=
TRIG (mmol/L)	-177	-177	-177	-180 3 <=	-176.1	-179.4
GLUC (mmol/L)	104	104	104	102.5	99.7 <=	100.7
UREA (mmol/L)	236.1	236 1	236.1 <=	238.5	243.3	247.5
CREA (µmol/L)	579.5	579 5	579.5	574.9 <=	582	575.9
TP (g/L)	399.8 <=	399.8	399.8	404.9	409.1	414.5
ALB (g/L)	400.1	400 1	400.1 <=	403.6	405.1	407.4
GLOB (g/L)	394.8 <=	394.8	394.8	395.4	398.2	398.2
A/G	44.7	44.7	44.7	37.1 <=	47.6	38.6
CA (mmol/L)	-179 2	-179.2	-179.2	-180.1	-183.6 <=	-182.9
PHOS (mmol/L)	-90.2	-90.2	-90.2 <=	-85.4	-83.8	-78.8
Na (mmol/L)	357.7	357.7	357.7	355.8	356	354.4 <=
K (mmol/L)	51.1	51.1	51.1	49.9	50.2	48.8 <=
Cl (mmol/L)	358.2	358 2	358.2	358.7	356.7	356.1 <=
LDHI2 (U/L)	1033.4	1033.4	1033.4	1023.1	1033.4	1022.9 <=
CK (U/L)	1249.6	1249.6	1249.6	1220.2	1249.1	1217.2 <=
TBA (µmol/L)	537.2	537 2	537.2	487 <=	537.1	487.1
AMYL (U/L)	1155.3	1155.3	1155.3	1117.3	1152.4	1110.5 <=
MG (mmol/L)	-348.4	-348.4	-348.4	-349 1 <=	-339.9	-340.6
HEMATOLOGY						
RBC (x10/L)	107	107	107	101.7 <=	112.9	105.6
HGB (g/L)	697.3	697 3	697.3	693.8 <=	701	695.7
HCT (L/L)	-395 3	-395.3	-395.3	-399.8 <=	-391.4	-398.9
MCV (fL)	341	341	341	336.7 <=	342.6	344.5
MCH (pg)	178.2	178 2	178.2 <=	180.6	189	187.7
MCHC (g/L)	629.2	629 2	629.2 <=	632.1	629.5	631.4
RDW (%)	244	244	244	232.9 <=	248.3	233.5
PLT (x10/L)	994.4	994.4	994.4	990.8	992.2	983.2 <=

<= - Selected model

SUMMARY RESULTS OF REPEATED TIME, THREE-WAY ANALYSIS OF VARIANCE
MODEL COVARIANCE STRUCTURE SELECTION - REML ESTIMATION METHOD
AKAIKE'S INFORMATION CRITERION (AICC, SMALLER IS BETTER) OBTAINED FROM THE FITTED COVARIANCE STRUCTURES
GENERATION F1 POST-WEANING

Covariance Structure	AICC Value					
	SP(POW) (Occasion)	SP(POWA) (Occasion)	AR(1)	ARH(1)	CS	CSH
WBC (x10/L)	416.4	416.4	416.4	420.2	416.3 <==	419.3
NEUT (x10/L)	362.4	362.4	362.4	365	360.6 <==	361.7
LYMPH (x10/L)	204.2	204 2	204.2	198.2 <==	207.5	202.1
MONO (x10/L)	-45	-45	-45	-49.7 <==	-43.9	-49.6
EOS (x10/L)	-158	-158	-158 <==	-152.4	-154.6	-149.1
BASO (x10/L)	-422 2	-422.2	-422.2	-430.4 <==	-417.4	-427.8
LUC (x10/L)	-455.7 <==	-455.7	-455.7	-452.5	-451.3	-447.2
NEUT (%)	614.5	614 5	614.5	616	610	609.7 <==
LYMPH (%)	618.9	618 9	618.9	619.6	614.1	612.4 <==
MONO (%)	298.3	298 3	298.3	293.2 <==	299.2	293.7
EOS (%)	295.5	295 5	295.5	287.2 <==	308	298.5
BASO (%)	-22.2	-22.2	-22.2	-34.3 <==	-18.4	-32 5
LUC (%)	-55.8	-55.8	-55.8	-57.7 <==	-48.6	-49 1
RETIC (x10/L)	951.6	951.6	951.6	938.9 <==	955.1	942.5
RETIC (%)	166.6	166.6	166.6	141.2 <==	168.3	143
COAGULATION						
PT (Sec)	45.5	45.5	45.5 <==	46.6	45.5	46.6
APTT (Sec)	246.3	246 3	246.3	244 <==	246.3	244
FIB (g/L)	41.3	41.3	41.3	37.4 <==	41.3	37.4
URINALYSIS						
VOL (mL)	501.2	501 2	501.2	489.7 <==	501.2	489.7
SG	-265.6	-265.6	-265.6 <==	-263.9	-265.6	-263.9
pH	33.7	33.7	33.6	30.8 <==	33.6	30.8

<= - Selected model

(b) (4)

PART C:

Analysis on Clinical Pathology Parameters on F_1 Generation after Weaning *p*-Values of the Main Effects

SUMMARY RESULTS OF REPEATED TIME, THREE-WAY ANALYSIS OF VARIANCE
MAIN EFFECTS P-VALUES FROM 3-WAY REPEATED MEASURES ANOVA
GROUP*SEX*DAY, GROUP*SEX, GROUP*DAY AND GROUP MAIN EFFECTS
GENERATION F1 POST-WEANING

Parameter	Effect (Pr > F)			
	Evaluation of GROUP*SEX*DAY Effect (Pr > F)	Evaluation of GROUP*SEX Effect (Pr > F)	Evaluation of GROUP*DAY Effect (Pr > F)	Evaluation of GROUP Effect (Pr > F)
CLINICAL CHEMISTRY				
AST (U/L)	0.8079	0.1830	**0.0382** [C]	-- [E]
ALT (U/L)	0.9940	0.9263	0.2555	**0.0148** [D]
ALP (U/L)	0.9343	0.9392	0.7711	0.6926
CHOL (mmol/L)	0.3462	0.3713	**0.0022** [C]	-- [E]
TRIG (mmol/L)	0.4281	0.7478	**0.0017** [C]	-- [E]
GLUC (mmol/L)	0.2619	0.8445	**0.0127** [C]	-- [E]
UREA (mmol/L)	0.8754	0.9359	**<.0001** [C]	-- [E]
CREA (µmol/L)	0.8293	0.3664	**0.0461** [C]	-- [E]
TP (g/L)	0.4984	0.3469	**0.0363** [C]	-- [E]
ALB (g/L)	0.9264	0.4306	0.1916	0.3641
GLOB (g/L)	0.9726	0.7873	**0.0045** [C]	-- [E]
A/G	0.9974	0.8274	0.1025	0.6823
CA (mmol/L)	0.4959	0.8477	0.3713	0.9972
PHOS (mmol/L)	0.6929	0.3153	0.5618	**0.0959** [D]
Na (mmol/L)	0.5623	0.8923	0.7964	**0.0774** [D]
K (mmol/L)	0.4664	0.9172	0.3784	0.1351
Cl (mmol/L)	**0.0397** [A]	-- [E]	-- [E]	-- [E]
LDHI2 (U/L)	0.3363	0.3403	**0.0943** [C]	-- [E]
CK (U/L)	0.4482	0.2423	**0.0435** [C]	-- [E]
TBA (µmol/L)	0.4915	0.6934	0.3098	0.4380
AMYL (U/L)	0.8265	0.2728	0.4052	0.1253
MG (mmol/L)	0.9453	0.7076	0.9291	**0.0017** [D]
HEMATOLOGY				
RBC (x10/L)	0.1927	0.6076	0.2847	**0.0153** [D]
HGB (g/L)	0.1072	0.3733	0.3817	**0.0312** [D]
HCT (L/L)	0.1669	0.3872	0.6363	**0.0207** [D]
MCV (fL)	0.8845	0.6016	**0.0512** [C]	-- [E]
MCH (pg)	0.9312	0.8138	0.5180	**0.0802** [D]
MCHC (g/L)	0.9961	0.5359	0.7302	0.1513
RDW (%)	0.9927	0.8187	0.1281	**0.0098** [D]
PLT (x10/L)	0.1013	0.3701	**0.0829** [C]	-- [E]
WBC (x10/L)	0.6443	0.9039	0.4627	0.6232
NEUT (x10/L)	0.8182	0.9645	0.6008	0.4720

P-values in bold-face indicate statistical significance effect:

[C] Significance GROUP*DAY Interaction Effect ($p \leq 0.1$). Follow up GROUP mean comparisons will be made within DAY.

[D] Significance GROUP Effect ($p \leq 0.10$). Follow up pairwise GROUP mean comparisons will be made averaged over SEX and DAY.

[E] P-values are excluded when there was a significant higher interaction level.

SUMMARY RESULTS OF REPEATED TIME, THREE-WAY ANALYSIS OF VARIANCE
MAIN EFFECTS P-VALUES FROM 3-WAY REPEATED MEASURES ANOVA
GROUP*SEX*DAY, GROUP*SEX, GROUP*DAY AND GROUP MAIN EFFECTS
GENERATION F1 POST-WEANING

	Effect (Pr > F)			
Parameter	**Evaluation of GROUP*SEX*DAY Effect (Pr > F)**	**Evaluation of GROUP*SEX Effect (Pr > F)**	**Evaluation of GROUP*DAY Effect (Pr > F)**	**Evaluation of GROUP Effect (Pr > F)**
LYMPH (x10/L)	0.2372	0.7182	0.1122	0.3592
MONO (x10/L)	0.1861	0.5600	0.5137	0.9961
EOS (x10/L)	0.7902	0.7892	**0.0317** [C]	-- [E]
BASO (x10/L)	0.5536	0.4919	0.2022	0.5221
LUC (x10/L)	0.8801	0.5674	**0.0472** [C]	-- [E]
NEUT (%)	0.5506	0.9358	0.2582	0.3393
LYMPH (%)	0.4414	0.9516	0.2532	0.3079
MONO (%)	**0.0306** [A]	-- [E]	-- [E]	-- [E]
EOS (%)	0.3343	0.9245	**0.0193** [C]	-- [E]
BASO (%)	0.8640	0.6249	**0.0913** [C]	-- [E]
LUC (%)	0.3675	0.5302	**0.0168** [C]	-- [E]
RETIC (x10/L)	0.9674	0.7661	0.6309	**0.0065** [D]
RETIC (%)	0.9721	0.7981	0.5676	**0.0103** [D]
COAGULATION				
PT (Sec)	0.1234	0.9070	**0.0108** [C]	-- [E]
APTT (Sec)	0.6277	0.9796	**0.0529** [C]	-- [E]
FIB (g/L)	0.0626	0.3588	0.4032	0.1216
URINALYSIS				
VOL (mL)	0.5555	0.8364	0.1349	0.7176
SG	0.8674	0.3863	0.4467	**0.0493** [D]
pH	0.7991	0.7827	0.1767	**0.0602** [D]

P-values in bold-face indicate statistical significance effect:

[C] Significance GROUP*DAY Interaction Effect ($p \leq 0.1$). Follow up GROUP mean comparisons will be made within DAY.

[D] Significance GROUP Effect ($p \leq 0.10$). Follow up pairwise GROUP mean comparisons will be made averaged over SEX and DAY.

[E] P-values are excluded when there was a significant higher interaction level.

PART D:

Analysis on Clinical Pathology Parameters on F_1 Generation after Weaning
Selection of the Covariance Structure

SUMMARY RESULTS OF REPEATED TIME, THREE-WAY ANALYSIS OF VARIANCE
MAIN EFFECTS P-VALUES FROM 3-WAY REPEATED MEASURES ANOVA
GROUP MEAN COMPARISONS WITHIN SEX AND DAY.
GENERATION F1 POST-WEANING

		Evaluation of GROUP Effect (Pr > F)			
Parameter	**SEX**	Day 56	Day 112	Day 168	Day 224
AST (U/L)	Combined	**<.0001** [B]	0.3219	0 1203	**<.0001** [B]
CHOL (mmol/L)	Combined	**<.0001** [B]	**0.0079** [B]	0 1390	0.3033
TRIG (mmol/L)	Combined	**0.0097** [B]	**0.0122** [B]	**0.0004** [B]	0.4009
GLUC (mmol/L)	Combined	**0.0016** [B]	0.2185	**0.0408** [B]	0.2263
UREA (mmol/L)	Combined	**<.0001** [B]	0.4077	**0.0190** [B]	**0.0573** [B]
CREA (µmol/L)	Combined	0.3100	**0.0582** [B]	**0.0225** [B]	**0.0202** [B]
TP (g/L)	Combined	0.4063	0.7311	0.4830	**0.0317** [B]
GLOB (g/L)	Combined	0.4606	0.9106	**0.0473** [B]	**0.0147** [B]
Cl (mmol/L)	Females	0.3555	**0.0067** [A]	0.6727	0.8603
	Males	0.4042	0.3477	0 3326	0.4430
LDHI2 (U/L)	Combined	**0.0136** [B]	0.5773	0 1568	**0.0446** [B]
CK (U/L)	Combined	0.1042	0.1736	0 5831	0.2632
HEMATOLOGY					
MCV (fL)	Combined	**0.0434** [B]	0.2394	**0.0367** [B]	**0.0978** [B]
PLT (x10/L)	Combined	**0.0237** [B]	0.1328	0 1884	0.3738
EOS (x10/L)	Combined	0.5221	0.2745	**0.0547** [B]	0.1497
LUC (x10/L)	Combined	0.2533	0.1734	0 3853	0.4085
MONO (%)	Females	0.5433	0.4561	0.4799	**0.0002** [A]
	Males	0.1654	0.9626	0.8170	**0.0375** [A]
EOS (%)	Combined	0.6564	0.1136	**0.0658** [B]	0.2805
BASO (%)	Combined	0.4417	0.1568	0.8932	0.1896
LUC (%)	Combined	**0.0964** [B]	0.1988	0.7856	0.3781

		Evaluation of GROUP Effect (Pr > F)	
Parameter	**SEX**	Day 91	Day 238
COAGULATION			
PT (Sec)	Combined	0.5009	**0.0282** [B]
APTT (Sec)	Combined	**0.0857** [B]	0.7424

P-values in bold-face indicate statistical significance GROUP effect ($p \leq 0.1$):
[B] Follow up pairwise GROUP mean comparisons will be made for corresponding DAY averaged over SEX.

PART E:

Analysis on Clinical Pathology Parameters on F_1 Generation after Weaning Pairwise Comparisons

SUMMARY RESULTS OF REPEATED TIME, THREE-WAY ANALYSIS OF VARIANCE
PAIRWISE GROUP MEAN COMPARISONS ON GENERATION F1 POST-WEANING

Parameter	Source of Effect	SEX	DAY	Group 1	Group 2		Group 3		Group 4	
				LSMean	LSMean	*p*-Value *	LSMean	*p*-Value *	LSMean	*p*-Value *
AST (U/L)	Group*Day	Combined	Day 56	28.0000	34.2500	**0.0042** C	30.2500	0.2648	39.1470	**<.0001** C
			Day 224	28.3750	30.3750	**0.0937** A	28.0000	0.7460	35.5000	**<.0001** C
ALT (U/L)	Group	Combined	Combined	32.3437	35.2188	0.6920	32.5625	0.9759	54.1839	**0.0055** C
CHOL (mmol/L)	Group*Day	Combined	Day 56	4.8813	4.6775	0.3813	4.7963	0.7131	3.4046	**<.0001** C
			Day 112	6.3125	6.3750	0.8312	5.9688	0.2473	5.3775	**0.0036** C
TRIG (mmol/L)	Group*Day	Combined	Day 56	0.4325	0.5413	**0.0630** A	0.5888	**0.0101** B	0.4028	0.6085
			Day 112	0.3950	0.3850	0.7871	0.3963	0.9730	0.2825	**0.0053** C
			Day 168	0.3638	0.4850	**0.0008** C	0.4213	**0.0838** A	0.3375	0.4200
GLUC (mmol/L)	Group*Day	Combined	Day 56	7.0500	6.2625	**0.0002** C	6.7625	0.1462	6.5249	**0.0110** B
			Day 168	6.2375	5.6625	**0.0049** C	5.8750	**0.0688** A	5.9125	0.1016
UREA (mmol/L)	Group*Day	Combined	Day 56	3.3375	4.4250	**0.0030** C	4.2250	**0.0144** B	6.2920	**<.0001** C
			Day 224	4.9875	5.5000	0.1516	5.3375	0.3256	5.9625	**0.0074** C
			Day 168	4.7375	4.6125	0.7248	5.0875	0.3256	5.6625	**0.0109** B
CREA (µmol/L)	Group*Day	Combined	Day 224	53.5000	54.3750	0.7474	58.5000	**0.0740** A	49.3750	0.1368
			Day 112	32.7500	33.1250	0.8215	32.3750	0.8215	28.8750	**0.0267** B
			Day 168	45.7500	46.1250	0.8701	49.2500	0.1356	41.6250	**0.0811** A
TP (g/L)	Group*Day	Combined	Day 224	55.1250	53.4750	**0.0624** A	54.4875	0.4663	56.0625	0.2852
GLOB (g/L)	Group*Day	Combined	Day 224	19.7875	17.8375	**0.0132** B	17.4625	**0.0034** C	18.8625	0.2335
			Day 168	17.1625	18.1000	0.2273	19.2375	**0.0085** C	17.5375	0.6279
PHOS (mmol/L)	Group	Combined	Combined	2.3394	2.3719	0.4046	2.3338	0.8847	2.2722	**0.0923** A
Na (mmol/L)	Group	Combined	Combined	146.19	146.25	0.8609	147.03	**0.0247** B	146.71	0.1531
Cl (mmol/L)	Group*Sex*Day	Females	Day 112	105.43	105.75	0.7198	108.10	**0.0063** C	108.03	**0.0077** C
LDHI2 (U/L)	Group*Day	Combined	Day 56	75.5000	145.00	**0.0369** B	80.0000	0.8871	172.78	**0.0068** C
			Day 224	51.5000	80.1250	**0.0556** A	58.0000	0.6518	89.0000	**0.0145** B
MG (mmol/L)	Group	Combined	Combined	0.7419	0.7303	0.3583	0.7384	0.7833	0.7810	**0.0040** C
HEMATOLOGY										
RBC (x10/L)	Group	Combined	Combined	6.4306	6.5953	0.2674	6.1888	0.1080	6.1495	**0.0644** A
HGB (g/L)	Group	Combined	Combined	146.31	144.94	0.6935	139.28	**0.0519** A	136.78	**0.0105** B
HCT (L/L)	Group	Combined	Combined	0.4494	0.4481	0.9052	0.4259	**0.0326** B	0.4219	**0.0137** B
MCV (fL)	Group*Day	Combined	Day 56	71.0875	68.0125	**0.0061** C	70.0250	0.3032	69.8543	0.2404
			Day 168	70.0250	68.0625	**0.0078** C	68.5125	**0.0352** B	68.4000	**0.0245** B
			Day 224	69.9500	68.1500	**0.0137** B	68.9625	0.1609	69.0750	0.2125
MCH (pg)	Group	Combined	Combined	22.7219	21.9125	**0.0156** B	22.4719	0.4294	22.1870	**0.0986** A
RDW (%)	Group	Combined	Combined	13.2781	13.7750	**0.0589** A	12.8500	0.1008	13.1782	0.6969
PLT (x10/L)	Group*Day	Combined	Day 56	295.75	342.13	0.1219	333.00	0.2101	394 14	**0.0027** C
EOS (x10/L)	Group*Day	Combined	Day 168	0.3538	0.2513	**0.0377** B	0.2525	**0.0400** B	0.2288	**0.0120** B
MONO (%)	Group*Sex*Day	Females	Day 224	6.3250	4.4500	**0.0001** C	4.4000	**<.0001** C	5.1250	**0.0070** C
		Males	Day 224	4.2250	4.3250	0.8079	4.9500	**0.0873** A	5.3250	**0.0124** B
EOS (%)	Group*Day	Combined	Day 168	3.9250	2.4500	**0.0172** B	2.6875	**0.0423** B	2.6375	**0.0352** B
LUC (%)	Group*Day	Combined	Day 56	0.7250	0.5000	**0.0315** B	0.5000	**0.0315** B	0.5460	**0.0903** A
RETIC (x10/L)	Group	Combined	Combined	107.77	97.5719	0.3315	75.4781	**0.0043** C	74.3723	**0.0035** C
RETIC (%)	Group	Combined	Combined	1.7625	1.5500	0.1776	1.2781	**0.0040** C	1.2831	**0.0047** C

p-Values in bold-face indicate statistical significance group mean differences ($p \leq 0.10$)
[a] Significantly different from group 1: A - $p \leq 0.10$, B - $p \leq 0.05$, C - $p \leq 0.01$

SUMMARY RESULTS OF REPEATED TIME, THREE-WAY ANALYSIS OF VARIANCE
PAIRWISE GROUP MEAN COMPARISONS ON GENERATION F1 POST-WEANING

Parameter	Source of Effect	SEX	DAY	Group 1	Group 2		Group 3		Group 4	
				LSMean	LSMean	*p*-Value *	LSMean	*p*-Value *	LSMean	*p*-Value *
COAGULATION										
PT (Sec)	Group*Day	Combined	Day 238	7.8875	8.1500	**0.0889** A	8.3625	**0.0029** C	8.1500	**0.0889** A
APTT (Sec)	Group*Day	Combined	Day 91	26.9500	24.8500	**0.0673** A	24.1625	**0.0178** B	24.7500	**0.0561** A
URINALYSIS										
SG	Group	Combined	Combined	1.0355	1.0447	**0.0400** B	1.0394	0.3579	1.0469	**0.0120** B
pH	Group	Combined	Combined	5.7188	5.5092	**0.0341** B	5.5000	**0.0234** B	5.6562	0.4949

p-Values in bold-face indicate statistical significance group mean differences ($p \leq 0.10$)
[a] Significantly different from group 1: A - $p \leq 0.10$, B - $p \leq 0.05$, C - $p \leq 0.01$

(b) (4)

APPENDIX NO. 65
STUDY PLAN, STUDY PLAN AMENDMENTS



CONFIDENTIAL

FINAL STUDY PLAN

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

Test Facility:





Sponsor:
DSM Nutritional Products AG



Issue Date: July 5, 2017

(b) (4)

GENERAL INFORMATION

Study Director	(b) (4), (b) (6)
Supporting Scientist	
Study Monitor and Sponsor's Representative	

(b) (4) **Participating Managers**

Senior Director, Toxicology	(b) (4), (b) (6)
Director, Toxicology (Test Facility Management)	
Senior Director, Scientifi Operations and Veterinary Services	
Associate Director, Toxicology	
Vice President, Operations	

Director, Pathology Services	(b) (4), (b) (6)
Head, Veterinary Services	
Senior Director, Global Laboratory Operations	
Head, Statistics and Report Production	

(b) (4) **Participating Staff**

Statistics	(b) (4), (b) (6)

External Contributing Scientists

Consulting Toxicology Expert	(b) (4), (b) (6)
Clinical Pathology Data Interpretation	

(b) (4)

Principal Investigators (Test Sites – Sponsor Designate)

Diet analysis	(b) (4), (b) (6)
Bioanalysis	
Interpretation of Bioanalysis Data	

Principal Investigators (Test Sites – Test Facility Designate)

Pretreatment and Prior to shipment Study Phase	(b) (4), (b) (6)

TARGETED STUDY SCHEDULE

Start of feeding control diet*:	Week of July 10, 2017
Experimental start (1st mating start*):	July 17, 2017
Start of dosing (1st mating*):	July 17, 2017
Animal Arrival**:	August 21, 2017
Littering start (GD*** 56):	Week of September 11, 2017
Weaning start (PPD*** 56):	Week of November 6, 2017
Last observation on F_0 females and F_1 animals not selected (up to 2 months post-partum):	Week of November 6, 2017
Last observation F_1 animals (34 weeks old):	Week of May 11, 2018
Experimental completion:	July 30, 2018
Draft report:	Week of August 13, 2018

* Performed at (b) (4)
** Confirmed 4- to 5-week pregnant (GD 29 to 35)
*** GD = Gestation Day, PPD = Post-Partum Day

The actual dates for start of treatment (experimental start), last observation and experimental completion will be presented in the study report.

COMPLIANCE STATEMENT

This study will be conducted according to the Standard Operating Procedures of (b) (4) The study will not comply with Good Laboratory Practice regulations.

OBJECTIVE

The objective of this study is to evaluate safety and bioavailability of Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to Beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old).

EXPERIMENTAL DESIGN

The test and reference items will be administered as a diet as shown below:

Table 1: Study Design

Treatment Group [b]	Dosage Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F_0 Generation (dams)@	F_1 Generation (puppies) [a]	
					F	M(Spare)	F(Spare)
1. Control diet*	0	0	0.11%	0.12%	5	4(1)	4(1)
2. AOCED	½ X	0.75%	0.41%**	0.44%	5	4(1)	4(1)
3. AOCED	1X	1.5%	0.77% **	0.83%	5	4(1)	4(1)
4. AOCED	2X	3.0%	1.55%**	1.69%	5	4(1)	4(1)

* Group 1 animals will receive the control diet, which will be formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA level (0.11%) is achieved by using the chicken by-product meal as one of the ingredients.

** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content will be the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA) and from the chicken by-product meal (0.11%). Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.

*** Calculated based on dry matter basis (adjusted for moisture content).

[a] Two puppies per litter (1 male and 1 female), randomly selected, the spare will be randomly selected from any litter within each group.

[b] Since this study design include blinding to treatment groups, designations for individual animals will not be revealed during the conduct of the study and will only become available following the end of the data collection period and interpretation by the Study Director.

@ Six (6) females per group will be mated, as an attempt to have at least 5 females per group confirmed pregnant at GD 28. Only confirmed pregnant females (up to a maximum of 5/group, randomly selected) will be shipped to (b) (4)

M: male; F: female

Test Methods and/or Guidelines

This study was designed with reference to the following test methods and/or guidelines:

- CVM Guidance for Industry 56: Protocol Development Guideline for Clinical Effectiveness and Target Animal Safety Trials

- CVM Guidance 221: Recommendations for Preparation and submission of Animal Food additive petitions
- VICH GL43 (CVM GFI #185): Guidance for Industry. Target Animal Safety for Veterinary Pharmaceutical Products
- AAFCO Dog Food Gestation/Lacation and Growth Feeding Protocols

Justification for Dose Levels

Dose levels were selected by the Sponsor based on available marketing data. The recommended dose level (1X) was defined as the dose which provides the actual maximum dose of EPA and DHA currently available on the market worldwide. The survey of labels of dog food products was conducted by the DSM marketing team in December 2016. The high dose as a 2x multiple of the use dose was agreed upon with the CVM staff at the presubmission conference in June 2016. The ½ dose will provide information on dose-response relations of test item-related findings, if any.

Reason for Choice of Route of Administration

The dietary route is the intended route of administration of the test item in dogs.

Justification for Selection of the Test System

The dog (*Canis familiaris)* has been selected by the Sponsor to satisfy the regulatory requirements for safety testing in the selected species.

The current state of scientific knowledge and the applicable guidelines cited previously in this study plan do not provide acceptable alternatives, in vitro or otherwise, to the use of live animals to accomplish the purpose of this study. The development of knowledge necessary for the improvement of the health and well-being of other animals requires in vivo experimentation with a wide variety of animal species. Whole animals are essential in research and testing because they best reflect the dynamic interactions between the various cells, tissues, and organs comprising the dog body.

The dog was selected for use in this study by the Sponsor since the dog is the target animal for the investigated feed ingredient.

Justification for Numbers of Animals Selected

The number of animals used on the study is considered the minimum required to achieve the study objectives, based on regulatory requirements, statistical power and/or availability of historical data and are within IACUC and CVM approved guidelines. The Sponsor, by his or her signature, attests that the activities specified in this study plan do not unnecessarily duplicate any previous experiment.

TEST ITEM INFORMATION

Test Item Action Feed ingredient and a source of omega-3 fatty acids (EPA and DHA)

Characterization of Test Item, Test Item Diets and Control Diet

Test Item

Identity:	Algal Oil containing EPA and DHA
Alternative name:	AOCED
Batch/Lot No.:	(b) (4)
Correction Factor:	None
Storage conditions:	Room temperature
Expiry Date:	To be documented via study plan amendment

High Dose Diet**

Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	3.0%
Actual DHA+EPA content in diet (as it is):	1.55%
DHA+EPA content (on a dry matter basis):	1.69%
Storage conditions:	Room temperature
Best before:	October 14, 2018

Mid Dose Diet**

Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	1.5%
Actual DHA+EPA content in diet (as it is):	0.77%
DHA+EPA content (on a dry matter basis):	0.83%
Storage conditions:	Room temperature
Best Before:	October 14, 2018

Low Dose Diet**

Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	0.75%
Actual DHA+EPA content in diet (as it is):	0.41%
DHA+EPA content (on a dry matter basis):	0.44%
Storage conditions:	Room temperature
Best Before:	October 14, 2018

[redacted] (b) (4)

Control Diet**

Batch/Lot No.*:	Not applicable
Actual DHA+EPA content (as it is):	0.11%
Storage conditions:	Room temperature
Best Before:	October 14, 2018

*The diets were produced once for the entire study duration; therefore, lot numbers were not assigned.
**The diet identity and coding are not presented in this study plan in order to preserve blinding. A separate study document, with access restricted to unblinded personel, will be issued to document it.

Documentation characterizing AOCED, the test diets and the reference diet (control) will be supplied by the Sponsor for inclusion in the study report.

Upon receipt at [redacted] (b) (4) diets will be stored in a temperature controlled room (humidity not controlled/monitored), separated from any other diets.

Upon receipt at [redacted] (b) (4) diets will be stored in a room where other diets are stored. The room will only be controlled for temperature, but both the temperature and humidity will be monitored (daily).

Preparation of Dietary Admixtures

Extruded dry diets (one each for control, low, mid, and high concentrations of AOCED) will be provided by the Sponsor as ready-to-use.

The control diet will fulfill the 2016 AAFCO Dog Food Nutrient Profiles, which include recommendations for inclusion of EPA+DHA for puppies.

Stability of Test Item

Documentation of AOCED stability over the period of the study will be provided by the Sponsor.

Analysis of Diets

Representative samples (approximately 500 g, in duplicate) of each manufactured batch of each formulation will be taken from one bag used on Day 1 (at [redacted] (b) (4) from the first day of dosing at [redacted] (b) (4) (day of animal arrival), at two months intervals throughout the study, and at the end of treatment. If a batch is used for less or equal than two months, then samples will be taken at the beginning and at the end of the use period.

Additional samples may be collected and/or analyzed as necessary at the request of the Study Director (documented via study plan amendment).

The samples will be kept at room temperature.

(b) (4)

One set of the duplicate samples will be shipped at room temperature to the Sponsor-designated laboratory, for analysis:

(b) (4), (b) (6)

Following confirmation of safe and intact receipt of the first set of samples, the second set of samples may be shipped at room temperature to the Sponsor-designated laboratory, if required. If not required for analysis, the second set of samples will be kept a(b) (4) (b) (4) pending discard. The second set of samples collected at (b) (4) (b) (4), if not required for analysis, will be shipped to (b) (4) where it will be kept pending discard.

The analysis will be performed by the analytical laboratory to verify the DHA and EPA contents (DSM Nutritional Products SOP # (b) (4) (b) (4) and PV values (CDR FoodLabFat Analyzer for Measuring Peroxide Value – equivalent to AOCS Cd 8-53 reapproved 1997) in all diets. The acceptance criteria for the formulation will be ±15% of nominal.

Any analytical samples not employed in the primary analysis or required following completion of the primary analysis will be discarded prior to issuance of the final report (but after finalization of the Analysis Report).

Archive Sampling and Disposition of Diets

An adequate sample (minimum of 1 g) of each lot of each diet will be collected (at (b) (4) and stored in the archives of (b) (4) under the same storage conditions used during the study.

After completion of the study, any sealed bags of diet remaining at (b) (4) will be destroyed (incinerated), or will be returned to the Sponsor prior to finalization. Similarly, any individual amount of food remaining daily (at (b) (4)) will be retained for incineration at intervals or at completion of the study.

Any diets remaining at (b) (4) at shipment of animals will be discarded.

Administration of Diets

As the Sponsor will provide the diets already coded, each animal's actual treatment designation will be unknown to staff performing dosing or data collection.

As animals will be housed in different rooms (at (b) (4) due to the space restrictions), treatment will be done in a separate designated room. Treatment of the animals will be by each housing room (applicable to (b) (4) only), by ascending animal number (see Animal Assignment and Blinding Procedure).

A(b) (4) animals will be housed in separate pens from animals not assigned to the study, starting approximately 1 to 2 weeks (3-14 days) prior to Day 1, to receive the reference/control diet.

F_0 (at (b) (4)): During the acclimation/pre-treatment period, the females will receiv (b) (4) standard diet for breeders up until approximately 1 to 2 weeks prior to Day 1 (3-14 days) when they will receive the reference/control diet (approximately 400 g of food per day). Daily oral dietary administration to dams (approximately 600 g of food per day) will start on the day of the first successful mating* and will continue until shipment to the Test Facility. If appetence issues are observed, warm water can be added to the diet.

** Females will be mated 2 or 3 times, with one day of rest between each mating. Successful mating will be described as observation of the tie. Males used for mating will be proven breeders of at least 12 months of age and confirmed healthy (health record of both sires and dams will be provided to the Study Director – only the health record of dams will be reported, health records of sires will be retained on file).*

F_0 (at (b) (4): Daily oral dietary administration to dams will continue immediately after arrival and throughout gestation and lactation (approximately 15 weeks in total). Dams will receive approximately 600 g of food per day from arrival to parturition, and 900 g per day from parturition until weaning. More food can be added during the day if needed, but additional quantities will be measured/recorded. If appetence issues are observed, 100 mL of warm reverse osmosis water can be added to the diet.

F_1: Starting at 5 weeks of age and until weaning, puppies will be provided with a feeding pan. During that period, the daily food intake will be calculated for the dam plus its litter (i.e.: dam's bowl, plus feeding pan) since the dam will also have access to the feeding pan (approximately 300 g).
As of weaning, puppies selected for the study will continue on their mothers' respective diets (approximately 400 g per day/dog for a 6-8 hours daily feeding period) for the additional 6 months until they reach 34 weeks of age. Puppies will remain pair-housed for feeding during the first two weeks post-weaning to confirm ability to properly thrive, and will then be individually housed for feeding for the remainder of the study. If appetence issues are observed, 100 mL of warm reverse osmosis water can be added to the diet. Similarly,

(b) (4)

puppies not selected to continue on the study will continue on their mothers' respective diets until release from the study (approximately 2 weeks after weaning).

The remaining puppies will be released from the study once ability to thrive of all randomly selected puppies is confirmed (transferred to (b) (4) dog colony where they will receive the standard commercially available diet).

TEST SYSTEM

Species:	Dog (*Canis familiaris*)
Strain:	Beagle
Source:	(b) (4)
Total animal No. on study*:	24 females
Target age range:	1.5 to 3 years old at start of treatment (assumed GD 0)
Target body weight range:	9 to 12 kg at start of treatment (assumed GD 0)

* Six (6) females per group will be mated, as an attempt to have at least 5 females per group confirmed pregnant at GD 28. Only confirmed pregnant females (up to a maximum of 5/group, randomly selected) will be shipped to (b) (4) (confirmed 4- to 5-week pregnant (GD 29 to 35).

The actual age and body weight ranges at the start of treatment will be presented in the study report. Bitches must be in at least their second heat period when they are mated and at least one year of age.

Health Status

Animals will be vaccinated and dewormed at (b) (4) (standard program) prior to dosing start, and free of infectious diseases which could complicate the interpretation of the study results.

Following arrival, all animals will be subject to a health assessment (including weight measurement). The evaluation will be performed in accordance with the standard operating procedures by technical staff. The results of the evaluations (including body weight) will be reviewed by the Clinical Veterinarian to confirm that animals are healthy and were not affected by transportation.

Puppies will be vaccinated, dewormed and examined at (b) (4) as per SOPs (data retained on file).

Identification

Each dam will arrive from the supplier individually identified by means of a tattoo. Each dam will be assigned an animal number to be used (as described in the following table and in the Animal Assignment and Blinding Procedure section).

(b) (4)

Group	Animal Numbers*
	Females
1	(b) (4)
2	
3	
4	

* Number of animals at assignment. The identification of animals received at (b) (4) will vary since (b) (4) will only ship confirmed pregnant females (up to a maximum of 5/group).

The first number corresponds to the respective dose group while the second number identifies the gender of the animal (numbers 5 to 9 will be used for females). The third and fourth number identifies the animal's rank per gender within each group.

The puppies (F_1) will be identified as per relevant (b) (4) SOPs (i.e.: paper collar on PPD 0, then microchip from PPD 1).

For the second generation, the utilization of animal number with 3 numbers can be used. Animal identification will be interpreted using example below (animal 1501).

i.e.: First generation (F_0) = 1501 for Dam
Second generation (F_1) = 151 or 101 for Puppies

Housing

Animals will be assigned to cages/pens in order of ascending animal mating number (for blinding).

Dams (F_0) will be housed individually in pens (at (b) (4) or in European cages (at (b) (4)) (dimensions: approximately 3 by 6 feet for d approximately 5 by 6 feet for European cages) equipped with an automatic watering system due to the nature of this study which does not permit group housing (i.e.: pregnant animals, dams with litter) and study requirements (i.e.: diet study).

Approximately 2 weeks prior to parturition, a nesting box will be offered to each dam. In addition, a litter pan will be given to the puppies from weaning until they reach approximately 3 to 4 months of age.

After weaning, puppies selected to continue on the study (F_1) will be pair housed in stainless steel dog cages (dimensions: approximately 3 by 3 feet) equipped with an automatic watering system, but will be separated during the 6-8 hour daily feeding period (separation starting at the third week post-weaning), to acquire individual food consumption data (i.e.: diet study). If possible, one male and one female will be housed together in each group to harmonize the food consumption values between cages during the first two weeks post-weaning. Throughout the weaning process and after weaning, dams will be individually housed in stainless steel dog cages (dimensions: approximately 3 by 3 feet) equipped with an automatic

[redacted] (b) (4)

watering system. Puppies not selected to continue on the study will remain in European cages until their release from the study (approximately 2 weeks after weaning).

All pens/cages will be clearly labeled with cage cards, indicating the study number, animal tattoo number, blinded animal assignment number, sex and replicate.

Due to space restrictions, at [redacted] (b) (4), animals will be housed in different rooms, but all rooms will be of the same type, within the same building, and will have the same environmental controls, water sources, and daily routines for care and cleaning. Every room will include animals from each treatment group (designated by unblinded technical staff not involved in data collection), such that the rooms will be balanced for sex (applicable to puppies only), and treatment. Within each room (at [redacted] (b) (4), animals will be assigned to cages by ascending animal arrival number (*e.g.*, in clockwise placement around the room) in order to maintain the study blind. Approximately 1 week after weaning, selected pups will be consolidated into a single room.

At [redacted] (b) (4), animals will be assigned to pens by ascending animal mating number (e.g., in rows of ascending blinded animal assignement number) in order to maintain the study blind.

Room Environment

At [redacted] (b) (4) a commercial breeder facility, the temperature, humidity and air changes per hour are not controlled (set) but the temperature is monitored (once a day). The light dark cycle is set to 14 hours light/10 hours dark.

At [redacted] (b) (4) the animal room environment will be set to maintain a relative humidity of 50 ± 20%; a light dark cycle of 12 hours light/12 hours dark, except during Study Plan-designated procedures; and 10 - 15 air changes per hour. The room temperature will be set to maintain 21 ± 3°C from arrival until approximately 2 weeks prior to parturition when it will be increased to maintain 24 ± 3°C until at least PPD 42. From PPD 43 (of the youngest litter) until the end of the study, the temperature will be returned to 21 ± 3°C.

At [redacted] (b) (4), the temperature and relative humidity will be monitored continuously. Room environmental conditions will be reported to the Study Director, and excursions from the prescribed ranges will be included in the study report. Records will be kept on file at [redacted] (b) (4).

Facility diagram, building orientation, ventilation and lighting procedures will be provided to CVM (as an Appendix to the report). The housing rooms at [redacted] (b) (4) will measure 14 by 33 feet.

Diet/Water

Throughout the pretreatment period until approximately 1 week prior to mating, animals will receive (b) (4) standard diet. For approximately 1 to 2 weeks (3-14 day) prior to Day 1 (day of first successful mating), the females will receive the reference/control diet, except during designated procedures. During the treatment period, animals in each group will be provided access to the Sponsor-provided dietary mixtures (one specific for each group – See Administration of Diets section for details).

No treats will be provided to the dams. A very small amount of treats will be provided to the puppies as part of the animal enrichment program. The provision of the treats will be approved by the Study Director prior to being given.

Municipal tap water (which has been exposed to ultraviolet light and purified by reverse osmosis, at (b) (4) nly) will be provided to the animals *ad libitum*, via automatic water system or via water bottles, if required. A bowl of water will also be placed in the cage until weaning. Periodic analyses of the municipal tap water (purified water) will be performed by a (b) (4) designated facility and the results are retained on file at (b) (4). Identified contaminants, if any, in the water will be assessed for concentrations that could interfere with the objectives of the study. Similarly, at (b) (4) periodic analyses of the municipal tap water will be performed and the results will be provided to the Study Director (retained on file).

Acclimation/Socialization

While at the breeding facility, animals will be socialized per (b) (4) relevant standard procedures (retained at (b) (4)) to ensure they are relaxed and calm when handled by caretakers in a laboratory setting.

There will be no acclimation period upon arrival at the Test Facility, as daily oral dietary administration started at (b) (4) is to be continued immediately after arrival. Nevertheless, the activities in the animal housing room(s) will be minimized for the 7 days following arrival to accustom the animals to the laboratory environment.

Dams will be socialized by the key technicians (no more than 4) at least twice weekly throughout the gestation period starting 7 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. Only the key technicians are allowed to take the puppies out of the cage.

Secondary technicians (no more than 6) will socialize with the dams at least once weekly during the gestation period starting 7 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. The secondary technicians are only allowed to manipulate the puppies if a key technician has taken them out of the cage first.

Puppies will also be socialized per SOP (submission technique).

(b) (4)

Animal Assignment and Blinding Procedure

The animal assignment will be performed at (b) (4). The order of the animal number assignement was randomly determined. In order to preserve the blinding, the table describing the assignment of animals based on timing of mating confirmation will be maintained in a separate document, with access restricted to unblinded personel.

(b) (4) will test for pregnancy approximately 28 days after mating. If all 6 dams within a group are confirmed pregnant, 1 dam will be randomly selected using a dice and will be released from the study, so that a maximum of 5 pregnant dams per group will be shipped to (b) (4). The dams will be shipped to (b) (4) in one shipment.

One or two puppy/sex/litter will be randomly retained for the F_1 assessments (See Weaning section for details). Additional puppies/sex/litter may be selected if less than 4 litters/group are obtained.

During the in-life portion of the study, each animal's treatment designation will be unknown to the staff who will be blinded.

The animal cage cards will only display the study number, animal sex, the blinded animal identification numbers (i.e., mating number) and the animal tattoo number.

Blinding in the study will be applied to the identity of the test item or reference item (control) assigned to each experimental dose group (i.e., Group 1 through Group 4). As the animal arrival numbers (e.g., 1, 2, etc.) will be maintained in Provantis for the in-life portion of the study, there will be no indicator of the animal assignment to treatment groups in Provantis until the study will be unblinded. Note that the Provantis system will only be used at (b) (4), not at (b) (4) where all data capture will be performed manually.

Personnel involved in the in-life data collection will be blinded to the experimental groups. However, the Study Director, the Principal Investigator (at (b) (4)), the Clinical Pathologist, the pharmacy staff and the departmental team leaders will not be blinded. These unblinded personnel will not participate in direct evaluation of the animals/data collection. This relaxation in requirement will be necessary in order to permit adequate monitoring and quality checks during the course of the study. For ethical reasons, the Veterinarian staff will not be blinded, since access to an animal's identification and treatment type could be required in order to assess the correct interventions that are needed and to properly fulfill animal care requirements.

Animal Replacement

Any dam considered unsuitable for use on study may be excluded prior to assignment (day of 1st mating). There will be no replacement of dams after initiation of treatment.

(b) (4)

Any dam confirmed not pregnant on GD 28 will not be shipped to (b) (4)

Any puppy (F_1) considered unsuitable for use on study may be excluded at selection (PPD 56). There will be no replacement of puppies after the first two weeks of weaning (once ability to thrive is confirmed).

Fluid Replacement

Fluid replacement (0.9% sodium chloride USP administered subcutaneously or Lactate Ringers administered intravenously) may be performed as required based on blood sample volumes collected during the study. The volume of fluid to be administered will be documented in the study data.

Animal Care Compliance

Procedures involving the care and use of animals in this study will be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) prior to conduct. During the study, the care and use of animals will be conducted in accordance with the principles outlined in the current Guidelines published by the Canadian Council on Animal Care and the Guide for the Care and Use of Laboratory Animals, an NRC publication and/or USDA regulations. (b) (4) facility is accredited by the Canadian Council on Animal Care and AAALAC. Per the Canadian Council on Animal Care guidelines, this study is considered as a category of invasiveness B. The portion of the study to be performed at (b) (4) is considered a category C for USDA Pain and Distress classification.

As a study in the field of regulated research, this study is expected to significantly contribute to medical advancement and improving the quality of animal life through animal use based on the intended purpose of the test item.

IN-LIFE OBSERVATIONS

Signed and dated records of activities relating to the day-to-day running and maintenance of the study within the animal room as well as the activities relating to the observations and examinations outlined in this Study Plan will be recorded. Observations will be made and data collections will be performed by blinded trained technicians (i.e., without knowledge of the treatment groups for individual animals). During the course of the study, additional evaluations to those described below and/or scheduled and considered necessary by the Study Director and the Veterinarian, as applicable, to assess health status will be conducted and duly documented in the study file and included in the study report.

Mortality

Mortality checks will be recorded concomitantly with the cage-side observations (see below), during all phases of the study.

Animals in unrelievable pain or distress will be euthanized at the discretion of the Study Director or based on the clinical judgment of the Clinical Veterinarian in consultation with the Study Director and the Sponsor, if possible. Euthanasia endpoints are described in facility Standard Operation Procedures.

For animals euthanized for humane reason, a blood sample (unfasted) will be collected for clinical pathology investigations, when possible.

Animals pre-terminally euthanized or found dead will be processed as detailed in the Terminal Procedures section.

Clinical Observations

Animals will be observed on multiple occasions for clinical signs that may indicate ill health or other changes; observations are planned to be made at the cage-side, and during scheduled detailed clinical examinations, but additional clinical observations may be conducted if warranted to properly monitor animals health condition. Clinical observations will be conducted by blinded trained technicians and per facility SOPs (or (b) (4)) and this study plan; the occasions are described in further detail below. Clinical findings may be referred to the Clinical Veterinarian.

Clinical signs (ill health, behavioral changes, etc.) will be recorded on all animals twice daily throughout the study. The nature of these observations will include evaluation of general appearance, activity, and other indicators of changes in animal health and behavior, including fur condition, gait and mobility. Litter checks will be performed once daily (concurrently with a clinical sign activity) until PPD 56.

A detailed clinical examination (DCE) will be performed on each animal at least on the day of estrous and on the day of treatment initiation and once within the week prior to shipment (at (b) (4), concurrently with body weight measurements), and monthly thereafter (at (b) (4). A DCE will also be performed on the day prior to release from the study.

Detailed clinical examinations will be conducted per facility SOPs (or (b) (4), which describe that during the detailed clinical examination, animals will be observed while in the cage for behavior, general appearance, coordination, etc., and then will be removed from the cage for close evaluation of general condition of the whole body including (but not limited to) head, thoracic, and abdominal areas through examination and palpation. Body temperature, heart rate and respiratory rate (counts per minute) will also be evaluated.

(b) (4)

For puppies, height and head circumference will also be measured weekly starting on PPD 7.

In addition, a detailed examination will also be performed on all puppies selected to continue on the study (F_1) by blinded technical staff once a month from weaning thereafter, including within 3 days prior to release from the study. This evaluation will be conducted per facility SOPs which include assessment of the general body condition, autonomic and central nervous system, somatomotor activity, gait, skin/fur condition, lymph nodes, eyes, mucus membranes, respiration, behavior, circulatory system, state of hydration, and lungs, bladder, reproductive system and gastrointestinal auscultation and/or palpation. Particular attention should be directed to observations of central nervous system signs (seizures, tremors, salivation), vomiting and diarrhea. Additional observations may be performed as deemed necessary.

Animals whose health condition warrants further evaluation will be examined. Initiation of medical treatments, as recommended, will begin only following authorization (with the exception of pre-approved treatments) by the Study Director (in consultation with the Sponsor, if possible). Whenever possible, the Sponsor will be consulted prior to administration of systemic therapeutic drugs (i.e. other than topical). In the event that medical intervention is necessary, all medications and treatments, and reason for administration will be recorded and included in the study report.

Body Weights

Body weights will be recorded for all dams at least on the day of estrous and on the day of treatment initiation (at (b) (4), concurrently with (b) (4), and weekly thereafter.

Puppies will be weighed on PPD 0, 4, 7, 10, 14, 17, 21, etc. until weaning, and weekly thereafter.

A body weight measurement will also be performed on dams and puppies on the day prior to release from the study.

Food Consumption

Individual food intake will be measured on all animals at least daily (except on days of food deprivation) throughout the study, starting at initiation of feeding the reference/control diet (3-14 days prior to treatment start). In addition to the daily food consumption, achieved intakes will be calculated on a weekly basis (calculations performed at (b) (4)

The average of daily individual achieved intake of the test item in mg/kg/body weight per week will be calculated for both generations based on daily food consumption using the following formulas:

- On dams from Day 1 until puppies are 5 weeks of age (without feeding pan)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

- On dams with puppies, from 5 weeks of age until weaning (with feeding pan, including puppies body weight), and for the first two weeks post-weaning (2 puppies/cage)

$$\frac{\text{Dietary concentration (mg/kg/cage) x food consumption (kg)}}{\text{Start-week body weight (kg/cage)}}$$

- On selected puppies, from the 3rd week post-weaning (1 puppy/cage)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

For reporting purposes weekly average of daily food consumption and achieved intakes will be presented.

Parturition Observations

Dams will be observed for parturition at least 3 times a day starting from GD 55 until GD 71 (as applicable), as per standard operating procedures. Body temperature will be measured twice daily (12 hours ± 1 hour apart) starting on GD 55 until the first signs of parturition are observed. Body temperature will also be measured daily from GD 52-54 for baseline acquisition. The time of onset and completion of delivery will be recorded for each animal whenever possible. The day parturition is completed will be termed as PPD 0. Any signs of difficulty in parturition will be recorded.

Litter Size

Following the littering, the number of live, dead and malformed puppies at birth of F_1 puppies will be recorded daily from PPD 0 until weaning on PPD 56. Gross abnormalties, if any, will be recorded.

External Sex Determination Puppies (F_1 generation)

The number of male and female puppies in each litter will be determined as per (b) (4) SOP, by visually judging the anogenital distance and/or presence of a vulva or penis.

Standardization of Litter (Culling)

If a dam has more than 6 puppies, on PPD 1, the litter will be randomly adjusted to 6 puppies.

(b) (4)

On PPD 4, the size of each litter may be adjusted by eliminating extra puppies by random selection to yield, as closely as possible, 4 puppies/litter (with at least 1 male and 1 female puppy where the number of puppies allows).

The culled puppies will be randomly selected and no criteria (e.g.: body weights or similar) used for selection, and they will be euthanized (intracardiac injection of sodium pentobarbital solution – 240 mg/mL – dose volume based on the SOP, unless the animal`s body weight is less than 0.5 kg, in which case the dose volume will be 0.6 mL).

The puppies will be identified as per relevant (b) (4) operating procedures.

Weaning

The puppies will be weaned on PPD 56 and separated from the dams. One puppy/sex/litter will be randomly retained for the F_1 assessments.

In case of fewer than 4 litters obtained per group, two males and two females from the same litter can be selected for the same treatment group. Puppies not selected will be released from the study.

Starting on PPD 49, the daily period of separation of the puppies from their mother will be introduced. It will gradually increase until complete separation on PPD 56. At all time while separated from their mother during gradual weaning process, the puppies will have access to a bowl of electrolytes solution.

Clinical Pathology

Clinical pathology evaluations (hematology and clinical chemistry) will be performed on all dams (F_0) once during pretreatment (a (b) (4) and at weaning.

In addition, on all puppies continued on the study (F_1), coagulation and urinalysis will be performed during Weeks 13 and 34; while hematology and clinical chemistry evaluation will be performed at weaning and every two months thereafter for the 4 total times during the growth phase.

Blood samples will be collected from the jugular vein (the cephalic vein may be used if required). Food will be removed overnight prior to blood collections (required for clinical chemistry). Urine will be collected overnight (targeted 10 hours ± 1 hour) from individually housed (in stainless steel dog cages) animals that will be deprived of food and water. The urine collection period may be extended in the event a sufficient urine sample volume is not collected within the time frame permitted.

Repeat for hematology and/or coagulation can be repeated with or without food and/or water deprivation if permissible sampling frequency and blood volume are not exceeded.

(b) (4)

a) **Hematology**

The following parameters will be measured on blood samples collected into tubes containing K_3-EDTA as anticoagulant. The target volume of blood collected for each sample will be 1.3 mL a (b) (4) and 3 mL at (b) (4).

Cell morphology *	Platelet count
Hematocrit	Red blood cell count
Hemoglobin	Red cell distribution width
Mean corpuscular volume	Reticulocyte counts (absolute and relative)
Mean corpuscular hemoglobin	White blood cell count (WBC)
Mean corpuscular hemoglobin concentration	WBC differential (absolute and relative)

* Manual reading of smears for morphology check only carried out as necessary, in accordance with (b) (4) standard operating procedures. At (b) (4), if manual reading of smears for morphology check is required, it will be performed (b) (4)'s designated laboratory (b) (4)

b) **Coagulation**

The following parameters will be measured on blood samples collected into tubes containing citrate as anticoagulant. The target volume of blood collected for each sample will be 1.0 mL.

Sample Appearance (when abnormal)	Fibrinogen
Activated partial thromboplastin time	Prothrombin time

c) **Clinical Chemistry**

The following parameters will be measured on blood samples collected into tubes containing clotting activator gel. The target volume of blood collected for each sample will be 1.1 mL at (b) (4) and 4 mL at (b) (4). At [(b) (4)], the obtained serum will be separated into two aliquots. One aliquots will be shipped to (b) (4) designated laboratory (b) (4) for analysis of the parameters with an '*' below. The other aliquot will be analyzed at (b) (4) for the remaining parameters.

Sample Appearance (when abnormal)	Creatine kinase
A/G ratio (calculated)	Gamma glutamyltransferase (GGT)
Alanine aminotransferase	Globulin (calculated)
Albumin	Glucose
Alkaline phosphatase	Lactate dehydrogenase (LDH)*
Amylase	Magnesium
Aspartate aminotransferase	Phosphorus (inorganic)
Bile acids (total)	Potassium
Bilirubin (total)	Sodium
Total Calcium	Total protein
Chloride	Triglycerides*
Cholesterol (total)	Urea
Creatinine	

[redacted]

d) **Urinalysis**

Minimum volume of approximately 1.0 mL. The following parameters will be measured on urine samples:

Bilirubin
Blood
Color and appearance
Glucose
Ketones
Leukocytes
Microscopic analysis (sediments)
Nitrites
pH
Protein
Specific gravity
Urobilinogen
Volume

Buccal mucosal bleeding time

Buccal mucosal bleeding time will be measured on all puppies continued on the study (F_1) during Week 34, on the same day (+/- 1 day) as the clinical pathology occasion (coagulation).

Bioanalysis

Blood samples (a target of 3 mL each) will be collected from dams during the pretreatment period for a baseline (at [redacted], after 4 to 5 weeks of treatment (at [redacted] and at weaning (at [redacted]). Blood samples (a target of 2 mL each) will also be collected from all selected weaned puppies (F_1) at weaning and during Weeks 13 and 34, at approximately the same time on each occasion.

Each blood sample will be collected by jugular venipuncture (or any other vein may be used if required) into tubes containing K_2-EDTA (alternatively, K_3-EDTA can also be used, but the tube type should be consistent throughout the study) as anticoagulant and kept on wet ice pending centrifugation. Samples will be centrifuged at 1500 g RCF for targeted 10 minutes. Centrifugation will be refrigerated (set to +4°C) at [redacted], but not at [redacted] where it will be performed at room temperature.

Excursions from the target volume will be documented in the raw data. In the event samples must be re-centrifuged, the times of sample processing will be documented. Plasma will be transferred into 2 separate tubes, placed on dry ice pending storage in a freezer set to maintain -70°C until shipment. One set of samples will be shipped on dry ice, to the Sponsor-designated laboratory for analysis at the following address:

Attn o [redacted]

(b) (4)

Samples should be shipped by FedEx overnight on dry ice. An email should be sent to (b) (4) (b) (4), (b) (6) alerting him of the shipment. An electronic list of samples should be included in the e-mail and with the shipment.

Following confirmation of safe and intact receipt of the first set of samples, the second set of the duplicate samples may be shipped to the Sponsor-designated laboratory on dry ice or may be discarded at the request of the Sponsor.

Samples will be analyzed using a validated assay (b) (4) or measurement of DHA and EPA plasma concentrations.

Remaining Sample Disposal Policy Statement

All remaining unanalyzed biological samples (if any) will be discarded prior to finalization, unless specifically instructed otherwise in writing, by the Sponsor. In the event the Sponsor requests, in writing, prolonged storage time of the above material it will be documented via a study plan amendment (at additional cost).

TERMINAL PROCEDURES

At weaning (for dams) or two weeks after weaning (for puppies), all dams and all puppies not selected for the growth phase of the study (once ability to thrive of selected puppies is confirmed, i.e. 2 weeks post-weaning) will be transferred to the (b) (4) animal colony. Similarly, at the completion of the study, all surviving selected puppies will be transferred to the (b) (4) animal colony.

Dams found dead or euthanized for humane reasons will be processed as per relevant standard operating procedures. Necropsy of the dams will consist of an external macroscopic examination, including identification of all clinically recorded lesions, as well as a detailed internal examination and the reprodutive tract dissected out, the ovaries removed and corpora lutea counted, and processed as per standard operating procedures. Grossly abnormal tissues will be retained for possible future histopathology.

Similarly, any puppies found dead or euthanized for humane reasons will be processed as per relevant standard operating procedures. Necropsy of the puppies will consist of an external macroscopic examination, including identification of all clinically recorded lesions, as well as a detailed internal examination, and processed as per standard operating procedures. Grossly abnormal tissues will be retained for possible future histopathology.

In order to avoid autolytic changes, the macroscopic examination of the carcass will be conducted, as soon as possible, on all animals which die or are euthanized prematurely. Should an animal be found dead or euthanized outside regular working hours, necropsy will be completed as soon as possible after the time of death. Pending necropsy, the carcass will be stored in a refrigerator (set to 2-8°C).

(b) (4)

Photographs of individual macroscopic or microscopic findings may be taken at the discretion of the attending Pathologist and/or the Study Director for illustrative purposes only. Photographs (if any) will not routinely be reported but will be kept in the study file. Photographs may be reported at the discretion of the Sponsor or Study Pathologist, at additional cost.

Histopathology

No histopathological preparation or evaluation will be performed (except at the request of the Sponsor and at additional cost).

DATA HANDLING AND REPORTING

Data Capture

The following data capture systems may be used during the conduct of this study. Version numbers of the systems will be specified in the study report.

In-life data collection	Provantis (at (b) (4))
Pathology (if any)	Provantis (at (b) (4))
Clinical pathology	Provantis (at (b) (4) custom-designed animal management database)
Analytical Chemistry	Agilent OpenLab CDS, version C.01.07
Bioanalytical	Shimadzu Lab Solutions, version 5.81
Statistical analysis	SAS (at (b) (4))
Room environment	Siemens Insight (at (b) (4) , none at (b) (4))

Various parameters, not mandated by the Study Plan, will be automatically measured and recorded by the instrumentation(s), but will not be reported.

Manual or computerized recording (in-life data collection and pathology, if any) in accordance with the standard operating procedures may be used to ensure data capture as necessary. At (b) (4) , most data will be manually collected and subsequently entered in Provantis (by (b) (4)) for reporting purposes.

All data collected at (b) (4) will be transferred to (b) (4) prior to and/or at shipment of the animals.

A quality check of the raw data will be performed prior to unblinding of the animal identification information.

Data Analysis

The statistical analysis approach for this study was designed with reference to Guidance for Industry #226: Target Animal Safety Data Presentation and Statistical Analysis. The statistical reporting will be done in compliance with the Guidance for Industry #197: "Documenting Statistical Analysis Programs and Data Files".

Data recorded at unscheduled occasions will be reported on an individual basis but will not be included in the analysis described below.

Whenever a continuous variable is measured on more than one pup per litter, an average per litter and sex will be computed, reported and the statistical analysis will be performed using the average per litter and sex.

Continuous variables specified in the study plan and collected during the conduct of the study will be subjected to calculation of group means, standard deviations, minimum and maximum values and will be reported by group and sex on each occasion. The calculation of group descriptive statistics will also be presented by group on combined occasions and/or combined sexes when a non significant occasion and\or sex interaction with the treatment effect is detected by the respective statistical analysis.

Categorical and dichotomous data specified in the study plan and obtained during the conduct of the study will be reported as individual results and, if deemed appropriate for interpretation, as group incidences by group on occasion and combined occasions for each sex and combined sexes.

The individual food consumption will be reported and analyzed as weekly average of daily food intake and as weekly average of achieved food intake.

To keep the statistical model as simple as possible and, considering that the inclusion of data from both sexes and across time in the same analysis would increase the power of the analysis, considering the group and the sex are the most relevant factors of interest and considering the the inclusion of more factors may over parameterize the statistical model, only the group, the sex and the time effects will be considered as fixed factors in the statistical models.

Statistical analysis will be independantly performed for the three periods: gestation, pre and post weaning.

To get a data distribution more closely to a normal one, data transformation may be used before doing the statistical comparisons when the data distribution is clearly skewed, e.g. for percentages approaching 0% or 100%.

One-Way ANOVA/ANCOVA

A one-way analysis of variance (ANOVA) will be performed for the following datasets:

- average of pre-treatment individual results of body weights F0;
- average of pre-treatment individual results of food and water consumption F0;
- mean day per litter and sex of positive development of vaginal opening and preputial separation;
- percentage live pups by litter, percentage malformed pups per litter at PPD0.
- clinical pathology parameters of F0

Two-Way Repeated Measures ANOVA/ANCOVA

A **two-way repeated measures** analysis of variance (ANOVA) will be performed for the following datasets:

- body weight changes for F0 during gestation;
- post-start of treatment results of food consumption F0 pre-weaning

A **two-way repeated** measures analysis of covariance (**ANCOVA**) will be performed for the following datasets:

- post-start of treatment results of body weights F0 during gestation
- post-start of treatment results of food consumption F0 during gestation

Three-Way Repeated Measures ANOVA/ANCOVA

A **three-way repeated measures** analysis of variance (ANOVA) will be performed for the following datasets:

- body weight and body weight change for F1 post-weaning
- food consumption, achieved food intake F1 post-weaning
- numerical clinical pathology data for F1
- buccal mucosal bleeding time for F1

A **three-way nested repeated measures** analysis of variance (ANOVA) will be performed for the following datasets (pups nested within litter):

- body weight and body weight change for F1 pre-weaning

Statistical methods

One-Way ANOVA/ANCOVA

The following statistical group comparison will not include groups with less than three observations or with zero variance.

For each data set with more than two groups to compare, a one-way analysis of variance (ANOVA) will be performed with group as fixed effect. When significant differences among the group means are indicated by the ANOVA overall F-test ($p \leq 0.10$), a t-test will be used to perform the group mean comparisons between the control diet group and each test item treated group.

For datasets with only two groups to compare (including the control diet group), a two-sample t-test will replace the one-way ANOVA F-test.

Two-Way Repeated Measures ANOVA/ANCOVA

Whenever possible, the pre-treatment results (i.e. prior to first treatment) will be used as covariate. The average of pre-treatment results will be used as covariate if there is more than one result.

The fixed effects in the model will be the group, the time and their interaction with the animal as subject and, when applicable, the pre-treatment as covariate. For the pre-weaning period, subject will be the pup nested within litter. The repeated measures analysis of variance will be performed using each of the following four covariance structures: the first-order autoregressive (AR(1)), the heterogeneous first-order autoregressive (ARH(1)), the compound symmetry (CS) and the heterogeneous (CSH) in order to determine which one would best express the pattern of measurement correlations across time. A common covariance matrix for all groups will be used. The Kenward and Roger's (or the alternative Satterthwaite's) method will be used when computing the denominator degrees of freedom for the tests involving the fixed effects. If the final Hessian is not positive definite or computational limitation/convergence problems are encountered while fitting a model, the model will not be considered in the following steps. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) will be selected.

If the retained two-way repeated measures ANOVA/ANCOVA indicates that the group-by-time interaction is significant ($p \leq 0.10$), the group effect will be assessed within each time point using F-test on least-squares means. If there is no significant group-by-time interaction ($p \leq 0.10$), then the group effect will be assessed across pooled time points using the F-test from the retained three-way repeated measure ANOVA/ANCOVA.

When the group effect is significant ($p \leq 0.10$), t-test on least-squares means will be performed to compare control diet group with each of the test item treated groups. The pairwise group comparisons will be assessed at an alpha level of 0.10. Significant differences from group mean comparisons will be reported as $p \leq 0.10$, $p \leq 0.05$, $p \leq 0.01$, where p represents the t-test probability. Least-square means related to the pairwise group comparisons will be presented with p-values.

Three-Way Repeated Measures ANOVA/ANCOVA

Whenever possible, the pre-treatment results (i.e. prior to first treatment) will be used as covariate. The average of pre-treatment results will be used as covariate if there is more than one result.

The fixed effects in the model will be the group, the sex, the time and their two-way and three-way interactions with the animal as subject and, when applicable, the pre-treatment as covariate. For the pre-weaning period, subject will be the pup nested within litter. The repeated measures analysis of variance will be performed using each of the following six covariance structures: the spatial power (SP(POW)), the spatial anisotropic power (SP(POWA)), the first-order autoregressive (AR(1)), the heterogeneous first-order autoregressive (ARH(1)), the compound symmetry (CS) and the heterogeneous (CSH) in order to determine which one would best express the pattern of measurement correlations across time. A common covariance matrix for all group-sex levels will be used. The Kenward and Roger's (or the alternative Satterthwaite's) method will be used when computing the denominator degrees of freedom for the tests involving the fixed effects. If the final Hessian is not positive definite or computational limitation/convergence problems are encountered while fitting a model, the model will not be considered in the following steps. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) will be selected.

If the retained three-way repeated measures ANOVA/ANCOVA indicates that the group-by-sex-by-time interaction is significant ($p \leq 0.05$), the group effect will be assessed within each sex-time combination using F-test on least-squares means. If there is no significant group-by-sex-by-time interaction ($p > 0.05$), then the group-by-sex and the group-by-time interactions will be assessed using the F-test from the retained three-way repeated measure ANOVA/ANCOVA.

If the group-by-sex interaction is significant ($p \leq 0.10$), the group effect will be assessed within each sex using F-test on least-squares means. If the group-by-time interaction is significant ($p \leq 0.10$), the group effect will be assessed within each time using F-test on least-squares means. If both group-by-sex and group-by-time interactions are not significant ($p > 0.10$), then the group effect will be assessed on pooled sexes and pooled time points using the F-test i.e. the main group effect from the retained three-way repeated measure ANOVA/ANCOVA.

When the group effect is significant ($p \leq 0.10$), t-test on least-squares means will be performed to compare control diet group with each of the test item treated groups. The pairwise group comparisons will be assessed at an alpha level of 0.10. Significant differences from group mean comparisons will be reported as $p \leq 0.10$, $p \leq 0.05$, $p \leq 0.01$, where p represents the t-test probability. Least-square means related to the pairwise group comparisons will be presented with p-values.

(b) (4)

Profile plots

For continuous variables measured repeatedly, the individual and group mean variations across time will be presented in graphs.

Reporting

Study updates will be provided to the Sponsor on a biweekly basis, or as required during the study.

A draft report will be submitted electronically to the Sponsor. Should external contributing reports be unavailable for inclusion in the initial draft of the report, the draft report will be issued on schedule, unless otherwise directed by the Sponsor. Following Sponsor (and/or Sponsor designate) review, appropriate modifications will be made to the draft report and a revised version (Word) of the draft report will be issued for review. Following agreement to the final content of the report by the Sponsor and (b) (4), the report will be finalized and one electronic copy (PDF and Word format) of the final version of the report will be issued and sent to the Sponsor.

The raw data and the statistical analysis will be provided in compliance with GFI #197 to facilitate the submission of the dossier to CVM.

(b) (4) expects that the draft report will be commented upon by the Sponsor and finalized within 6 months of issuance. Should the Sponsor fail to contact (b) (4) to make alternate arrangements, within the above referenced period, (b) (4) will consider that the draft report is acceptable and proceed with the finalization of the report. If such a case occurs, the Sponsor will be notified in writing at least 30 days prior to finalization of the report.

Archives

The following study materials (including but not limited to) generated during this study will be retained at (b) (4) archive and/or subcontracted archive facility for a period of 5 years after the signature of the study report by the Study Director:

Study Plan and Study Plan Amendments (if any)
Receiving and shipping records
Records of room maintenance and environmental data
Records of test system and animal care
Records of day to day activities
Final Report
Test material and formulation records
Records of laboratory analysis
Records of histopathology (if any) and clinical pathology
Statistical analysis
Appropriate samples and specimens (if any)

(b) (4)

(b) (4) agrees to give the Sponsor sufficient advance notification of any intended disposal of such materials after the 5-year holding period, to allow the Sponsor to secure alternative storage facilities.

All study material generated by the (b) (4) (b) (4) will be retained in the archives of (b) (4).

All study material generated by (b) (4) will be transferred to (b) (4) for archiving.

Communication

Any untoward changes occurring during the conduct of the study will be communicated to the Sponsor by phone, e-mail, or facsimile, and discussed. All mutually-agreed changes to the Study Plan or study conduct will be duly documented in the form of a Study Plan amendment and signed by the signatories of the Study Plan (as appropriate). Any additional costs associated with these changes will be communicated to the Sponsor.

If the Sponsor cannot be reached immediately or if there is insufficient time to contact the Sponsor, the Study Director will take all steps necessary to ensure continuity and viability of the study and/or the general well-being of the animals. If such action is taken, the Study Director will notify the Sponsor as soon as possible.

Copies of any Study Plan amendments will be sent to the Sponsor, whose formal approval will be indicated by the return of one signed copy to (b) (4).

Regulatory

Although this is a non-GLP study, the Quality Assurance Program of (b) (4) (b) (4) may undertake and document inspections and audits of critical aspects of the study during its conduct. The results of all the study audits will be reported to the Study Director. The Sponsor study monitor or authorized designate(s) may inspect this study during regular working hours for quality assurance purposes and copy any study-related original data.

Multisite

For any portion of the study conducted by a subcontractor (i.e.: (b) (4) , the Study Director will ensure that a qualified Principal Investigator will be identified by the site conducting that portion of the study, prior to the start of the study phase analysis.

For any portions of the study conducted by a test site (i.e.: analytical, bioanalytical), a sub-report will be provided by the Principal Investigator to the Study Director for inclusion in the study report.

(b) (4)

Standard Operating Procedures

All activities of this study will be performed according to standard operating procedures (SOPs) and/or Study Specific Procedures (SSPs), which will be maintained on-file at (b) (4) and at the location of any subcontracting laboratories.

Government Inspection

(b) (4) agrees to notify the Sponsor promptly of any government inquiry or proposed inspections with respect to this study. The Sponsor shall have the right to participate in (b) (4) response to the inquiry, when time permits.

(b) (4)

Approved by:

(b) (4), (b) (6)

July 05, 2017
Date

July 05, 2017
Date

Reviewed by:

(b) (4), (b) (6)

July 05, 2017
Date

July 6, 2017
Date

STUDY PLAN AMENDMENT NO. 1

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety

(b) (4)[S]

Study Plan Date: July 5, 2017

Study Plan Amendment Date: July 24, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 2 of 33, under GENERAL INFORMATION:

Amended as follows:

Study Director (b) (4)

Reason for Amendment:

Study director responsibilities will be transferred to (b) (4), (b) (6) due to return from vacation.

STUDY PLAN AMENDMENT NO. 1

2 Page 2 of 33, under GENERAL INFORMATION:

Amended as follows:

Supporting Scientist (b) (4), (b) (6)

Reason for Amendment:

Supporting scientist responsibilities will be transferred to (b) (4), (b) (6) due to change in supporting scientist.

(b) (4)

[redacted]

STUDY PLAN AMENDMENT NO. 1

Approved by:

(b) (4), (b) (6)

[redacted]

July 24, 2017
Date

July 24, 2017
Date

July 24, 2017
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

[redacted]

July 25, 2017
Date

[redacted] (b) (4)

STUDY PLAN AMENDMENT NO. 2

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

[redacted] (b) (4)

Study Plan Date: July 5, 2017

Study Plan Amendment Date: August 14, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 3 of 33, under External Contributing Scientists:

Amended as follows:

(…)

Clinical Pathology Data Interpretation

[redacted] (b) (4), (b) (6)

Reason for Amendment:

To document a change in the scientist responsible for clinical pathology data interpretation.

2 Page 9 of 33, under Analysis of Diets:

Amended as follows:

Representative samples (approximately 500 g, in duplicate) of each manufactured batch of each formulation will be taken from one bag used on Day 1 (at [redacted] (b) (4), from the first day of dosing at [redacted] (b) (4) (day of animal arrival), at two months intervals throughout the study, and at the end of treatment. If a batch is used for

less or equal than two months, then samples will be taken at the beginning and at the end of the use period.

Additional samples may be collected and/or analyzed as necessary at the request of the Study Director (documented via study plan amendment).

The samples will be kept at room temperature.

One set of the duplicate samples will be shipped at room temperature to the Sponsor-designated laboratory, for analysis:
(b) (4)

The samples collected at (b) (4) will transit through (b) (4) prior to shipment to the analytical laboratory.

Following confirmation of safe and intact receipt of the first set of samples, the second set of samples may be shipped at room temperature to the Sponsor-designated laboratory, if required. If not required for analysis, the second set of samples will be kept a (b) (4) (b) (4) pending discard. The second set of samples collected not required for analysis, will be shipped to (b) (4) where it will be kept pending discard.

(…)

Reason for Amendment:

To clarify that the samples collected at (b) (4) will not be shipped directly to the analytical laboratory, but will rather transit through the Test Facility due to permit issues.

3 Page 12 of 33, under Identification:

Amended as follows:

Each dam will arrive from the supplier individually identified by means of a tattoo**, and will be implanted with a microchip**. Each dam will be assigned an animal number to be

used (as described in the following table and in the Animal Assignment and Blinding Procedure section).

Group	Animal Numbers* Females
1	(b) (4)
2	
3	
4	

* Number of animals at assignment. The identification of animals received at (b) (4) will vary since (b) (4) will only ship confirmed pregnant females (up to a maximum of 5/group).

The first number corresponds to the respective dose group while the second number identifies the gender of the animal (numbers 5 to 9 will be used for females). The third and fourth number identifies the animal's rank per gender within each group.

The puppies (F_1) will be identified as per relevant (b) (4) SOPs (i.e.: paper collar on PPD 0, then microchip from PPD 1).

For the second generation, the utilization of animal number with 3 numbers can be used. Animal identification will be interpreted using example below (animal 1501).

i.e.: First generation (F_0) = 1501 for Dam

Second generation (F_1) = 151 or 101 for Puppies

Reason for Amendment:

To document that each dams will have a microchip implanted following arrival at (b) (4).

4 Page 15 of 33, under Acclimation/Socialization:

Amended as follows:

While at the breeding facility, animals will be socialized per (b) (4), relevant standard procedures (retained at (b) (4)) to ensure they are relaxed and calm when handled by caretakers in a laboratory setting.

There will be no acclimation period upon arrival at the Test Facility, as daily oral dietary administration started at (b) (4) is to be continued immediately after arrival. Nevertheless, the activities in the animal housing room(s) will be minimized for the 7 days following arrival to accustom the animals to the laboratory environment.

Dams will be socialized by the key technicians (no more than 4) at least twice weekly throughout the gestation period starting ~~7~~ **4** days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. Only the key technicians are allowed to take the puppies out of the cage.

Secondary technicians (no more than 6) will socialize with the dams at least once weekly during the gestation period starting ~~7~~ **4** days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. The secondary technicians are only allowed to manipulate the puppies if a key technician has taken them out of the cage first.

Puppies will also be socialized per SOP (submission technique).

Reason for Amendment:

To document that socialization will start sooner following arrival.

5 Page 19 of 33, under Food Consumption:

Amended as follows:

Individual food intake will be measured on all animals at least daily (except on days of food deprivation) throughout the study, starting at initiation of feeding the reference/control diet (3-14 days prior to treatment start). In addition to the daily food consumption, achieved intakes will be calculated on a weekly basis (calculations performed at (b) (4)]. **Throughout the phase conducted at** (b) (4)**, any spilled food will also be weighed daily for each cage, unless clearly contaminated with liquid or solid material (e.g. water, urine, feces, etc.). The amount of contaminated food (excluded from the spillage measured value) will be visually estimated and documented.**

The average of daily individual achieved intake of the test item in mg/kg/body weight per week will be calculated for both generations based on daily food consumption **(taking into account the weighed spilled food, if any)** using the following formulas:

- On dams from Day 1 until puppies are 5 weeks of age (without feeding pan)

$$\frac{\text{Dietary concentration (mg/kg)} \times \text{food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

- On dams with puppies, from 5 weeks of age until weaning (with feeding pan, including puppies body weight), and for the first two weeks post-weaning (2 puppies/cage)

$$\frac{\text{Dietary concentration (mg/kg/cage)} \times \text{food consumption (kg)}}{\text{Start-week body weight (kg/cage)}}$$

- On selected puppies, from the 3rd week post-weaning (1 puppy/cage)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

For reporting purposes weekly average of daily food consumption and achieved intakes will be presented.

Reason for Amendment:

To document that spilled food will be weighed as well and taken into account for calculation of daily food consumption, per Sponsor`s request.

6 Page 27 of 33, under Data Analysis:

Amended as follows:

(…)

One-Way ANOVA/ANCOVA

A one-way analysis of variance (ANOVA) will be performed for the following datasets:

- average of pre-treatment individual results of body weights F0;
- average of pre-treatment individual results of food ~~and water~~ consumption F0;
- mean day per litter and sex of positive development of vaginal opening and preputial separation;
- percentage live pups by litter, percentage malformed pups per litter at PPD0.
- clinical pathology parameters of F0

(…)

Reason for Amendment:

To remove statistical analysis of water consumption data since no such dataset will be collected on this study.

(b) (4)

STUDY PLAN AMENDMENT NO. 2

Approved by:

(b) (4)

August 14, 2017
Date

August 14, 2017
Date

Reviewed by:

(b) (4)

August 14, 2017
Date

August 15, 2017
Date

(b) (4)

STUDY PLAN AMENDMENT NO. 3

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

(b) (4)

Study Plan Date: July 5, 2017

Study Plan Amendment Date: August 18, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 5 of 33, under TARGETED STUDY SCHEDULE:

Amended as follows:

Start of feeding control diet*:	Week of July 10, 2017
Experimental start (1st mating start*):	July 17, 2017
Start of dosing (1st mating*):	July 17, 2017
Animal Arrival**:	~~August 21, 2017~~ **August 22, 2017**
Littering start (GD*** 56):	Week of September 11, 2017
Weaning start (PPD*** 56):	Week of November 6, 2017
Last observation on F_0 females and F_1 animals not selected (up to 2 months post-partum):	Week of November 6, 2017
Last observation F_1 animals (34 weeks old):	Week of May 11, 2018
Experimental completion:	July 30, 2018
Draft report:	Week of August 13, 2018

* Performed at (b) (4)
** Confirmed 4- to 5-week pregnant ~~(GD 29 to 35)~~ **(GD 32 to 39)**
*** GD = Gestation Day, PPD = Post-Partum Day

The actual dates for start of treatment (experimental start), last observation and experimental completion will be presented in the study report.

Reason for Amendment:

To update the animal arrival date and the Gestation Day at arrival based on the actual mating dates.

STUDY PLAN AMENDMENT NO. 3

2 Page 11 of 33, under Administration of Diets:

Amended as follows:

(…)

F_0 (at (b) (4) Daily oral dietary administration to dams will continue immediately after arrival and throughout gestation and lactation (approximately 15 weeks in total). Dams will receive approximately 600 g of food per day from arrival to parturition, and 900 g per day from parturition until weaning. More food can be added during the day if needed, but additional quantities will be measured/recorded. If appetence issues are observed, 100 mL of warm reverse osmosis water can be added to the diet.

F_1: Starting at 5 weeks of age and until weaning, puppies will be provided with a feeding pan. During that period, the daily food intake will be calculated for the dam plus its litter (i.e.: dam's bowl, plus feeding pan) since the dam will also have access to the feeding pan (approximately 300 g**, taken from the 900 g measured for the dam**).
As of weaning, puppies selected for the study will continue on their mothers' respective diets (approximately 400 g per day/dog for a 6-8 hours daily feeding period) for the additional 6 months until they reach 34 weeks of age. Puppies will remain pair-housed for feeding during the first two weeks post-weaning to confirm ability to properly thrive, and will then be individually housed for feeding for the remainder of the study. If appetence issues are observed, 100 mL of warm reverse osmosis water can be added to the diet. Similarly, puppies not selected to continue on the study will continue on their mothers' respective diets until release from the study (approximately 2 weeks after weaning).

The remaining puppies will be released from the study once ability to thrive of all randomly selected puppies is confirmed (transferred to (b) (4) B dog colony where they will receive the standard commercially available diet).

Reason for Amendment:

To clarify that the 300 g of diet placed in the feeding pan will not be in addition to the 900 g given to the dam but will rather be taken from the measured 900 g (i.e., 600 g in the dam`s food hopper and 300 g in the puppies' feeding pan).

3 Page 15 of 33, under Acclimation/Socialization:

Amended as follows:

(…)

There will be no acclimation period upon arrival at the Test Facility, as daily oral dietary administration started at (b) (4) is to be continued immediately after

arrival. Nevertheless, the activities in the animal housing room(s) will be minimized for the 7 days following arrival to accustom the animals to the laboratory environment.

Dams will be socialized by the key technicians (no more than 4) at least twice weekly throughout the gestation period starting 4 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. Only the key technicians are allowed to take the puppies out of the cage.

Secondary technicians (no more than 6) will socialize with the dams at least once weekly during the gestation period starting 4 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. The secondary technicians are only allowed to manipulate the puppies if a key technician has taken them out of the cage first.

Puppies will also be socialized per SOP (submission technique).

Throughout the study conduct (at (b) (4), and especially prior to weaning, access to the housing rooms will be restricted to the minimum feasible amount of personnel in order to minimize the stress to the animals.

Reason for Amendment:

To document restricted room access.

4 Page 16 of 33, under Animal Assignment and Blinding Procedure:

Amended as follows:

The animal assignment will be performed at (b) (4). The order of the animal number assignement was randomly determined. In order to preserve the blinding, the table describing the assignment of animals based on timing of mating confirmation will be maintained in a separate document, with access restricted to unblinded personnel.

(b) (4) will test for pregnancy approximately 28 days after mating. If all 6 dams within a group are confirmed pregnant, 1 dam will be randomly selected using a dice and will be released from the study, so that a maximum of 5 pregnant dams per group will be shipped to (b) (4). **Alternatively, a dam could be excluded from the study (not selected for shipment) based on an undesirable behavior (e.g., propensity to spill food).** The dams will be shipped to (b) (4) in one shipment.

(…)

Reason for Amendment:

To add a selection criterion.

(b) (4)

STUDY PLAN AMENDMENT NO. 3

Approved by:

(b) (4), (b) (6)

August 18, 2017
Date

August 18, 2017
Date

Reviewed by:

(b) (4)

August 18, 2017
Date

August 18, 2017
Date

STUDY PLAN AMENDMENT NO. 4

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

(b) (4)

Study Plan Date: July 5, 2017

Study Plan Amendment Date: September 14, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 12 of 33, under Identification:

Amended as follows:

Each dam will arrive from the supplier individually identified by means of a tattoo, and will be implanted with a microchip. Each dam will be assigned an animal number to be used (as described in the following table and in the Animal Assignment and Blinding Procedure section).

Group	Animal Numbers*
	Females
1	(b) (4)
2	
3	
4	

* Number of animals at assignment. The identification of animals received at (b) (4) will vary since (b) (4) will only ship confirmed pregnant females (up to a maximum of 5/group).

The first number corresponds to the respective dose group while the second number identifies the gender of the animal (numbers 5 to 9 will be used for females). The third and fourth number identifies the animal's rank per gender within each group.

The puppies (F_1) will be identified as per relevant (b) (4) SOPs (i.e.: paper collar on PPD 0, then microchip from PPD 1).

For the second generation, the utilization of animal number with 3 numbers can be used. Animal identification will be interpreted using example below (animal 1501).

i.e.: First generation (F_0) = 1501 for Dam

Second generation (F_1) = ~~151 or 101~~ **100, 101, etc.** for **male** Puppies **and 150, 151, etc. for female Puppies**

Reason for Amendment:

To modify the identification of puppies based on the study design.

2 Page 19 of 33, under Body Weights:

Amended as follows:

Body weights will be recorded for all dams at least on the day of estrous and on the day of treatment initiation (at (b) (4), concurrently with DCE), and weekly thereafter.

Puppies will be weighed on PPD 0, 4, 7, 10, 14, 17, 21, etc., **and as per** (b) (4) **SOP** until weaning, and weekly thereafter.

A body weight measurement will also be performed on dams and puppies on the day prior to release from the study.

Reason for Amendment:

To clarify that the frequency of body weight measurements on puppies after Day 21 will be as per SOP.

3 Page 24 of 33, under Terminal Procedures:

Amended as follows:

At weaning (for dams) or two weeks after weaning (for puppies), all dams and all puppies not selected for the growth phase of the study (once ability to thrive of selected puppies is confirmed, i.e. 2 weeks post-weaning) will be transferred to the (b) (4) animal colony. Similarly, at the completion of the study, all surviving selected puppies will be transferred to the (b) (4) animal colony.

In addition, any dams with no puppies after whelping is completed (litter of zero live puppies) will be released from the study and transferred to (b) (4) **animal colony.**

Reason for Amendment:

To document the fate of dams without live puppies once parturition is completed.

4 Page 27 of 33, under Data Analysis:

Amended as follows:

(…)

One-Way ANOVA/ANCOVA

A one-way analysis of variance (ANOVA) will be performed for the following datasets:

- average of pre-treatment individual results of body weights F0;
- average of pre-treatment individual results of food consumption F0;
- ~~mean day per litter and sex of positive development of vaginal opening and preputial separation;~~
- percentage live pups by litter, percentage malformed pups per litter at PPD0.
- clinical pathology parameters of F0

(…)

Reason for Amendment:

To remove statistical analysis of vaginal opening and preputial separation data since no such dataset will be collected on this study.

(b) (4)

STUDY PLAN AMENDMENT NO. 4

Approved by:

(b) (4), (b) (6)

September 14, 2017
Date

September 14, 2017
Date

Reviewed by:

(b) (4), (b) (6)

September 14, 2017
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

September 14, 2017
Date

(b) (4)

STUDY PLAN AMENDMENT NO. 5

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

(b) (4)

Study Plan Date: July 5, 2017

Study Plan Amendment Date: September 28, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 15 of 33, under Acclimation/Socialization:

Amended as follows:

(…)

Dams will be socialized by the key technicians (no more than 4) at least twice weekly throughout the gestation period starting 7 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. Only the key technicians are allowed to take the puppies **(until 1 week old)** out of the cage.

Secondary technicians (no more than 6) will socialize with the dams at least once weekly during the gestation period starting 7 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. The secondary technicians are only allowed to manipulate the puppies if a key technician has taken them out of the cage first. **For logistical convenience, once the youngest puppy in the room reaches 1 week of age, both key and secondary technicians are allowed to take the puppies out of the cage.**

Puppies will also be socialized per SOP (submission technique).

Reason for Amendment:

To clarify that the restriction for the puppies to be taken out of the cage solely by the key technicians is only applicable until the youngest puppy in the room is 1 week old; after that, secondary technicians can also take puppies out of the cage.

(b) (4)

STUDY PLAN AMENDMENT NO. 5

Approved by:

(b) (4), (b) (6)

September 28, 2017
Date

September 28, 2017
Date

Reviewed by:

(b) (4), (b) (6)

September 28, 2017
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

September 28, 2017
Date

[redacted] (b) (4)

STUDY PLAN AMENDMENT NO. 6

Study Title:	Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies [redacted] (b) (4)
Study Plan Date:	July 5, 2017
Study Plan Amendment Date:	October 02, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 23 of 33, under Bioanalysis:

Amended as follows:

Blood samples (a target of 3 mL each) will be collected from dams during the pretreatment period for a baseline (at [redacted] (b) (4)), after 4 to 5 weeks of treatment (at [redacted] (b) (4)) and at weaning (at [redacted] (b) (4)). Blood samples (a target of 2 mL each) will also be collected from all selected weaned puppies (F_1) at weaning and during Weeks 13 and 34, at approximately the same time on each occasion.

Each blood sample will be collected by jugular venipuncture (or any other vein may be used if required) into tubes containing K_2-EDTA (alternatively, K_3-EDTA can also be used, but the tube type should be consistent throughout the study) as anticoagulant and kept on wet ice pending centrifugation. Samples will be centrifuged at 1500 g RCF for targeted 10 minutes. Centrifugation will be refrigerated (set to +4°C) at [redacted] (b) (4), but not at [redacted] (b) (4) where it will be performed at room temperature.

Excursions from the target volume will be documented in the raw data. In the event samples must be re-centrifuged, the times of sample processing will be documented. Plasma will be transferred into 2 separate tubes, placed on dry ice pending storage in a freezer set to maintain -70°C until shipment. One set of samples will be shipped on dry ice, to the Sponsor-designated laboratory for analysis at the following address:

Attn of [redacted] (b) (4), (b) (6)

STUDY PLAN AMENDMENT NO. 6

(b) (4)

Samples should be shipped by FedEx overnight on dry ice. An email should be sent to (b) (4), (b) (6) alerting him of the shipment. An electronic list of samples should be included in the e-mail and with the shipment.

Samples will be analyzed using a validated assay (OMQ-MTD-003, Whole Plasma Fatty Acid Concentrations) for measurement of DHA and EPA plasma concentrations.

Following confirmation of safe and intact receipt of the first set of samples, the second set of the duplicate samples **(if not required by** (b) (4) **for analysis)** ~~may~~ **will** be shipped to the Sponsor ~~designated laboratory~~ on dry ice ~~or may be discarded at the request of the Sponsor.~~ **at the following address, for possible future analysis:**

Attention of (b) (4), (b) (6)
Analytical Sciences
DSM Nutritional Products AG
(b) (4), (b) (6)

Reason for Amendment:

To document a change in the fate of back-up samples, per Sponsor request.

STUDY PLAN AMENDMENT NO. 6

Approved by:

(b) (4), (b) (6)

October 02, 2017
Date

October 02, 2017
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

October 2, 2017
Date

(b) (4)

STUDY PLAN AMENDMENT NO. 7

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety (b) (4) Puppies

Study Plan Date: July 5, 2017

Study Plan Amendment Date: November 9, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 11 of 33, under Administration of Diets

Amended as follows:

As the Sponsor will provide the diets already coded, each animal's actual treatment designation will be unknown to staff performing dosing or data collection.

(…)

F_1: Starting at 5 weeks of age and until weaning, puppies will be provided with a feeding pan. During that period, the daily food intake will be calculated for the dam plus its litter (i.e.: dam's bowl, plus feeding pan) since the dam will also have access to the feeding pan (approximately 300 g, taken from the 900 g measured for the dam).

As of weaning, puppies selected for the study will continue on their mothers' respective diets (approximately 400 g per day/dog for a 6-8 hours daily feeding period) for the additional 6 months until they reach 34 weeks of age. Puppies will remain pair-housed for feeding during the first two weeks post-weaning to confirm ability to properly thrive, and will then be individually housed for feeding for the remainder of the study **(including for some individuals, while waiting for the youngest litter to complete the first two weeks post-weaning)**. If appetence issues are observed, 100 mL of warm reverse osmosis water can be added to the diet. Similarly, puppies not selected to continue on the study **(spares)** will continue on their mothers' respective diets until release from the study (approximately 2 weeks after weaning).

The remaining puppies will be released from the study once ability to thrive of all randomly selected puppies is confirmed (transferred to (b) (4) dog colony where they will receive the standard commercially available diet).

Reason for Amendment:

To clarify that although the puppies will be pair housed with an animal of same group and sex only after the youngest litter has completed the 2-week post-weaning period, individual food consumption will be obtained for each puppy starting after completion of the 2-week post-weaning period. To clarify that only selected puppies and spare puppies will be retained on the study at weaning.

2 Page 13 of 33, under Housing

Amended as follows:

(…)

After weaning, puppies selected to continue on the study (F_1) will be pair housed in stainless steel dog cages (dimensions: approximately 3 by 3 feet) equipped with an automatic watering system, but will be separated during the 6-8 hour daily feeding period (separation starting at the third week post-weaning), to acquire individual food consumption data (i.e.: diet study). If possible, one male and one female will be housed together in each group to harmonize the food consumption values between cages during the first two weeks post-weaning **(of the youngest litter)**. **Thereafter, puppies will be pair housed by sex and by group.** Throughout the weaning process and after weaning, dams will be individually housed in stainless steel dog cages (dimensions: approximately 3 by 3 feet) equipped with an automatic watering system. Puppies not selected to continue on the study will remain in European cages until their release from the study (approximately 2 weeks after weaning).

(…)

Due to space restrictions, at (b) (4), animals will be housed in different rooms, but all rooms will be of the same type, within the same building, and will have the same environmental controls, water sources, and daily routines for care and cleaning. Every room will include animals from each treatment group (designated by unblinded technical staff not involved in data collection), such that the rooms will be balanced for sex (applicable to puppies only), and treatment. Within each room (at (b) (4) (b) (4), animals will be assigned to cages by ascending animal arrival number (*e.g.*, in clockwise placement around the room) in order to maintain the study blind. Approximately 1 week after **completion of** weaning, selected pups **(excluding spares)** will be consolidated into a single room.

(…)

Reason for Amendment:

To clarify that the puppies will be pair-housed with an animal of same group and sex only after the youngest litter has completed the 2-week post-weaning period, as puppies of same

dosage level and sex may not be available for pairing after the 2-week post-weaning period of each animal. This is due to dams staggered mating and random group assignment, as well as staggered parturition. To clarify the timing for selected puppies all housed in a single room.

3 Page 16 of 33, under Animal Replacement:

Amended as follows:

(…)

Any puppy (F_1) considered unsuitable for use on study may be excluded at selection (PPD 56). There will be no replacement of puppies after the first two weeks of weaning (once ability to thrive **of the youngest litter** is confirmed).

Reason for Amendment:

To clarify the duration of the replacement period for the puppies (growth phase).

4 Page 18 of 33, under Clinical Observations:

Amended as follows:

(…)

Clinical signs (ill health, behavioral changes, etc.) will be recorded on all animals twice daily throughout the study. The nature of these observations will include evaluation of general appearance, activity, and other indicators of changes in animal health and behavior, including fur condition, gait and mobility. Litter checks will be performed once daily (concurrently with a clinical sign activity) until PPD 56.

A detailed clinical examination (DCE) will be performed on each animal at least on the day of estrous and on the day of treatment initiation and once within the week prior to shipment (at (b) (4), concurrently with body weight measurements), and monthly thereafter (at (b) (4)). A DCE will also be performed on the day prior to **(or on the day of)** release from the study.

Detailed clinical examinations will be conducted per facility SOPs (or (b) (4)), which describe that during the detailed clinical examination, animals will be observed while in the cage for behavior, general appearance, coordination, etc., and then will be removed from the cage for close evaluation of general condition of the whole body including (but not limited to) head, thoracic, and abdominal areas through examination and palpation. Body temperature, heart rate and respiratory rate (counts per minute) will also be evaluated.

For puppies, height and head circumference will also be measured weekly starting on PPD 7.

In addition, a detailed examination **(including body temperature, heart rate and respiratory rate)** will also be performed on all puppies selected to continue on the study (F_1) by blinded technical staff **starting on PPD63 (1 week post-weaning) and** once a month ~~from weaning~~ thereafter, including within 3 days prior to release from the study. This evaluation will be conducted per facility SOPs which include assessment of the general body condition, autonomic and central nervous system, somatomotor activity, gait, skin/fur condition, lymph nodes, eyes, mucus membranes, respiration, behavior, circulatory system, state of hydration, and lungs, bladder, reproductive system and gastrointestinal auscultation and/or palpation. Particular attention should be directed to observations of central nervous system signs (seizures, tremors, salivation), vomiting and diarrhea. Additional observations may be performed as deemed necessary.

(…)

Reason for Amendment:

To document that DCE on puppies selected for the growth phase will start 1 week post-weaning since a DCE is already performed on PPD 56 (day of weaning), via the litter check; to clarify that DCE on weaned puppies will also include measurement of body temperature, heart rate and respiratory rate; and to clarify that the last DCE can also be performed on the day of release from the study.

5 Page 19 of 33, under Body Weights:

Amended as follows:

Body weights will be recorded for all dams at least on the day of estrous and on the day of treatment initiation (at (b) (4) concurrently with DCE), and weekly thereafter.

Puppies will be weighed on PPD 0, 4, 7, 10, 14, 17, 21, etc., and as per (b) (4) (b) (4) SOP until weaning **(in grams, 4 digits)**, and weekly thereafter **(in kilograms, with 2 decimals)**.

A body weight measurement will also be performed on dams and puppies on the day prior to **(or on the day of)** release from the study.

Reason for Amendment:

To clarify the body weight data units of measurement as a different balance will be used after weaning due to animal size; and to clarify that the last body weight measurement can also be performed on the day of release from the study.

STUDY PLAN AMENDMENT NO. 7

6 Page 19 of 33, under Food Consumption:

Amended as follows:

(…)

The average of daily individual achieved intake of the test item in mg/kg/body weight per week will be calculated for both generations based on daily food consumption (taking into account the weighed spilled food, if any) using the following formulas:

- On dams from Day 1 until puppies are 5 weeks of age (without feeding pan)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

- On dams with puppies, from 5 weeks of age until weaning (with feeding pan, including puppies body weight), and for the first two weeks post-weaning (2 puppies/cage)

$$\frac{\text{Dietary concentration (mg/kg/cage) x food consumption (kg)}}{\text{Start-week body weight (kg/cage)}}$$

- On selected puppies, from the 3rd week post-weaning (1 puppy/cage **during feeding**)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

(…)

Reason for Amendment:

To clarify that although the puppies will be pair-housed with an animal of same group and sex only after the youngest litter has completed the 2-week post-weaning period, individual food consumption will be obtained for each puppy starting after completion of the 2-week post-weaning period.

7 Page 24 of 33, under TERMINAL PROCEDURES:

Amended as follows:

At weaning (for dams **and puppies not selected for the growth phase**) or two weeks after weaning **of the youngest litter** (for **spare** puppies), all dams and all puppies not selected for the growth phase of the study (once ability to thrive of selected puppies is confirmed, i.e. 2 weeks post-weaning **of the youngest litter**) will be transferred to the (b) (4) animal colony. Similarly, at the completion of the study, all surviving selected puppies will be transferred to the (b) (4) animal colony.

(…)

Reason for Amendment:

To clarify the timing of release from the study for puppies.

STUDY PLAN AMENDMENT NO. 7

Approved by:

(b) (4), (b) (6)

November 9, 2017
Date

December 09, 2017
Date

Reviewed by:

(b) (4), (b) (6)

November 10, 2017
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

November 10, 2017
Date

[redacted] (b) (4)

STUDY PLAN AMENDMENT NO. 8

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

[redacted] (b) (4)

Study Plan Date: July 5, 2017

Study Plan Amendment Date: December 18, 2017

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 2 of 33, under GENERAL INFORMATION:

Amended as follows:

~~Study Director~~ [redacted] (b) (4), (b) (6)

(…)

Reason for Amendment:

Study Director responsibilities will be undertaken by [redacted] (b) (4), (b) (6) during the absence of [redacted] (b) (4), (b) (6) from December 23, 2017 to January 7, 2018, inclusively.

2 Page 19 of 33, under Food Consumption:

Amended as follows:

Individual food intake will be measured on all animals at least daily (except on days of food deprivation**, applicable to dams only**) throughout the study, starting at initiation of feeding the reference/control diet (3-14 days prior to treatment start). In addition to the daily food consumption, achieved intakes will be calculated on a weekly basis (calculations performed at (b) (4)ica). Throughout the phase conducted at (b) (4), any spilled food will also be weighed daily for each cage, unless clearly contaminated with liquid or solid material (e.g. water, urine, feces, etc.). The amount of contaminated food (excluded from the spillage measured value) will be visually estimated and documented.

(…)

Reason for Amendment:

To clarify that there will be no occasions throughout the study where food deprivation will prevent collection of individual food consumption data in puppies.

STUDY PLAN AMENDMENT NO. 8

Approved by:

(b) (4), (b) (6)

December 18, 2017
Date

December 18, 2017
Date

Acknowledged by:

(b) (4), (b) (6)

December 18, 2017
Date

December 18, 2017
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

December 18, 2017
Date

[redacted] (b) (4)

STUDY PLAN AMENDMENT NO. 9

Study Title: Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

[redacted] (b) (4)

Study Plan Date: July 5, 2017

Study Plan Amendment Date: March 2, 2018

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 24 of 33, under TERMINAL PROCEDURES:

Amended as follows:

At weaning (for dams and puppies not selected for the growth phase) or two weeks after weaning of the youngest litter (for spare puppies), all dams and all puppies not selected for the growth phase of the study (once ability to thrive of selected puppies is confirmed, i.e. 2 weeks post-weaning of the youngest litter) will be transferred to the [redacted] (b) (4) animal colony. Similarly, at the completion of the study, all surviving selected puppies will be transferred to the [redacted] (b) (4) animal colony.

In addition, any dams with no puppies after whelping is completed (litter of zero live puppies) will be released from the study and transferred to [redacted] (b) (4) colony.

Dams found dead or euthanized for humane reasons will be processed as per relevant standard operating procedures. Necropsy of the dams will consist of an external macroscopic examination, including identification of all clinically recorded lesions, as well as a detailed internal examination and the ~~reprodutive~~ **reproductive** tract dissected out, the ovaries removed and corpora lutea counted, and processed as per standard operating procedures. Grossly abnormal tissues will be retained for possible future histopathology.

Similarly, any puppies found dead or euthanized for humane reasons will be processed as per relevant standard operating procedures. Necropsy of the puppies will consist of an external macroscopic examination, including identification of all clinically recorded lesions, as well as a detailed internal examination, and processed as per standard operating procedures. Grossly abnormal tissues will be retained for possible future histopathology.

In order to avoid autolytic changes, the macroscopic examination of the carcass will be conducted, as soon as possible, on all animals which die or are euthanized prematurely. Should an animal be found dead or euthanized outside regular working hours, necropsy will be completed as soon as possible after the time of death. Pending necropsy, the carcass will be stored in a refrigerator (set to 2-8°C).

Any necropsy data generated will not be included in the report unless a death or pre-terminal euthanasia warrants further evaluation as judged by the Study Director, in which case the Study Director may choose to report the data.

(…)

Reason for Amendment:

To add that necropsy data will be retained on file by default, unless instructed otherwise by the Study Director.

2 Page 26 of 33, under Data Analysis:

Amended as follows:

The statistical analysis approach for this study was designed with reference to Guidance for Industry #226: Target Animal Safety Data Presentation and Statistical Analysis. The statistical reporting will be done in compliance with the Guidance for Industry #197: "Documenting Statistical Analysis Programs and Data Files".

Data recorded at unscheduled occasions will be reported on an individual basis but will not be included in the analysis described below.

Whenever a continuous variable is measured on more than one pup per litter, an average per litter and sex will be computed, reported and the statistical analysis will be performed using the average per litter and sex.

Continuous variables specified in the study plan and collected during the conduct of the study will be subjected to calculation of group means, standard deviations, minimum and maximum values and will be reported by group and sex on each occasion. The calculation of group descriptive statistics will also be presented by group on combined occasions and/or combined sexes when a non significant occasion and\or sex interaction with the treatment effect is detected by the respective statistical analysis.

Categorical and dichotomous data specified in the study plan and obtained during the conduct of the study will be reported as individual results and, if deemed appropriate for interpretation, as group incidences by group on occasion and combined occasions for each sex and combined sexes.

The individual food consumption will be reported and analyzed as weekly average of daily food intake and as weekly average of achieved food intake.

To keep the statistical model as simple as possible and, considering that the inclusion of data from both sexes and across time in the same analysis would increase the power of the analysis, considering the group and the sex are the most relevant factors of interest and considering the ~~the~~ inclusion of more factors may over parameterize the statistical model, only the group, the sex and the time effects will be considered as fixed factors in the statistical models.

Statistical analysis will be ~~independantly~~ **independently** performed for the three periods: gestation, pre and post weaning.

To get a data distribution more closely to a normal one, data transformation may be used before doing the statistical comparisons when the data distribution is clearly skewed, e.g. for percentages approaching 0% or 100%.

One-Way ANOVA/ANCOVA

A one-way analysis of variance (ANOVA) will be performed for the following datasets:

- average of pre-treatment individual results of body weights F0;
- average of pre-treatment individual results of food consumption F0;
- **average of pre-treatment individual results for body temperature F0;**
- **average of pre-treatment individual results for heart rate F0;**
- **average of pre-treatment individual results for respiratory rate F0;**
- percentage live pups by litter, percentage malformed pups per litter at PPD0;
- clinical pathology parameters of F0 **during pretreatment.**

A one-way analysis of covariance (ANCOVA) will be performed for the following datasets:

- **clinical pathology parameters of F0 at weaning**

Two-Way Repeated Measures ANOVA/ANCOVA

A two-way repeated measures analysis of variance (ANOVA) will be performed for the following datasets:

- **body weight for F0 during post-partum (lactation phase);**
- body weight changes for F0 during gestation **and post-partum (lactation phase)**;
- **body temperature for F0 during post-partum (lactation phase);**
- **heart rate for F0 during post-partum (lactation phase);**
- **respiratory rate for F0 during post-partum (lactation phase);**

- ~~post start of treatment results of~~ food consumption **for** F0 **and F1 combined (by cage)** ~~pre weaning~~ **during post-partum (PPD0 to weaning);**
- **food consumption F1 during the first 2 weeks post weaning**

A two-way repeated measures analysis of covariance (**ANCOVA**) will be performed for the following datasets:

- post-start of treatment results of body weights F0 during gestation;
- post-start of treatment results of food consumption F0 during gestation;
- **post-start of treatment results of body temperature F0 during gestation;**
- **post-start of treatment results of heart rate F0 during gestation;**
- **post-start of treatment results of respiratory rate F0 during gestation**

Three-Way Repeated Measures ANOVA/ANCOVA

A three-way repeated measures analysis of variance (ANOVA) will be performed for the following datasets:

- body weight and body weight change for F1 post-weaning;
- food consumption~~, achieved food intake~~ **for** F1 **after the first 2 weeks** post-weaning;
- numerical clinical pathology data for F1;
- buccal mucosal bleeding time for F1;
- **body temperature for F1 post-weaning;**
- **heart rate for F1 post-weaning;**
- **respiratory rate for F1 post-weaning;**
- **height for F1 post-weaning;**
- **head circumference for F1 post-weaning**

A three-way nested repeated measures analysis of variance (ANOVA) will be performed for the following datasets (pups nested within litter):

- body weight and body weight change for F1 pre-weaning;
- **body temperature for F1 pre-weaning;**
- **heart rate for F1 pre-weaning;**
- **respiratory rate for F1 pre-weaning;**
- **height for F1 pre-weaning;**
- **head circumference for F1 pre-weaning**

Reason for Amendment:

To correct typographical errors; to remove the achieved food intake from the statistical analysis since all group diets contain different test item levels; and to complete the lists of parameters to be submitted to statistical analysis.

STUDY PLAN AMENDMENT NO. 9

Approved by:

(b) (4), (b) (6)

March 2, 2018
Date

March 2, 2018
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

March 5, 2018
Date

(b) (4)

STUDY PLAN AMENDMENT NO. 10

Study Title:	Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

(b) (4)

Study Plan Date:	July 5, 2017
Study Plan Amendment Date:	March 21, 2018

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 26 of 33, under Data Analysis:

Amended as follows:

(…)

<u>One-Way ANOVA/ANCOVA</u>

A one-way analysis of variance (ANOVA) will be performed for the following datasets:

- average of pre-treatment individual results of body weights F0;
- average of pre-treatment individual results of food consumption F0;
- average of pre-treatment individual results for body temperature F0;
- average of pre-treatment individual results for heart rate F0;
- average of pre-treatment individual results for respiratory rate F0;
- percentage live pups by litter, percentage malformed pups per litter at PPD0;
- clinical pathology parameters of F0 during pretreatment **and, for parameters without baseline values, at weaning**.

A one-way analysis of covariance (ANCOVA) will be performed for the following datasets:

- clinical pathology parameters of F0 at weaning

<u>Two-Way ANOVA</u>

A two-way analysis of variance (ANOVA) will be performed for the following datasets:

- **body weight for F1 at PPD0**

STUDY PLAN AMENDMENT NO. 10

Two-Way Repeated Measures ANOVA/ANCOVA

A two-way repeated measures analysis of variance (ANOVA) will be performed for the following datasets:

- body weight for F0 during post-partum (lactation phase);
- body weight changes for F0 during gestation and post-partum (lactation phase);
- body temperature for F0 during post-partum (lactation phase);
- heart rate for F0 during post-partum (lactation phase);
- respiratory rate for F0 during post-partum (lactation phase);
- food consumption for F0 and F1 combined (by cage) during post-partum (PPD0 to weaning)
- food consumption F1 during the first ~~3~~ **2** weeks post-weaning

A two-way repeated measures analysis of covariance (ANCOVA) will be performed for the following datasets:

- post-start of treatment results of body weights F0 during gestation
- post-start of treatment results of food consumption F0 during gestation
- post-start of treatment results of body temperature F0 during gestation
- post-start of treatment results of heart rate F0 during gestation
- post-start of treatment results of respiratory rate F0 during gestation

Three-Way Repeated Measures ANOVA/ANCOVA

A three-way repeated measures analysis of variance (ANOVA) will be performed for the following datasets:

- body weight and body weight change for F1 post-weaning;
- food consumption for F1 after the first 2 weeks post-weaning;
- numerical clinical pathology data for F1;
- buccal mucosal bleeding time for F1;
- body temperature for F1 post-weaning;
- heart rate for F1 post-weaning;
- respiratory rate for F1 post-weaning;
- height **and height change** for F1 post-weaning;
- head circumference **and head circumference change** for F1 post-weaning

A three-way nested repeated measures analysis of variance (ANOVA) will be performed for the following datasets (pups nested within litter):

- body weight and body weight change for F1 pre-weaning **(including only selected animals at culling);**
- ~~body temperature for F1 pre-weaning;~~
- ~~heart rate for F1 pre-weaning;~~

~~– respiratory rate for F1 pre-weaning;~~
– height **and height change** for F1 pre-weaning;
– head circumference **and head circumference change** for F1 pre-weaning

Statistical methods

One-Way ANOVA/ANCOVA

The following statistical group comparison will not include groups with less than three observations or with zero variance.

For each data set with more than two groups to compare, a one-way analysis of variance (ANOVA) will be performed with group as fixed effect. When significant differences among the group means are indicated by the ANOVA overall *F*-test ($p \leq 0.10$), a *t*-test will be used to perform the group mean comparisons between the control diet group and each test item treated group.

For datasets with only two groups to compare (including the control diet group), a two-sample *t*-test will replace the one-way ANOVA *F*-test.

Two-Way Repeated Measures ANOVA/ANCOVA

The fixed effects in the model will be the group, the sex, their interaction and litter nested within group.

If the model indicates that the group-by-sex interaction is significant ($p \leq 0.10$), the group effect will be assessed within each sex using *F*-test on least-squares means. If there is no significant group-by-sex interaction ($p \leq 0.10$), then the group effect will be assessed for each sex using the *F*-test from the model.

When the group effect is significant ($p \leq 0.10$), *t*-test on least-squares means will be performed to compare control diet group with each of the test item treated groups. The pairwise group comparisons will be assessed at an alpha level of 0.10. Significant differences from group mean comparisons will be reported as $p \leq 0.10$, $p \leq 0.05$, $p \leq 0.01$, where *p* represents the *t*-test probability. Least-square means related to the pairwise group comparisons will be presented with *p*-values.

(…)

Reason for Amendment:

To clarify the analysis to be performed for clinical pathology parameters without baseline values; to update the list of parameters to be submitted to statistical analysis for the puppies (F1) since body temperature, heart rate and respiratory rate were not measured during the pre-weaning period; to add the calculation of change between measurement

intervals for height and head circumference as these parameters are growth indicators; and to complete the list of statistical analysis that can be performed.

STUDY PLAN AMENDMENT NO. 10

Approved by:

(b) (4), (b) (6)

March 21, 2018
Date

March 21, 2018
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

March 26, 2018
Date

(b) (4)

STUDY PLAN AMENDMENT NO. 11

Study Title:	Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

(b) (4)

Study Plan Date:	July 5, 2017
Study Plan Amendment Date:	July 30, 2018

Amendments to the study plan are detailed below. Additions or changes are identified by **bold** font; deletions are identified by ~~strikethrough~~. Unless otherwise stated, all amendments are effective as of the above-referenced Amendment Date.

1 Page 26 of 33, under Data Analysis:

Amended as follows:

(…)

Three-Way Repeated Measures ANOVA/ANCOVA

A three-way repeated measures analysis of variance (ANOVA) will be performed for the following datasets:

- body weight and body weight change for F1 post-weaning;
- food consumption for F1 after the first 2 weeks post-weaning;
- numerical clinical pathology data for F1;
- ~~buccal mucosal bleeding time for F1;~~
- body temperature for F1 post-weaning;
- heart rate for F1 post-weaning;
- respiratory rate for F1 post-weaning;
- height and height change for F1 post-weaning;
- head circumference and head circumference change for F1 post-weaning

A three-way nested repeated measures analysis of variance (ANOVA) will be performed for the following datasets (pups nested within litter):

- body weight and body weight change for F1 pre-weaning (including only selected animals at culling);
- height and height change for F1 pre-weaning;
- head circumference and head circumference change for F1 pre-weaning

Log-rank test

The Log-rank test will be performed for the following data set:

- **buccal mucosal bleeding time for F1;**

Statistical methods

Log-rank test

The statistical analyses for bleeding time will be performed on sexes combined due to the low number of animals. The stop of bleeding being the event, the time to event function of each group will be estimated using the Kaplan Meier product limit method applied on 1 min intervals. All animals still bleeding at the end of the observation period (30 min) will be censored at 30 min. A plot of the group time to event function based on Kaplan-Meier estimates will be produced.

Inter-group differences of the time to event curve estimates will be tested using the Log-Rank test. The log rank test will be applied to all groups in order to assess the significance of the overall group effect. If the overall log rank test reveals significant group differences ($p \leq 0.05$), then the control group will be compared to each of the other groups using a Peto two sided test. When performing a pairwise group comparison, only the data corresponding to the two compared groups will be submitted to the statistical analysis.

One-Way ANOVA/ANCOVA

The following statistical group comparison will not include groups with less than three observations or with zero variance.

For each data set with more than two groups to compare, a one-way analysis of variance (ANOVA) will be performed with group as fixed effect. When significant differences among the group means are indicated by the ANOVA overall *F*-test ($p \leq 0.10$), a *t*-test will be used to perform the group mean comparisons between the control diet group and each test item treated group.

For datasets with only two groups to compare (including the control diet group), a two-sample *t*-test will replace the one-way ANOVA *F*-test.

(…)

Reason for Amendment:

To specify the analysis to be performed for buccal mucosal bleeding time.

STUDY PLAN AMENDMENT NO. 11

Approved by:

(b) (4), (b) (6)

July 30, 2018
Date

July 31, 2018
Date

Approved on behalf of the Sponsor by:

(b) (4), (b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

July 31, 2018
Date

(b) (4)

APPENDIX NO. 66
FACILITY DIAGRAM, BUILDING ORIENTATION,
VENTILATION AND LIGHTING PROCEDURES

(b) (4)

STANDARD OPERATING PROCEDURE

Subject:	No.: (b) (4)
Light Intensity (Lux) Determination In Animal Rooms at (b) (4)	**Date of Issuance:** March 30, 2017
	Date effective: April 06, 2017
	Supersedes: (b) (4) / **Training required:** No
	Page 1 of 2

Prepared by:	QAP Review:	Management Approval: (b) (4), (b) (6)

Purpose:

To ascertain the animals are exposed to acceptable levels of luminosity and to describe the method to measure the level of luminosity (Lux) in the animal rooms.

Scope:

This SOP applies to all rooms where animals are housed and for animal activities.

Responsibilities:

It is the responsibility of trained personnel to assure this SOP is followed.

It is the responsibility of the trained personnel to perform the test and to record the results.

Materials:

Calibrated Light Meter

Acceptance criterion:

Since (b) (4) is accredited by AAALAC/CCAC, the low light intensity at one meter above ground should be between 130 to 325 lux for loaded animal rooms.

A high intensity is also available to allow technicians to perform their work, if needed. This high intensity is automatically turned OFF after one hour. The personnel can also turn it OFF if work lasts less than one hour. If the intensity is required for more than one hour, the personnel may turn it ON again. No acceptance criterion is applied for high light intensity.

If a specified high light intensity is required as per study plan, the Request for Environmental Conditions Set points form will be filled to advise Facility Management department of the settings required for the study.

Procedure:

1. A calibrated light meter is used to measure the luminosity.
2. Low light and high light intensities are tested in each room housing animals, if required.
3. The light meter is placed on a support that holds the light meter photo detector at approximately one meter above the ground. A reading is taken in the middle of the room.
4. The value is recorded when photo detector is stabilized.
5. The operator stands away from the light meter to avoid false readings.
6. Rooms with low light intensity outside established ranges are retested to confirm the results.
7. Inform Facility Management department of unacceptable results. Appropriate action will be taken to restore adequate light intensity.
8. Results are recorded on the "Request for Environmental Condition Set Points" form or on appropriate attachment.

Effective Date	Nature of Revision
April 06, 2017	3 year revision, no change.

[redacted] (b) (4)

STANDARD OPERATING PROCEDURE

Subject: Maintenance and Operation of critical Air Handling Units (Supply and Exhaust)		**No.:** BD.011.08
		Date of Issuance: July 20, 2017
		Date effective: July 27, 2017
		Supersedes: [redacted] (b) (4) **Training required:** No
		Page 1 of 5 plus 6 attachments (total 8 pages)
Prepared by:	**QAP Review:**	**Management Approval:** [redacted] (b) (4), (b) (6)

Purpose:
To describe and outline the maintenance and operation of critical Air Handling Units and critical exhaust systems.

Scope:
This SOP applies to the critical Air Handling Units Supply and Exhaust.

Equipment #	Model #	Function
Phase1		
Canatal	9AU12YEBHGX	Cooling unit for server room 146
A-1, A-2	ITF-VC-I-2	Supply
E-1, E-2	ITF-VC-I-2	Exhaust
Phase 2		
A-7, A-8	CAH-2SP-SF-CD-92.25"/196.0"-1	Supply
E-7, E-8	CAH-2SP-SF-CD-92.25"/95.0"-1	Exhaust
E-14	CURE-420-50	Exhaust
A-9	RPS080CSA	Supply
R-9	RPS080CSA	Exhaust

Phase 3

UVA-301	A4D-112/124-DI	Supply
UVA-302	A4D-112/124-DI	Supply
UVA-303	A4D-112/124-DI	Supply
UVE-301	A2D-111/124-DI	Exhaust
UVE-302	A2D-111/124-DI	Exhaust
UVE-303	A2D-111/124-DI	Exhaust
UCA 306		Cooling unit for server room G239

Responsibilities:

It is the responsibility of Facility Management to assure that provisions of this SOP are followed.

Description:

Air handling unit Canatal is used only too cool down the server room 146

Air handling unit UCA 306 is used only too cool down the server room G239

Air handling units A-1/E-1, A-2/E-2 are supplying and exhausting 100% fresh air in the animal Area (Phase 1), laboratories (phase 1), necropsy rooms (phase1 room #174) and cage wash (phase 1).

Air handling units A-7/E-7, A-8/E-8 are supplying and exhausting 100% fresh air in the animal Areas (phase II) and supply histology laboratories (phase II) but exhausting by units E-14.

The units A-9/R-9 is supplying and exhausting the immunology laboratories. The units A-9 is supplying necropsy room (phase1 room #170,173 and 175) and cage wash (phase 2) but exhausting by units E-14.

Air handling units UVA-301/UVE-301, UVA-302/UVE-302, UVA-303/UVE-303 are supplying and exhausting 100% fresh air in the animal Area (phase 3), laboratories (phase 3), necropsy rooms (phase 3) and cage wash (phase 3).

Air handling unit Canatal and UCA 306 are equipped with;

- **Filter:** filters 25 - 35%

Supply Air handling systems A-1, A-2, A-7, A-8, UVA-301, UVA-302 and UVA303 are equipped with;

- **Filter**: Pre-filters 25 - 35%, efficiency filters 95% and high capacity efficiency filters 99.97% (HEPA).

- **Coils:** Heat-recovery, cooling and heating coils use re-circulated glycol for the pre-heating, cooling and heating of fresh air.

- **Humidification unit**; steam headers supplied by HU-1and HU-2 (phase1), HU-4 and HU-5 (phase2), CH-3, CH-5 and CVA-301 (phase3)

Exhausts Air handling systems E1, E2, E7, E8, UVE-301, UVE-302, UVE-303, are equipped with;

- **Filter**: Pre-filters 25 - 35%.

- **Coils:** Heat-recovery, coils use re-circulated glycol for the pre-heating.

Supply Air handling systems A-9/R-9 is equipped with;

-Filter: Pre-filters 25 - 35%, efficiency filters 95%

- Coils: Air Conditioning cooling coil

-Gas furnace; forced draft burner.

- Humidification unit; steam headers supplied by HU-3

- Ventilator;

A-9/R-9 has a supplying and exhausting capacity of 21430 cubic feet per minute with a 30 horse power motor.

E-14 has an exhausting capacity of 13 980 cubic feet per minute with a 5 horse power motor.

Air handling unit's start/stop, heat recovery, heat, cooling and humidification are controlled by the Siemens Building Automation System (BAS) as per sequence of operation A-1/E-1, A-2/E-2, A-7/E-7, A-8/E-8, A-9/R-9, E-14, UVA-301/UVE-301, UVA-302/UVE-302 , UVA-303/UVE-303 and UCA 306. They are authorized to function on the emergency diesel generator electrical power when a hydro electrical power failure occurs. Alarms are triggered on non-authorized start/stop of the ventilators, filter pressure, humidity, temperature and static pressure. The BAS Remote Notification notifies (RENO) the Facility Management technician on call of impending alarms.

The Canatal is a stand-alone operating unit and it is authorized to function on the emergency diesel generators electrical power when a hydro electrical power failure occurs.

Differential Pressure Alarms on filters			
Systems	**Point Name**	**Alarm Maximum Value (Pa)**	**Filter Type**
A-1	445.A-1.MPF1	400	HEPA (99.97% efficacy)
A-2	445.A-2.MPF1		
A-7	445.A-7.MPF1		
A-8	445.A-8.MPF1		
UVA-301	445.UVA-301.MPF1		
UVA-302	445.UVA-302.MPF1		
UVA-303	445.UVA-303.MPF1		
A-1	445.A-1.MPF2	200	95% efficacy
A-2	445.A-2.MPF2		
A-7	445.A-7.MPF2		
A-8	445.A-8.MPF2		
UVA-301	445.UVA-301.MPF2		
UVA-302	445.UVA-302.MPF2		
UVA-303	445.UVA-303.MPF2		
A-1	445.A-1.MPF3	200	30% efficacy
A-2	445.A-2.MPF3		
A-7	445.A-7.MPF3		

A-8	445.A-8.MPF3		
UVA-301	445.UVA-301.MPF3		
UVA-302	445.UVA-302.MPF3		
UVA-303	445.UVA-303.MPF3		
E-1	445.A-1.MPF4	200	30% efficacy
E-2	445.A-2.MPF4		
E-7	445.A-7.MPF4		
E-8	445.A-8.MPF4		
UVA-301	445.UVA-301.MPF4		
UVA-302	445.UVA-302.MPF4		
UVA-303	445.UVA-303.MPF4		

Systems	Dynamics pressure Alarm (Pa) Outside range below
A-1	Between 150 and 350
A-2	
A-7	
A-8	
E-1	
E-2	
E-7	
E-8	
UVA-301	
UVA-302	
UVA-303	

Systems	Temperature Alarm (°C) Outside range below
A-1	Between 10 and 18
A-2	
A-7	
A-8	
UVA-301	
UVA-302	
UVA-303	
Canatal UCA 306	Between 15 and 21

Systems	Relative humidity Alarm (% RH) Outside range below
E-1	Between 30 and 70
E-2	
E-7	
E-8	
UVE-301	
UVE-302	
UVE-303	

Maintenance:

Maintenance is required every 3 months on Air handling units and is performed by the Facility management technicians. If abnormal conditions are detected by the facility management technician, proper action will be taken to correct the situation and will be reported on Attachment 6 for units A-1/E-1, A-2/E-2, A-7/E-7, A-8/E-8, UVA-301, UVA-302, UVA-303, UVE-301, UVE-302, UVE-303, in addition, for systems A9/R9 and E-14.

Effective Date	Nature of Revision
July 27, 2017	Three years revision

(b) (4)

Critical air handling unit (3 month maintenance)

use this attachment for unit A-1, A-2, A-7, A-8, UVA-301, UVA-302, UVA-303.

EQUIPMENT: _____ **MONTH:** _____

–CHECK DAMPER		( )
–LUBRIFICATE DAMPER		( )
–CHECK LIGHT		( )
–CHANGE 25-35% FILTER		( )
–CHECK 95% filter		( )
–CHECK HEPA FILTER		( )
–WASH FLOORS AND WALLS		( )
–CHECK HEATING COIL		( )
–CHECK COOLING COIL		( )
–CHECK RECOVERY COIL		( )
–CLEAN CONDENSING PAN		( )
–CLEAN HUMIDITY DIFFUSER		( )
–CHECK MOTOR PULLEY		( )
–CHECK BLOWER PULLEY		( )
–CHECK PULLEY ALIGNEMENT		( )
–CHECK MOTOR AMPERAGE	LINE 1	* ( )
	LINE 2	* ( )
	LINE 3	* ( )
–CHECK V-BELT		( )
GREASE BLOWER BEARING		
FRONT		( )
BACK		( )
GREASE MOTOR BEARING		
FRONT		( )
BACK		( )

Maintenance performed by : _____

Date: _____

(✓) = MA NTENANCE IS PERFORMED

* ( ) = READ NG VALUE

(N/A) = MA NTENANCE IS NOT APPLICABLE

Reviewed by:

Date:

(b) (4)

Critical air handling unit (3 month maintenance)

use this attachment for units:E-1; E-2; E-7; E-8; UVE-301; UVE-302; UVE-303.

EQUIPMENT: _____ **MONTH:** _____

–CHECK DAMPER		( )
–LUBRIFICATE DAMPER		( )
–CHECK LIGHT		( )
–CHANGE 25-35% FILTER		( )
–WASH FLOORS AND WALLS		( )
–CHECK RECOVERY COIL		( )
–CLEAN CONDENSING PAN		( )
–CHECK MOTOR PULLEY		( )
–CHECK BLOWER PULLEY		( )
–CHECK PULLEY ALIGNEMENT		( )
–CHECK MOTOR AMPERAGE	LINE 1	* ( )
	LINE 2	* ( )
	LINE 3	* ( )
–CHECK V-BELT		( )
– GREASE BLOWER BEARING		
FRONT		( )
BACK		( )
– GREASE MOTOR BEARING		
FRONT		( )
BACK		( )

Maintenance performed by : _____

Date: _____

(✓) = MAINTENANCE IS PERFORMED

* ( ) = READING VALUE

(N/A) = MAINTENANCE IS NOT APPLICABLE

Reviewed by _____

Date: _____

(b) (4)

Critical air handling unit (3 month maintenance)

use this attachment for unit A9/R9

EQUIPMENT: A9/R9 **MONTH:** _____

ONLY IN WINTER (February & December)

–CHECK FORCED DRAFT BURNER PROPER IGNITION ( )

ONLY IN SUMMER (Mai, August)

–CHECK FREON SIGHT GLASS	COMPRESSOR CIRCUIT 1, 3, 5	( )
(IF IT'S GREEN)	COMPRESSOR CIRCUIT 2, 4, 6	( )
–CHECK OIL LEAK	COMPRESSOR CIRCUIT 1, 3, 5	( )
	COMPRESSOR CIRCUIT 2, 4, 6	( )
–CLEAN CONDENSING PAN		( )
–CLEAN CONDENSOR COIL		( )

–CHECK COMPRESSOR AMPERAGE

	LINE 1	LINE 2	LINE 3
COMP 1	* ( )	* ( )	* ( )
COMP 2	* ( )	* ( )	* ( )
COMP 3	* ( )	* ( )	* ( )
COMP 4	* ( )		* ( )
COMP 5	* ( )	* ( )	* ( )
COMP 6	* ( )	* ( )	* ( )

–CHECK CONDENSOR FAN FOR PROPER FUNCTION

FAN 1 ( )	FAN 4 ( )	
FAN 2 ( )	FAN 5 ( )	
FAN 3 ( )	FAN 6 ( )	

Maintenance performed by : _____

Date: _____

(✓) = MAINTENANCE IS PERFORMED

* ( ) = READING VALUE

Reviewed by: _____

Date: _____

1959

(b) (4)

Critical air handling unit (3 month maintenance)

use this attachment for unit A9 and R9

EQUIPMENT: A9/R9 **MONTH:** _____

		SUPPLY	EXAUST
–CHECK MOTOR PULLEY		( )	( )
–CHECK BLOWER PULLEY		( )	( )
–CHECK PULLEY ALIGNEMENT		( )	( )
–CHECK MOTOR AMPERAGE	LINE 1	* ( )	* ( )
	LINE 2	* ( )	* ( )
	LINE 3	* ( )	* ( )
– **GREASE BLOWER BEARING**			
FRONT		( )	( )
BACK		( )	( )
– **GREASE MOTOR BEARING**			
FRONT		( )	
BACK		( )	( )
–CHECK V-BELT		( )	( )
–IF V-BELT ARE REPLACED		( )	( )
–CHECK BLOWER IMPELLER INTEGRITY		( )	( )
–CHECK LIGHT		( )	
–CHECK CRANK CASE HEATER		( )	
–CHANGE 25-35% FILTER		( )	
–CHECK 95% filter		( )	

Maintenance performed by : _____

Date: _____

(✓) = MAINTENANCE IS PERFORMED

* ( ) = READING VALUE

Reviewed by: _____

Date: _____

1960

(b) (4)

Critical air handling unit (3 month maintenance)

use this attachment for unit E-14

EQUIPMENT: E-14 **MONTH:** _____

– GREASE BLOWER BEARING	
FRONT	( )
BACK	( )
– GREASE MOTOR BEARING	
FRONT	( )
BACK	( )
–CHECK MOTOR PULLEY	( )
–CHECK BLOWER PULLEY	( )
–CHECK PULLEY ALIGNEMENT	( )
–CHECK V-BELT	( )
–IF V-BELT ARE REPLACED	( )

Maintenance performed by : _____

Date: _____

(✓) = MAINTENANCE IS PERFORMED

Reviewed by: _____

Date: _____

1961

(b) (4)

Critical air handling unit (3 month maintenance)

use this attachment for unit Canatal

EQUIPMENT: CANATAL **MONTH:** _____

– GREASE BLOWER BEARING	
FRONT	( )
BACK	( )
– GREASE MOTOR BEARING	
FRONT	( )
BACK	( )
–CHECK MOTOR PULLEY	( )
–CHECK BLOWER PULLEY	( )
–CHECK PULLEY ALIGNEMENT	( )
–CHECK V-BELT	( )
–IF V-BELT ARE REPLACED	( )
–CHANGE 25-35% FILTER	( )
–TEMPERATURE SET POINT COMPRESSOR 1	( )
–TEMPERATURE SET POINT COMPRESSOR 2	( )

Maintenance performed by : _____

Date: _____

(✓) = MAINTENANCE IS PERFORMED

Reviewed by: _____

Date: _____

1962

(b) (4)

Critical air handling unit (3 month maintenance)

use this attachment for unit UCA-306

EQUIPMENT: UCA-306 **MONTH:** _____

–CHECK MOTOR PULLEY	( )
–CHECK BLOWER PULLEY	( )
–CHECK PULLEY ALIGNEMENT	( )
–CHECK V-BELT	( )
–IF V-BELT ARE REPLACED	( )
–CHANGE 25-35% FILTER	( )

Maintenance performed by : _____

Date: _____

(✓) = MAINTENANCE IS PERFORMED

Reviewed by: _____

Date: _____

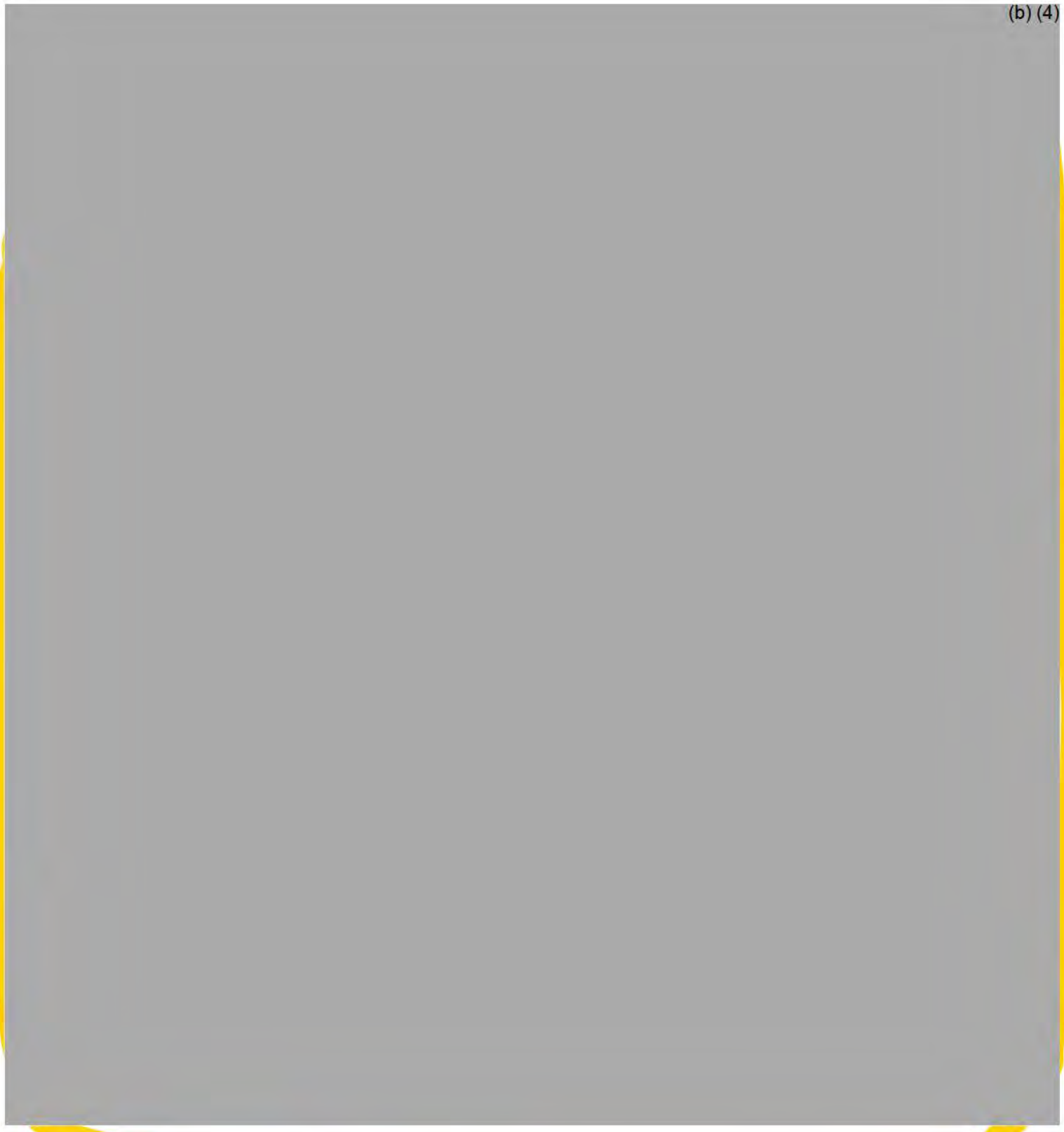
1963

(b) (4)

Description of Abnormal Conditions & Actions Taken		
Date	**Comments:**	**Initials & Date**

Reviewed by: _____

Date: _____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Annex 12- Canine Literature Search and Screen Protocol

Review Protocol: Canine Dietary Long-chain Omega-3 Safety and Bioavailability

Background

This systematic review is intended to update a prior literature search, conducted through January 2010, and used in support of an application to the United States FDA, Center for Veterinary Medicine, for use of long-chain omega-3 (n-3 LCPUFA)-rich algal products in animal feeds, particularly, canine diets.

Objective

Describe the justification for this review. In other words, describe why this review/the information it collects is important.

To verify that prior literature supporting the bioavailability and safe use of n-3 LCPUFA (i.e. DHA and/or EPA) in canine diets is consistent with current (2010-2018) published research.

Review Question

Full Review Question	
Are n-3 LCPUFA, particularly EPA and DHA, safe and bioavailable when added to canine diets?	
Population	Canine - Dog/puppy/bitch
Intervention	Dietary sources of Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA)
Comparison	Placebo; No treatment/intervention; Usual diet/standard of care
Outcome	Measures of bioavailability and safety

Search Strategy

Databases
PubMed, Embase, Web of Science, CAB, VetMed
Hand Searching
Hand searching of relevant narrative and systematic reviews and meta-analyses will be completed
Reference Searches
Reference lists of full text papers meeting inclusion criterial will be scanned

Eligibility Criteria

PICO	**Inclusion Criteria**	**Exclusion Criteria**

Population	Healthy populations (includes populations with disease risk factors, e.g. overweight), of any age: • Domestic canine/dog • Puppies • Bitches	• Wild/feral canine • Canines with chronic disease or congenital malformations • Non-canine species • In vitro studies
Intervention	Known amount of dietary n-3 LCPUFA (i.e. EPA/DHA) from a variety of sources including, but not limited to: • Fish/fish oil • Algal oil	• Source of omega-3 fatty acids other than marine type, i.e. ALA only such as flaxseed oil • Combination* of EPA/DHA with other omega-3 oils (see above) • Combination* of EPA/DHA with omega-6 oils • Concurrent use of EPA/DHA with other active ingredients (e.g. botanicals, therapeutics) • IV administration • Topical administration • Insufficient information provided to determine dose of EPA/DHA Note: *combinations considered supplemental, those required to meet essential fatty acid requirements not excluded
Comparison	• For Randomized controlled trials - Placebo; No treatment/intervention; Usual diet/standard of care • For Observational studies – stratified intake levels	• No control group
Outcomes	• Safety • Bioavailability • Adverse events/effects • Growth and development • Weaning • Body weight • Blood, plasma, serum, platelets • Blood coagulation • Platelet aggregation • Hematology • Hemoglobin • Serum albumin	• Outcomes related to efficacy including but not limited to: o cognitive function, o performance, o behavior,

	• Serum alkaline phosphatase • Packed cell volume • Clinical Chemistry • Blood chemical analysis, veterinary • Morbidity/mortality • Skin condition • Stool quality • Hair/coat condition • Poisoning • Toxicity • Dog disease/chemically induced • Physiology • Nutritional requirements • Nutrient deficiency/excess • Eicosanoid function • Immune function • Gestation • Lactation	
Study Design	• Randomized controlled trials o Of duration consistent with typical dietary regimen • Observational studies including prospective cohorts and case control o Of duration consistent with typical dietary regimen	• Acute feeding study, e.g. one time bolus dose, or acute administration (e.g. less than 7 days) • Open-label/No comparison group • Letters, • abstracts, • case reports, • case series, • position statements, • hypotheses, • study designs, • conference proceedings • Study results not available in English

Data Extraction

Provide a description of methods used to collect data from included studies (e.g. categories of data you intend to collect, how many people will conduct extraction, how disagreements will be resolved, etc).

Data extracted into an Excel spreadsheet. Variables of interest include: age, weight, sex, and breed of animals; dose of EPA/DHA; route of administration; variables of interest; length of trial, number of subjects, and others

Study Quality Assessment

If applicable, describe the tool(s) you will use to assess risk of bias.

No bias assessment planned

Data Synthesis

Describe how you will analyze and summarize the included study results.

Evidence tables and narrative summary

Annex 13
Domoic Acid Report 190919

Domoic Acid Report

Project: DSM Nutritional Products

Submitted to: (b) (4), (b) (6)
Organization: DSM Nutritional Products
Address: (b) (4)
Email:

Sample Receipt Date: 24 September 2019
Sample Condition: 27.3 ºC upon arrival
Report# (b) (4)
Date Prepared: 8 October 2019
Prepared by: (b) (4), (b) (6)

Table 1: Samples analyzed

Sample Identification	Site	Collection Date
B6 Whole Broth	Columbia	9/19/19
B7 Whole Broth	Columbia	9/19/19

Analytes: Domoic Acid (DA)

Sample Preparation

The samples were received, inverted for 60 seconds to mix and aliquots spiked (LFSM; Table 2). Acetonitrile was added (2:1) and samples were cold (5°C) centrifuged (3,000 RPM; 15 min). The supernatants were saved, diluted in deionized water and sent through preconditioned solid phase extraction Strata X (100 mg) cartridges. The columns were washed (water) and eluted (100% methanol), solvent removed (60°C, N_2) and reconstituted in 5% methanol at 1x.

Analytical Techniques

Liquid chromatography mass spectrometry/mass spectrometry (LC-MS/MS)

DA

A Phenomenex Kinetex 2.6µm 2.1 x 150 mm C18 column was used in separation with mobile phases acetonitrile and water containing 2 mM formic acid and 3.6 mM ammonium formate. The $[M+H]^+$ ion for domoic acid (*m/z* 312) was fragmented and the product ions (*m/z* 266, 248, 220, 146) were monitored. An external standard curve was used to determine LFSM returns.

Quality Control

Table 2: QA/QC samples prepared for analyses.

Analyte	Concentration (ng/mL)	Sample ID	QC Type	Return
DA	10	B6 Whole Broth	LFSM	35%[N]
DA	100	B7 Whole Broth	LFSM	42%[N]

Additional Quality Control/Quality Assurance checks included method blanks, LFBs, and standard curves.

Qualifier	Flag
CL	Analytical result is estimated due to ineffective quenching.
J	Analyte was positively identified; the associated numerical value is estimated.
PT	The reported result is estimated because the sample was not analyzed within required holding time.
B	Analytical result is estimated. Analyte was detected in associated reagent blank as well as the samples.
E	Analytical result is estimated. Values achieved were outside calibration range.
N	Spiked sample control was outside limits
T	The reported result is estimated because the sample exceeded temperature threshold when received

Abbreviations

NA	Not Applicable	LFSM	Lab Fortified Sample Matrix
MDL	Method Detection Limit	LFSMD	Lab Fortified Sample Matrix Duplicate
MQL	Method Quantification Limit	LD	Lab Duplicate
ND	Not Detected above the MDL	IS	Internal Standard
Blank	Regent Water free from interferences	—	Not Analyzed
LFB	Lab Fortified Blank	MRL	Method Reporting Limit

Summary of Results

Table 4: Summary of results in ng/mL

Sample ID	Domoic Acid (ng/mL)
B6 Whole Broth	ND
B7 Whole Broth	ND
MRL (ng/mL)	*10*
Analyst Initials	(b) (4), (b) (6)
Date Analyzed	*10/8/19*

Submitted by: (b) (4), (b) (6)

Date: October 8, 2019

The results in this report relate only to the samples listed above.
This report shall not be reproduced except in full without written approval of the laboratory.

[redacted] (b) (4)

Identification of MK27173

Provided by:
Günther Bahnweg, Ph.D.
Head of Plant Toxicology and Mycology

November 3rd, 2009

Observations:

Cultures of MK27173 were received from [redacted] (b) (4) during July 2008. Cells were transferred to petri dishes with (15 ml) half-strength seawater and (1 ml) of a suspension of autoclaved newly hatched brine shrimp larvae. The brine shrimp larvae were heavily overgrown with clusters of sporangia after 2-3 days.

Microscopic observation in flow-through slides: Zoospores settled on the substrate enlarged and rapidly underwent binary divisions leading to tetrads, octads, and finally to clusters of sporangia. Tetrad formation commenced at a very early stage prior to maturity. Spores were biflagellate at discharge, swimming actively away from the mature sporangium, wall remnants of which were clearly visible (in phase contrast) after spore discharge. Sporangia measured 12.5-25 µm in diameter, spore size was 2.5-2.8x4.5-4.8 µm. Numbers of spores per individual sporangium were 8-24. Individual sporangia enlarging to maturity without binary divisions (tetrad formation) have never been observed. No slug-like stages or naked protoplasts have been observed.

Conclusion:

Based on these observations, I conclude that MK27173 is definitely a member of the genus *Schizochytrium*. The characteristic of multiple binary cell divisions leading to clusters of sporangia is a hallmark characteristic of the genus.

The gene sequence characteristics provided by Martek do not correspond with any of the known species of the genus *Schizochytrium*, I further conclude that MK27173 is a new member of that genus. As a result the organism is referred to as *Schizochytrium* sp.

[redacted] (b) (4), (b) (6)

[redacted] (b) (4)

(b) (4)

Verification of Identity of *(Schizochytrium sp.)*

Provided by:
Günther Bahnweg, Ph.D.
Head of Plant Toxicology and Mycology

January 29th, 2010

Observations:

An algal culture was received from (b) (4) for the purpose of identification in January 2010. Colonies were transferred to new plates of FFM medium and also to petri dishes with (15 ml) half-strength seawater and (1 ml) of a suspension of autoclaved newly hatched brine shrimp larvae. The brine shrimp larvae were only poorly overgrown with clusters of sporangia after 2-3 days – Observations were therefore primarily based on colonies from FFM medium.

Microscopic observation in flow-through slides: Zoospores actively swimming for several minutes finally settled on the substrate, enlarged and rapidly underwent binary divisions leading to tetrades, octades, and finally to clusters of sporangia. Tetrade formation commenced at a very early stage prior to maturity. Ectoplasmic nets ("rhizoids") were well developed, often prominent). Spores developing within sporangia prior to discharge, drifting passively away from the mature sporangium, wall remnants of which were poorly visible (in phase contrast). Active swimming is retarded, commencing several minutes to an hour after spore release. Sporangia measured 7.5-8.5 µm in diameter, cluster size ranged from 15-25 µm i.d. Spore size was 2.0-2.5x2.5-3.5 µm. Numbers of spores per individual sporangium were 8-16 (-32). Individual sporangia enlarging to maturity without binary divisions (tetrade formation) have not been observed. Naked protoplasts occasionally seen at the edge of colonies on FFM rounded off and underwent binary fission to produce further tetrades.

Conclusion:

Based on these observations, I conclude that the examined organism is definitely a member of the genus *Schizochytrium*. The characteristic of multiple binary cell divisions leading to tetrades and clusters of sporangia is a hallmark characteristic of the genus.

The examined organism shares some characters with other species of the genus *Schizochytrium* and with *Thraustochytrium aggregatum* Ulken, in particular the unique formation of tetrades, octades and clusters of sporangia. Zoospore motility is retarded at discharge just like in *T. aggregatum* Ulken, the latter differing, however, in its ability to alternatively develop mature sporangia without prior binary fission. The examined organism differs from *Schizochytrium aggregatum* Goldstein & Belsky, by the presence of vigorously swimming zoospores just before and at discharge through a fissure of the persistent sporangium wall. Zoospore motility and fate of the sporangium wall at discharge is considered a key character for species definition in the Thraustochytriales. The examined organism also differs considerably from *Schizochytrium minutum* Gaertner (now *Oblongichytrium minutum* Yokoyama & Honda), *S. octosporum* Raghukumar and *S.*

mangrovei Raghukumar (now *Aurantiochytrium mangrovei* Yokoyama & Honda) in the size of sporangia and the number of zoospores per sporangium. *Schizochytrium limacinum* Honda et al. (now *Aurantiochytrium limacinum* Yokoyama & Honda) is different from the examined organsm in its discharge of limax amoebae from mature primary sporangia.

Since morphological and developmental characteristics do not fully agree with any of the known species of the genus *Schizochytrium*, I further conclude that the examined organsim is a new member of that genus. As a result the organism is properly referred to as *Schizochytrium* sp.

(b) (4), (b) (6)



Cerrito, Chelsea

From: Das, Manisha
Sent: Wednesday, July 15, 2020 11:58 AM
To: Animalfood-premarket
Cc: Wong, Geoffrey K
Subject: FW: AGRN 36
Attachments: 2016-3002 - Draft Study Plan ES - JW.docx; 2016-3002 Final Study Plan Signed.pdf; SP signature page.pdf

Please log into STARS as an amendment to M-88.

Thanks,
Manisha.

From: Turney, William <William-George.Turney@DSM.COM>
Sent: Tuesday, July 14, 2020 7:19 AM
To: Das, Manisha <Manisha.Das@fda.hhs.gov>
Cc: Wong, Geoffrey K <Geoffrey.Wong@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Donnelly, Karen (CVM) <Karen.Donnelly2@fda.hhs.gov>
Subject: RE: AGRN 36

For Internal Use Only

Dear Manisha,

In response to Dr. Donnelly's inquiry below, DSM has conducted a thorough investigation an hereby confirms that the final disposition of the puppies was carried out in accordance with the GLG protocol and was accurately reflected in the GLG study final report. DSM fully recognizes that the disposition described in the publication and in the GRAS notice under section 7.4.2 was erroneously reported. As a formal corrective action Dr. Dahms has a submitted a corrigendum to the journal to correct the publication. The Journal PlosOne received the corrigendum on 7/8/2020. Below is the excerpt of the rationale for the error provided by Dr. Dahms to the journal.

Excerpt of response from Dr. Dahms to PlusOne:

Please see the experimental protocol (study plan) attached along with the signature page.

Please note that it was reviewed and signed by the IACUC chairperson (p. 33). Also, there is a chapter on Animal Care Compliance (p. 17 of the final study plan).

Additionally, I attached the initial draft of the protocol last modified 01.03.2017. On page 18 in the Section "Standardization of Litter (Culling)" you will see that the initial plan was to (b) (4) *Unfortunately, this changed later when we realized that the testing site did not have any spare dams to foster as they do not breed themselves. Puppies at this age cannot survive without a nursing dam.* (b) (4)

The mistake happened because I used the initial protocol for writing the methods part of the manuscript instead of the final version. I sincerely apologize for this error.

Please be assured that DSM is taking this oversight seriously and is instituting further corrective action to prevent reoccurrence in the future.

I would like to review with the CVM via a conference call the above findings and obtain further direction how the agency would prefer to administratively manage the correction.

I have availability for a call anytime Wednesday July 15th before 3 pm or Friday July 17th before 11 am or after 1 pm.

Sincerely,
Bill

William Turney| Head of Regulatory Affairs and Product Quality Management|DSM Nutritional Products LLC | 45 Waterview Blvd | Parsippany, NJ 07054 | USA | T 973-257-8325 | M 908-283-1067 | william-george.turney@dsm.com | Stay connected:



From: Das, Manisha <Manisha.Das@fda.hhs.gov>
Sent: Friday, June 19, 2020 11:00 AM
To: Turney, William <William-George.Turney@DSM.COM>
Cc: Wong, Geoffrey K <Geoffrey.Wong@fda.hhs.gov>; Burkholder, William <William.Burkholder@fda.hhs.gov>; Donnelly, Karen (CVM) <Karen.Donnelly2@fda.hhs.gov>
Subject: AGRN 36

CAUTION - This email originated from outside DSM
Please forward suspicious emails as attachments to phishing@dsm.com

Dear Bill,

Thank you for speaking with us today. I have provided the summary of Dr. Donnelly's request below.

> There is a discrepancy regarding the disposition of puppies used in the AOCED GLG study. (b) (4) However, in the GLG Final Report (Annex 11 of the notice), section 7.9 is titled "Standardization of Litter (Culling)" and it says the removed puppies were euthanized. This same information about culling appears in Appendix 65 of the Final Report, the Final Study Plan. The Study Monitor and Sponsor Representative, Dr. Irina Dahms, has signed off on the Final Study Plan and is the lead author on the published paper.

We need you to resolve this discrepancy in writing, telling us what actually happened with the removed puppies and explaining how information different from the GLG Study Final Report ended up in the GRAS notice.

It would be great if you can get back to us in a couple of weeks.

Have a good weekend.

Kind Regards,
Manisha Das.

Manisha Das, Ph.D.
Chemist

Center for Veterinary Medicine
Office Surveillance and Compliance, Division of Animal Feeds
U.S. Food and Drug Administration
Tel: 240-402-5920
manisha.das@fda.hhs.gov

RECEIVED DATE
JUL 15, 2020



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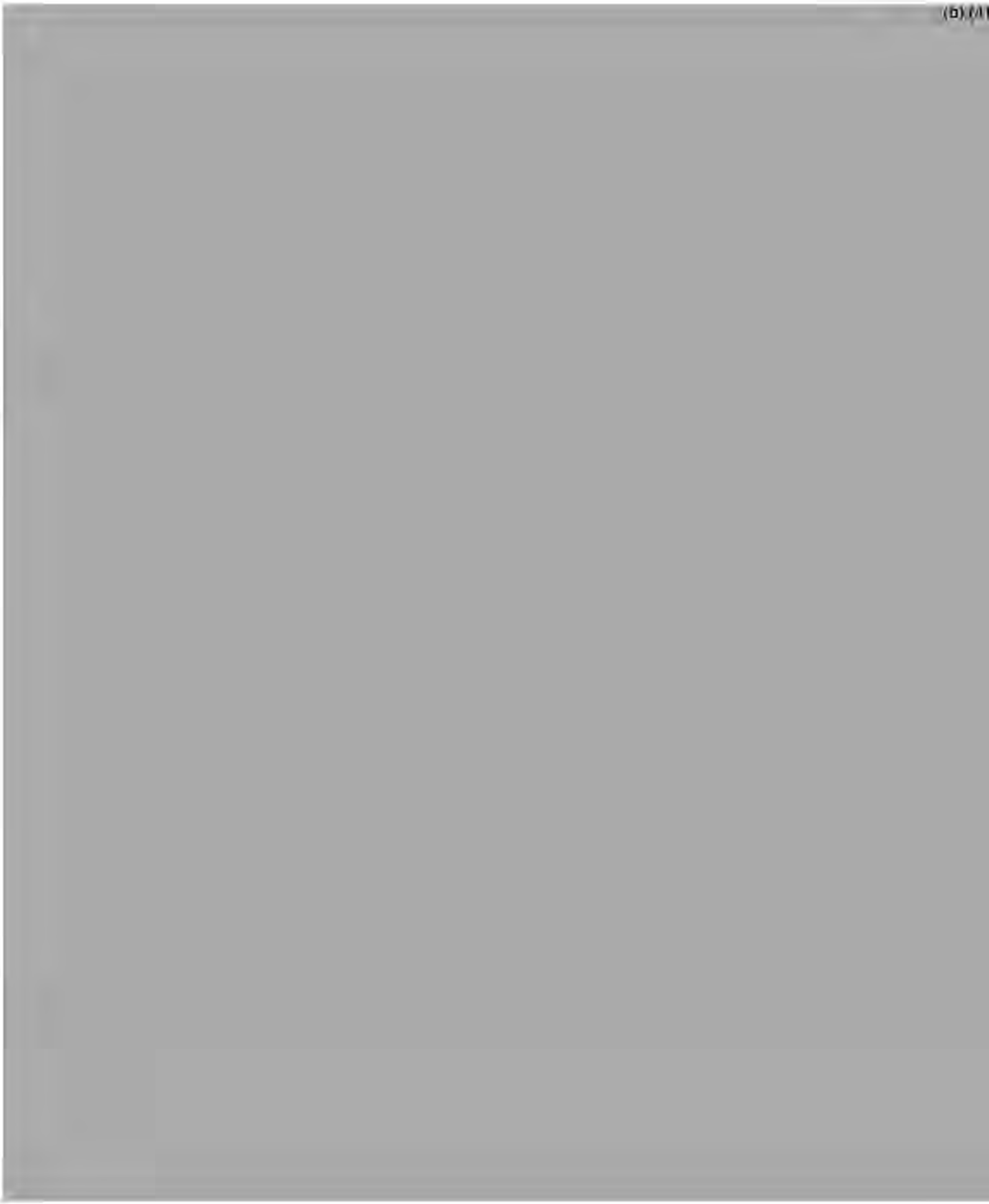
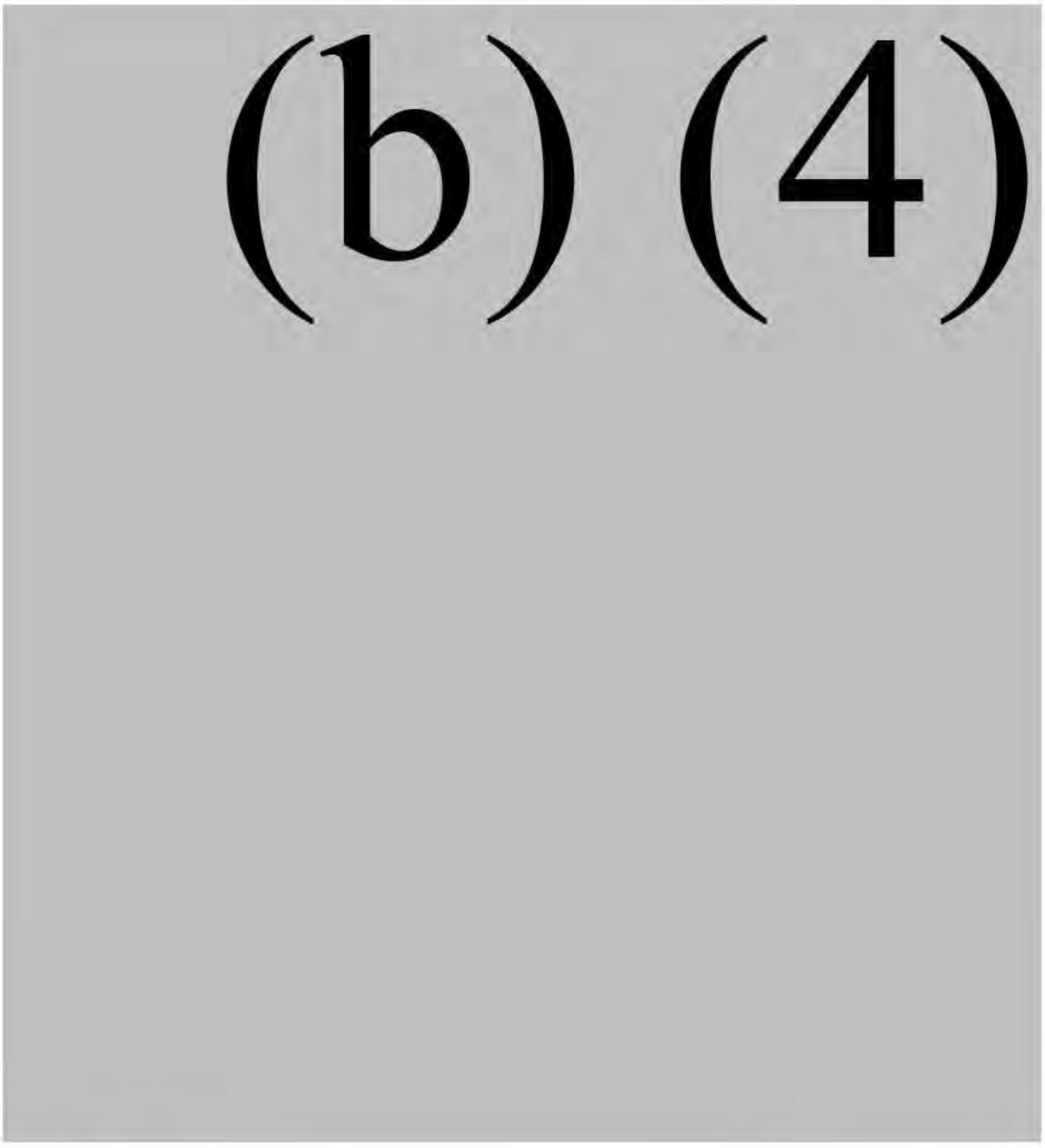
(b)(4)

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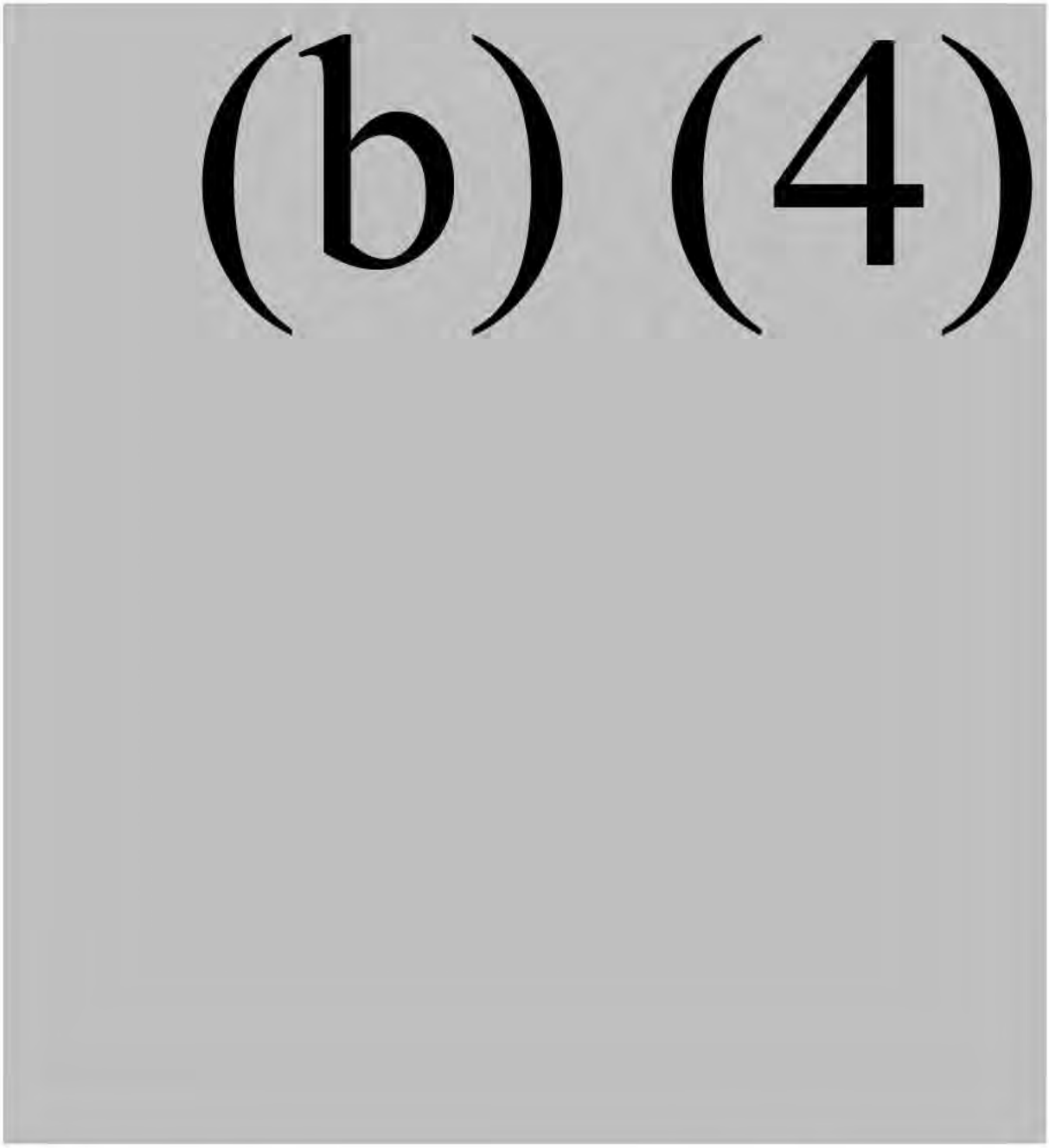
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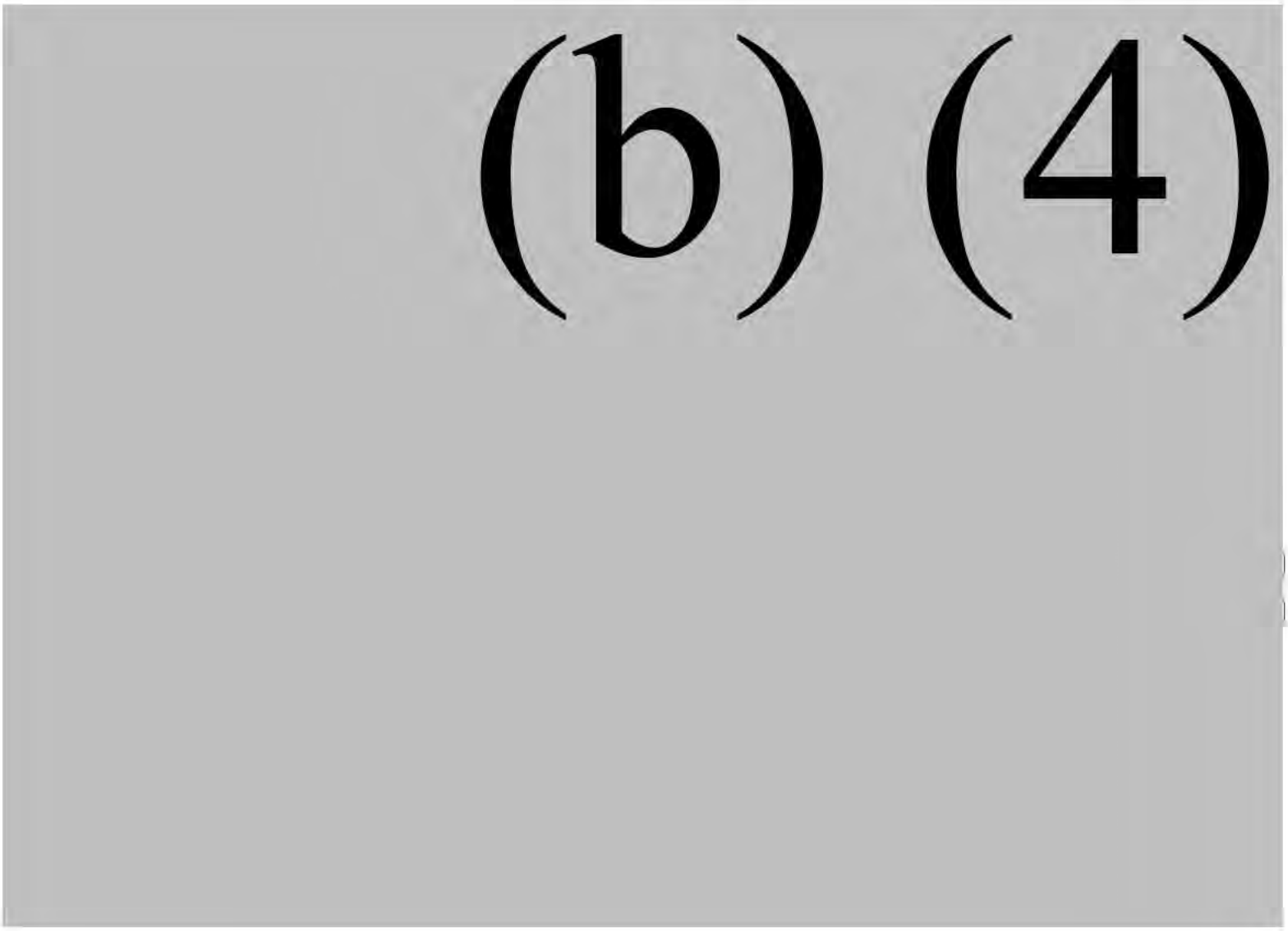
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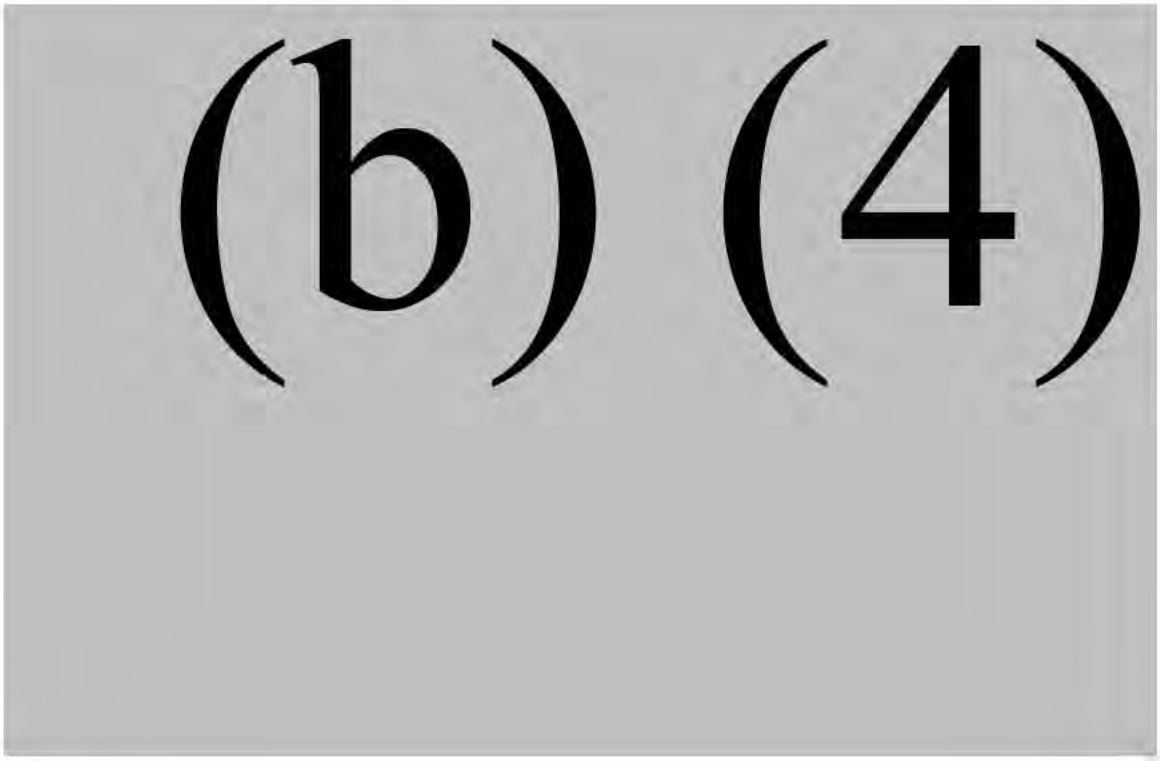
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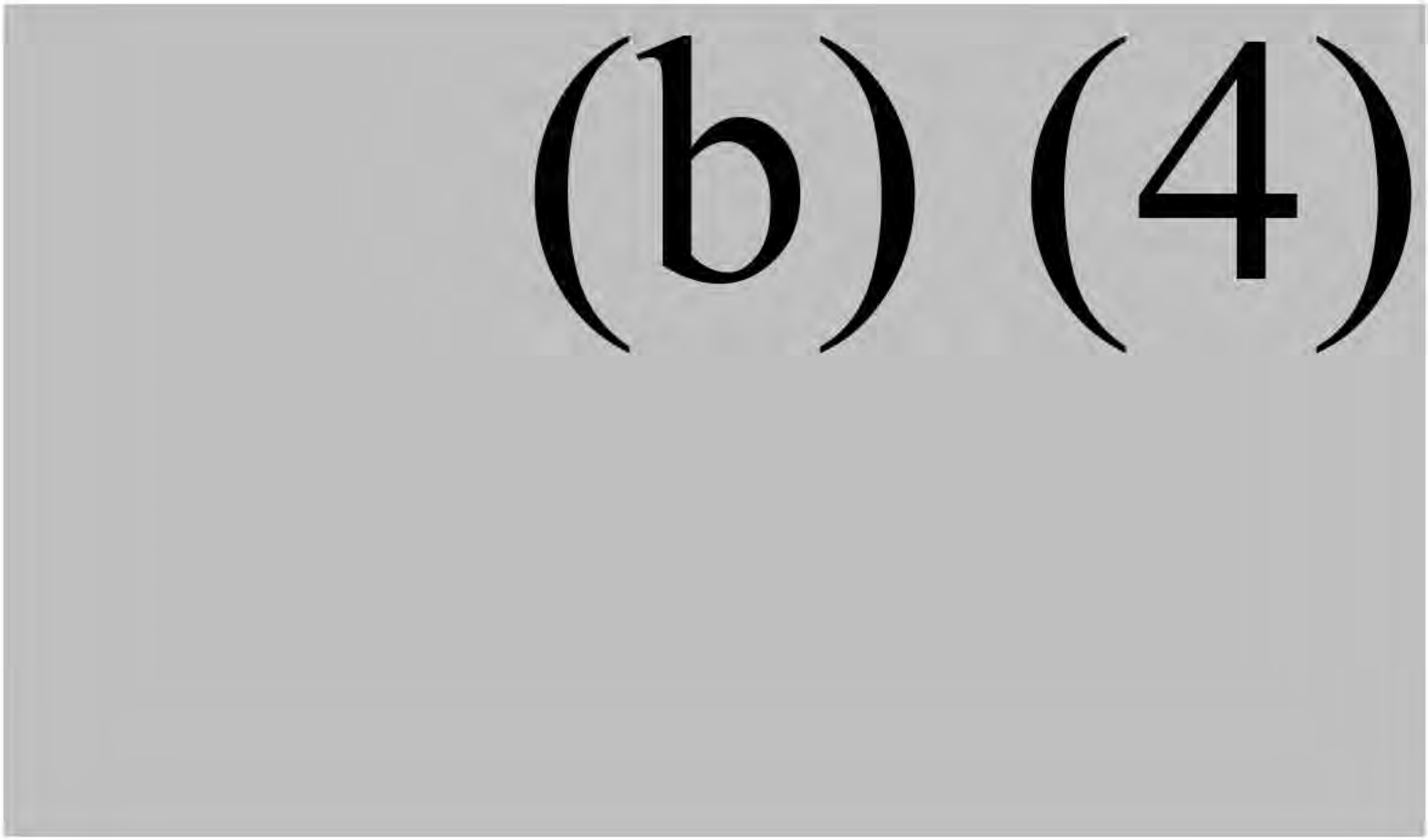
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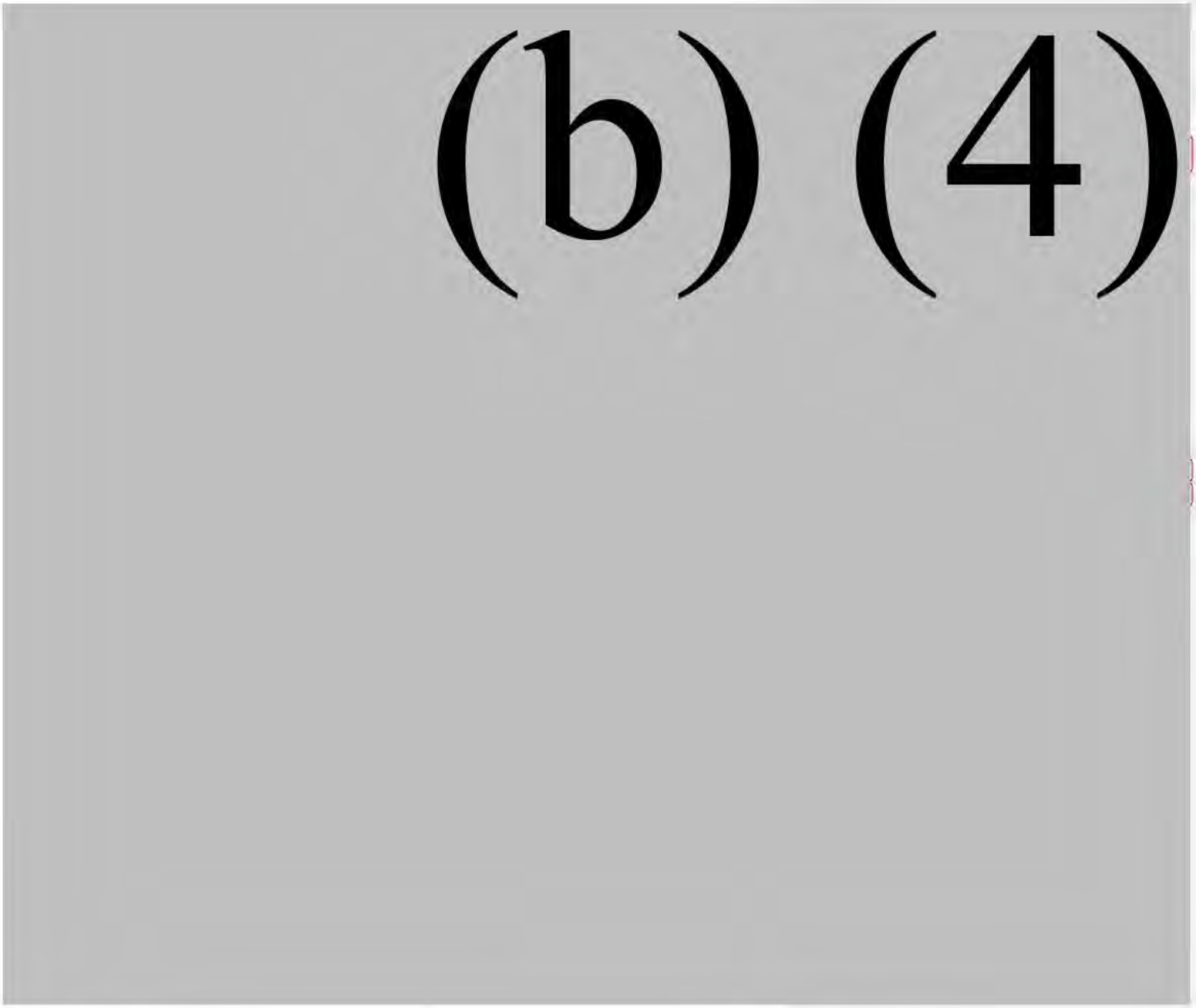
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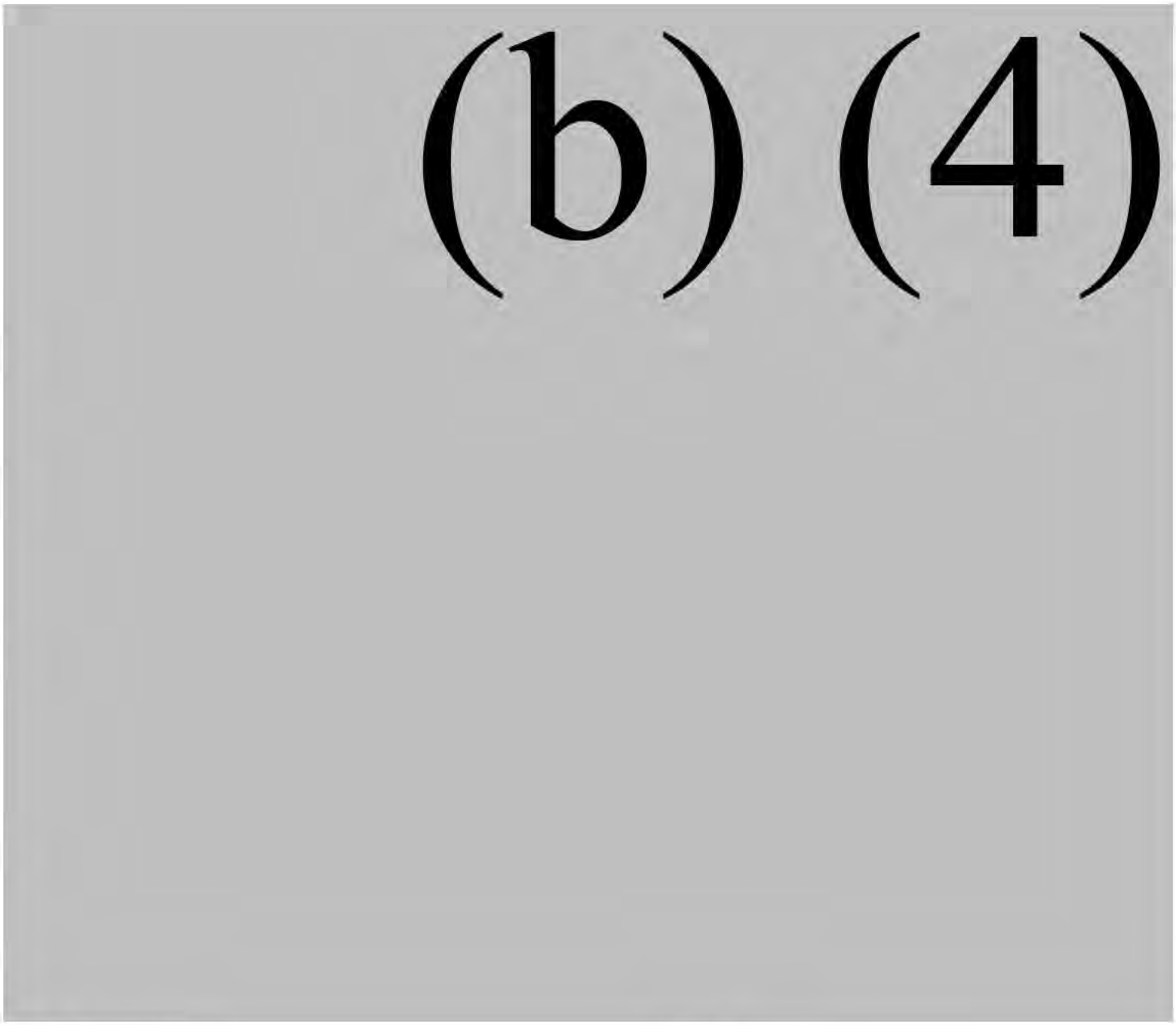
(b) (4)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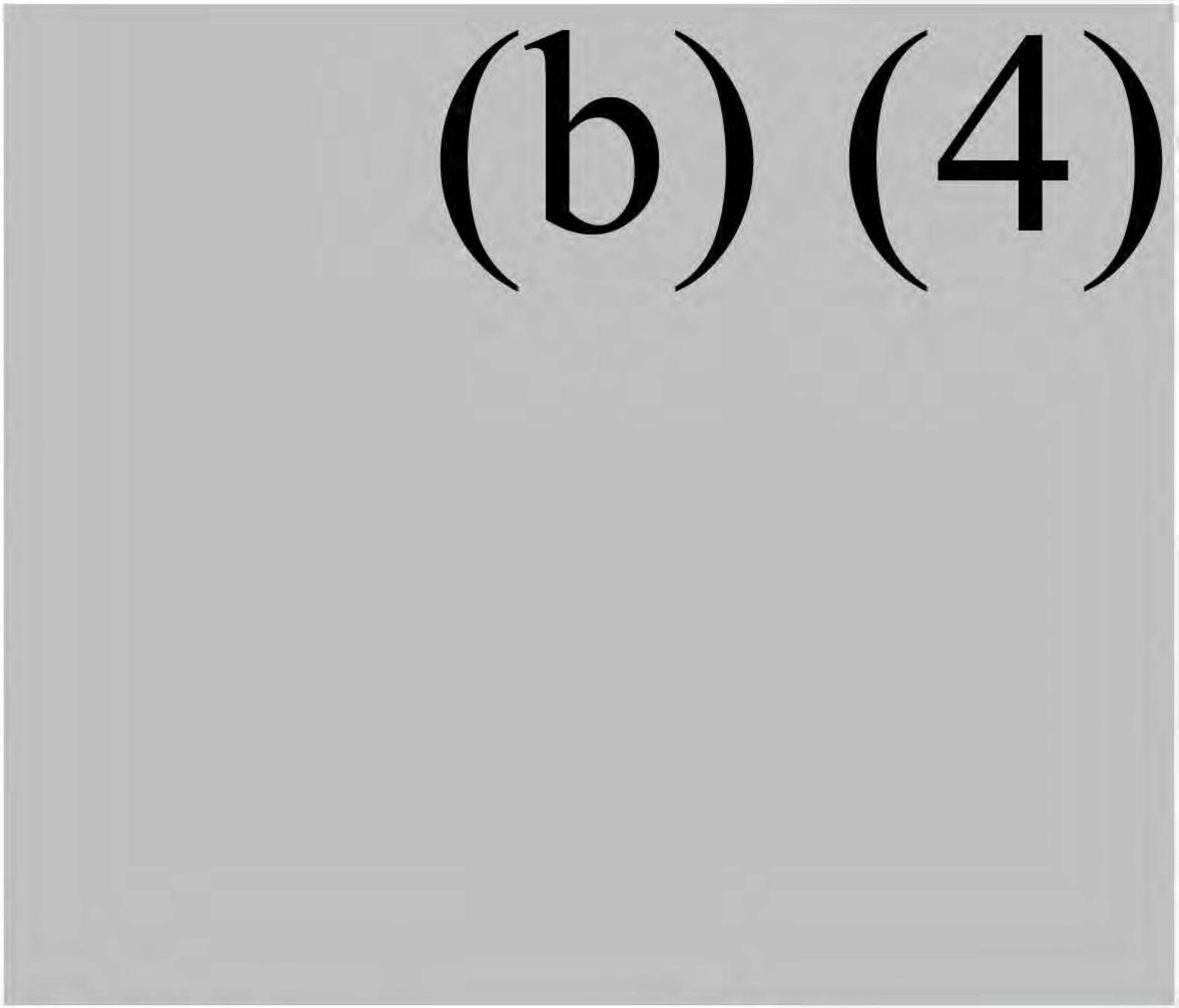
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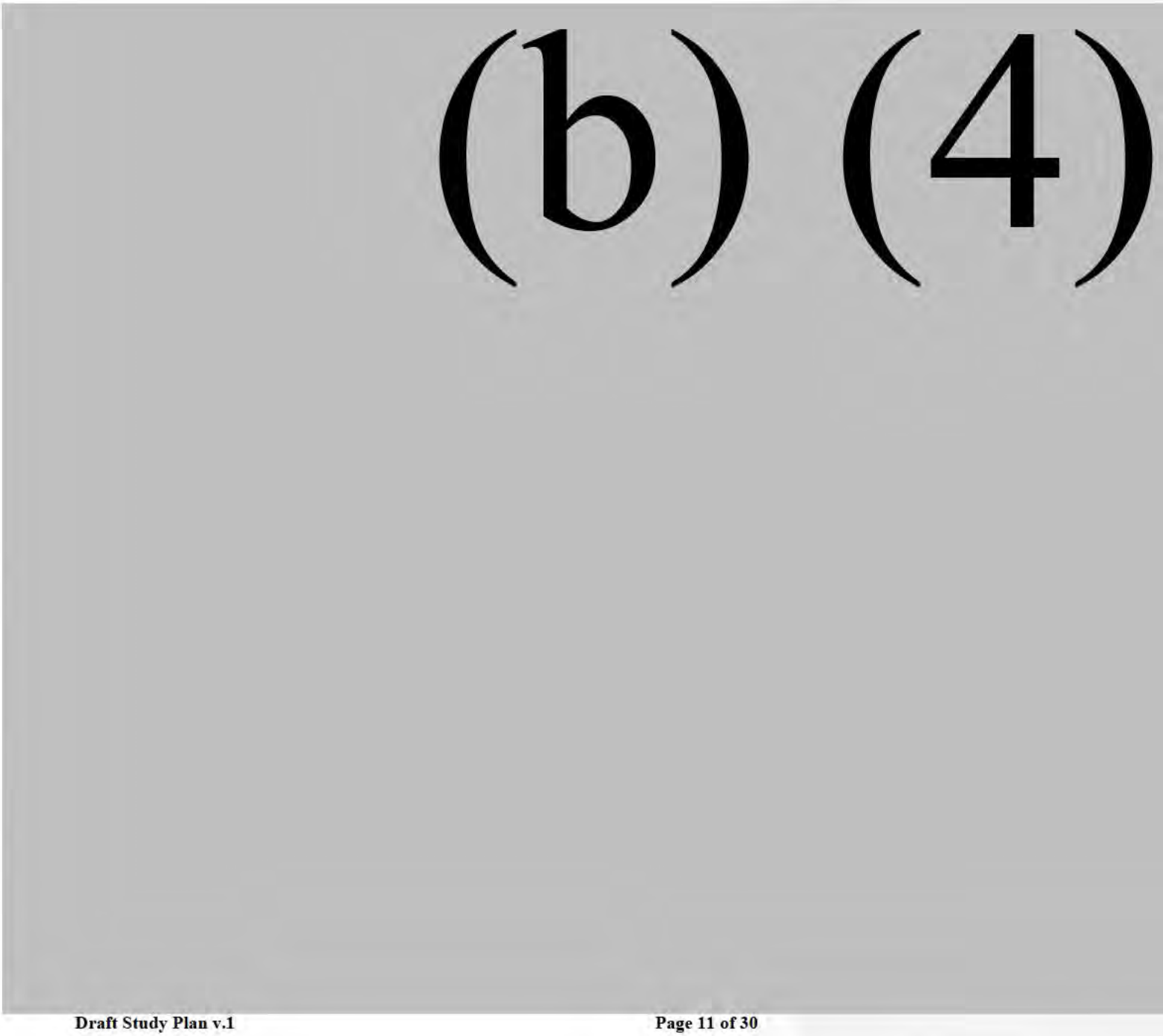
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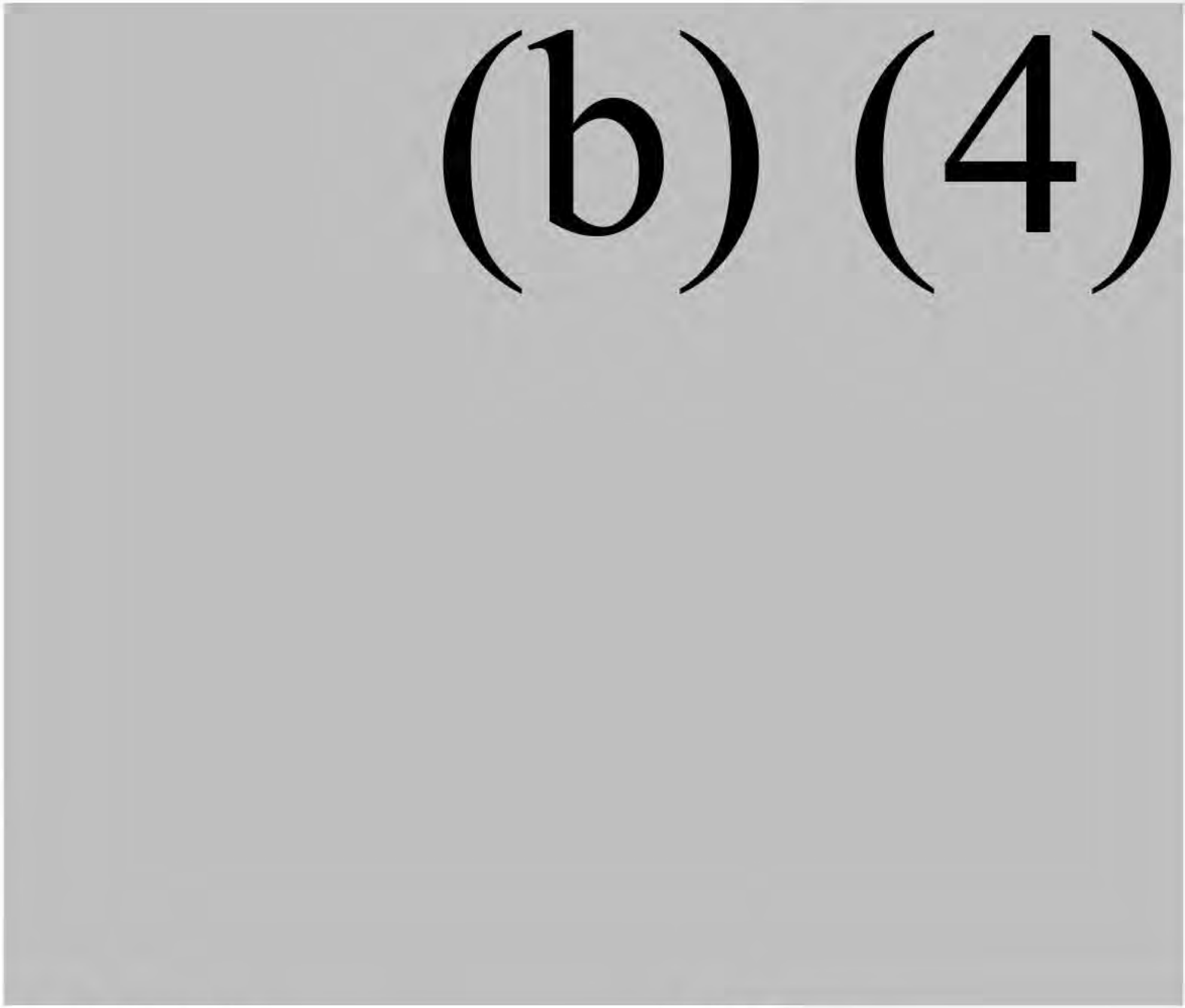
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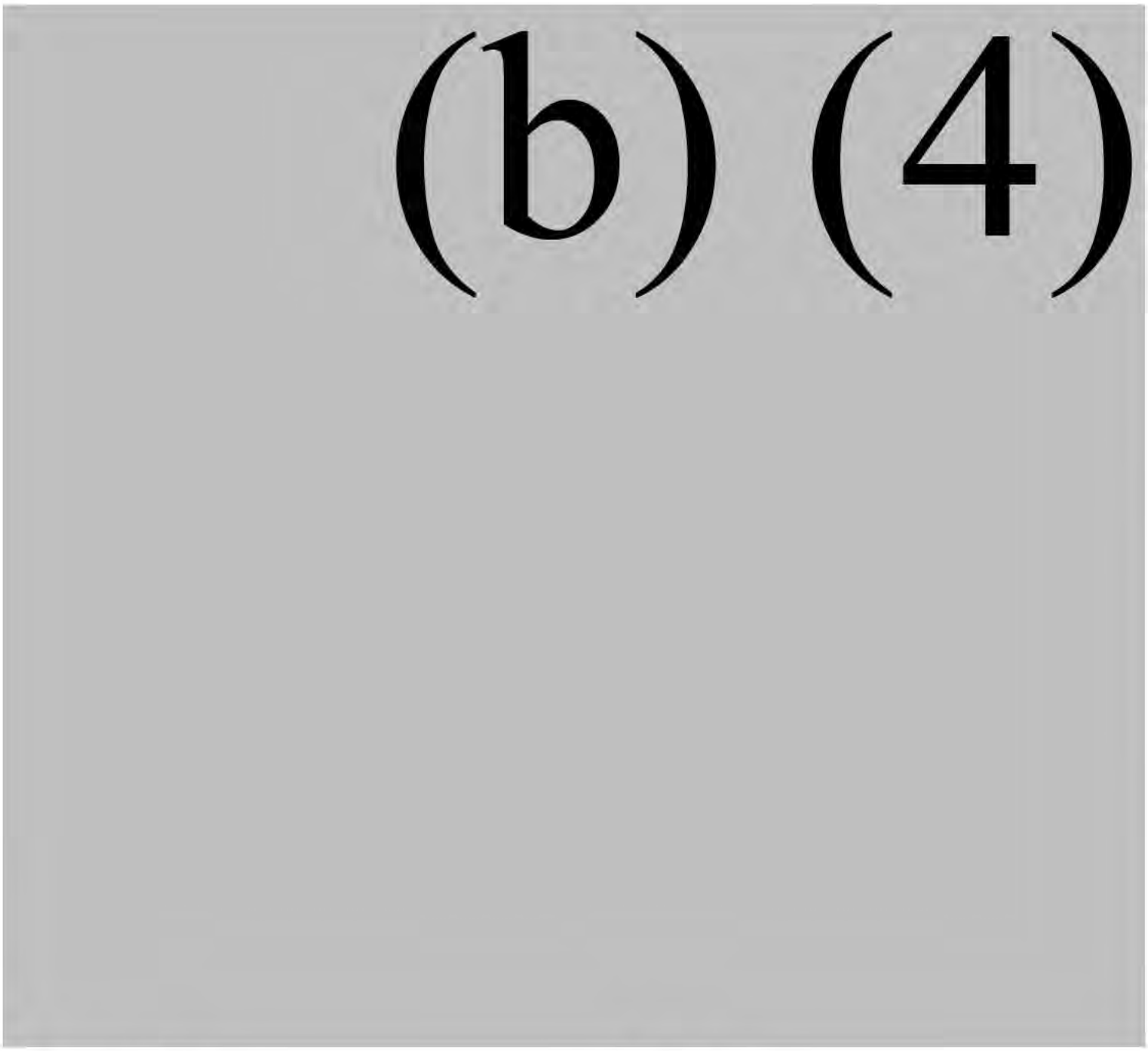
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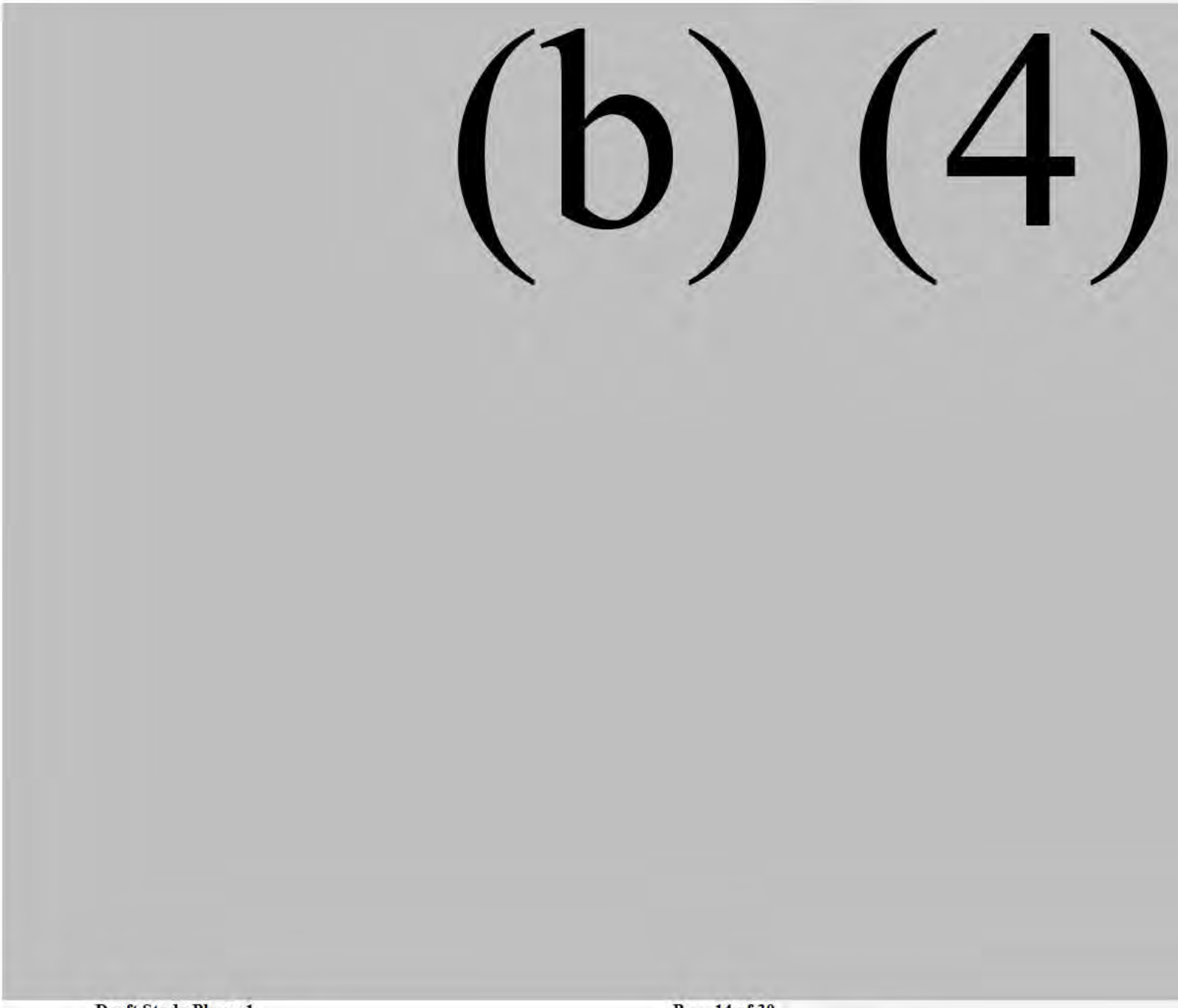
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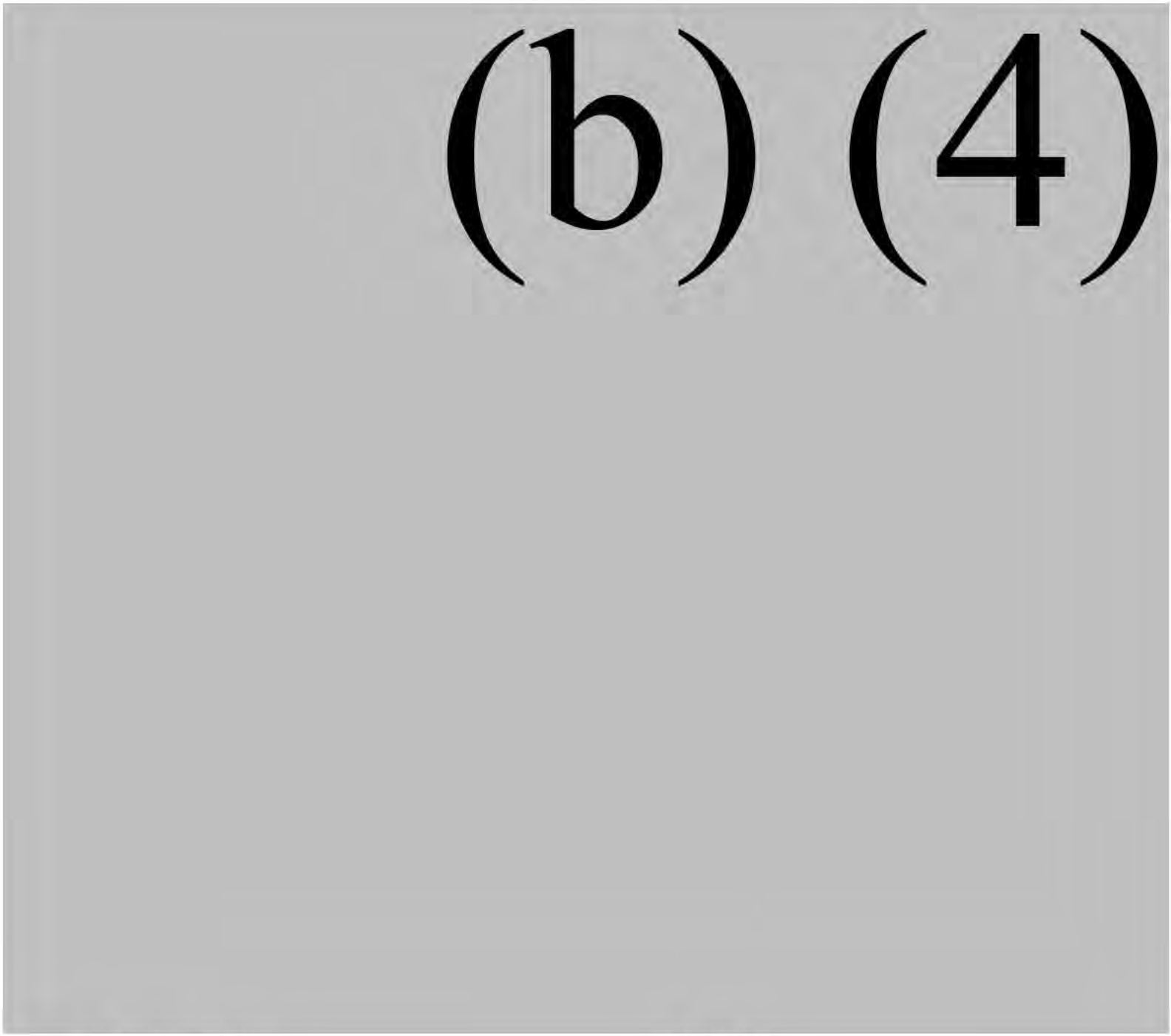
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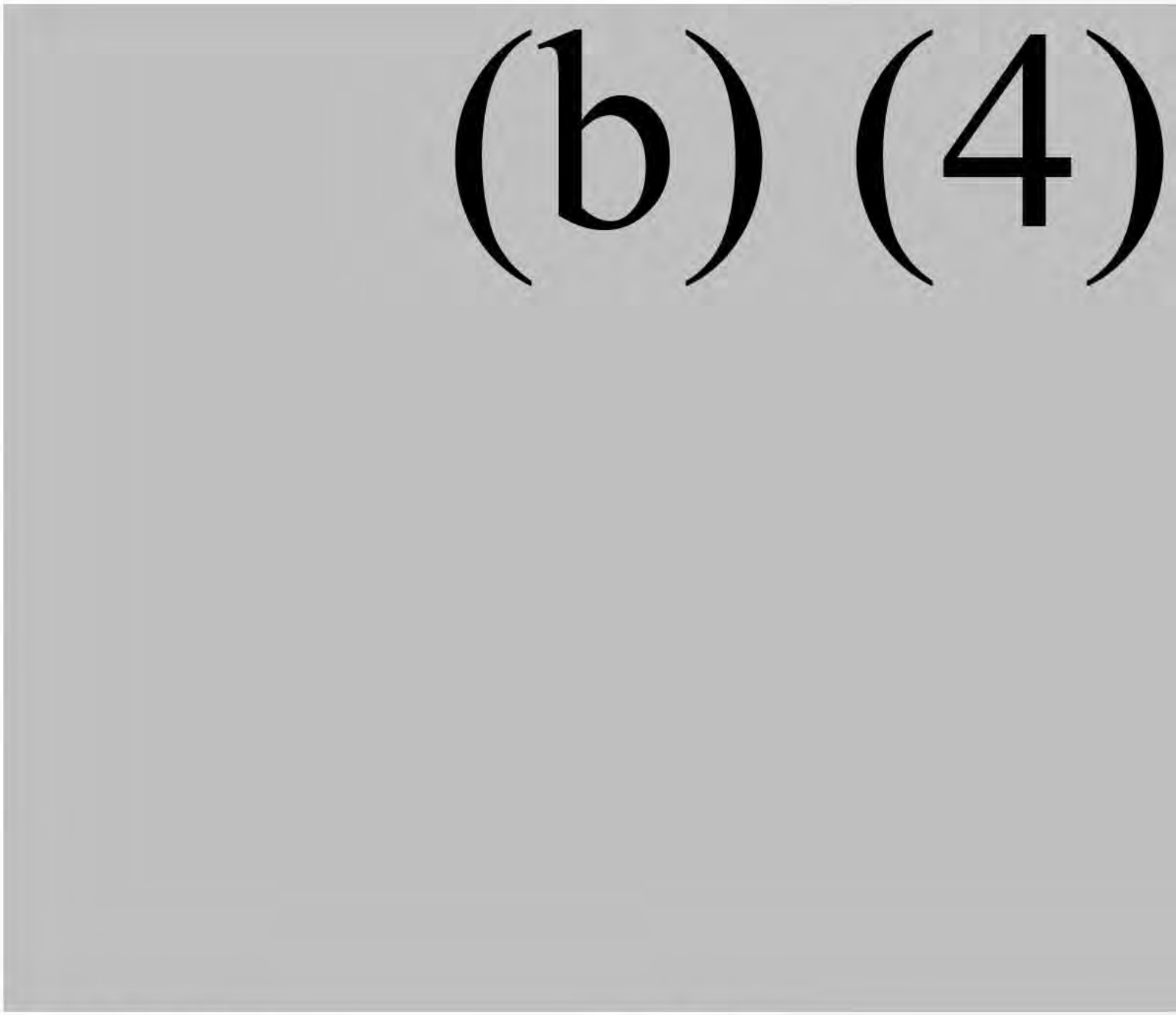
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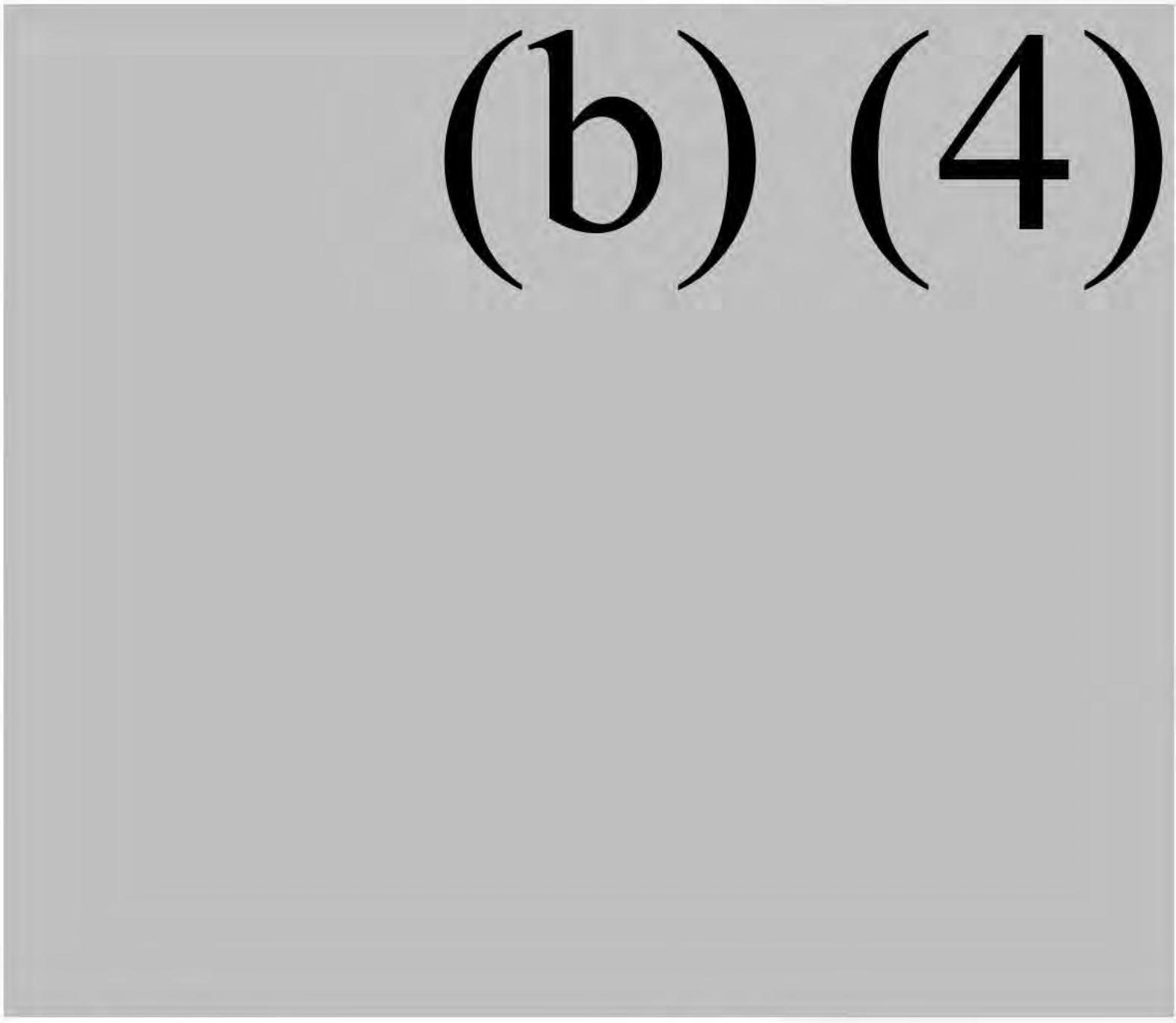
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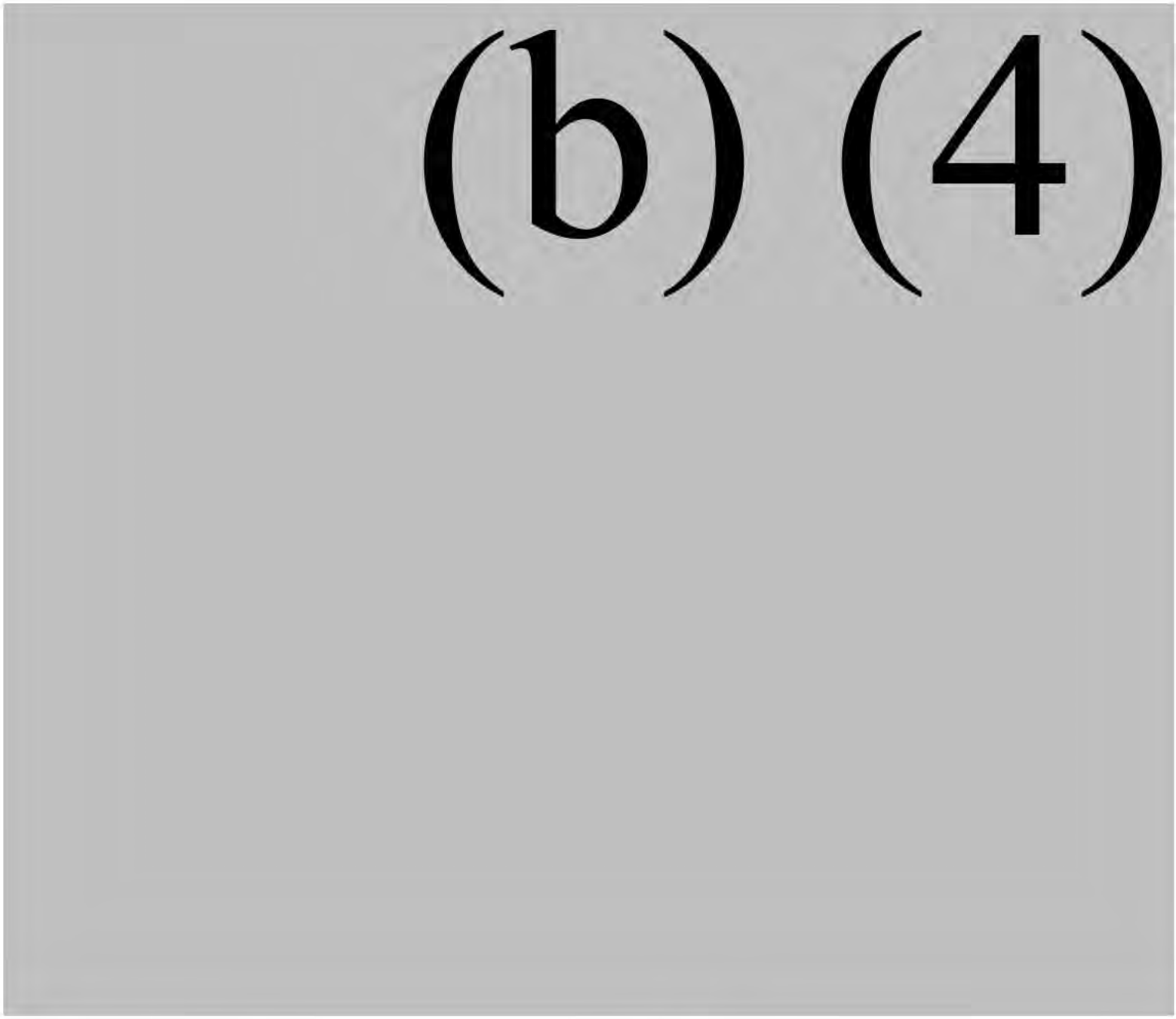
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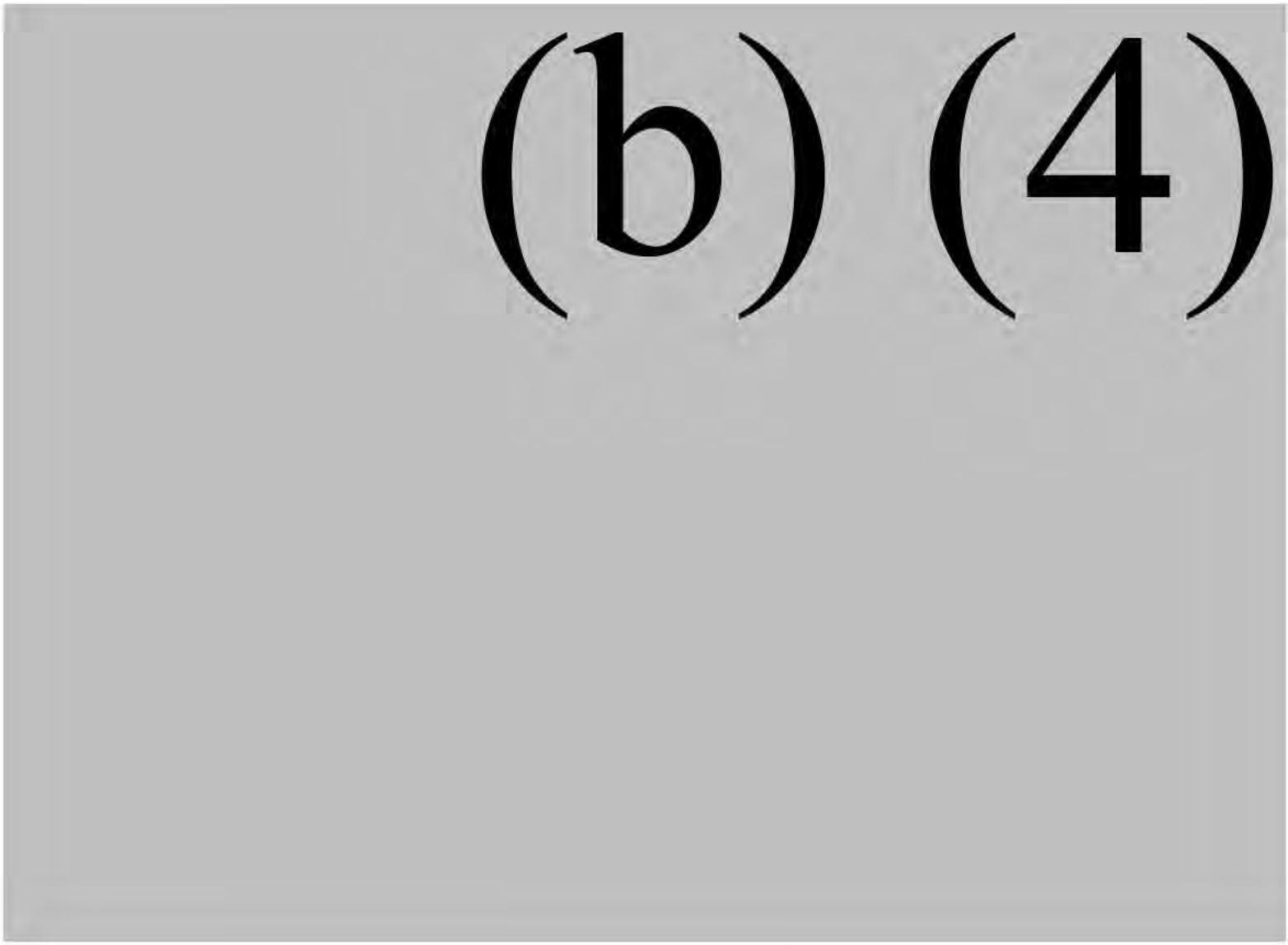
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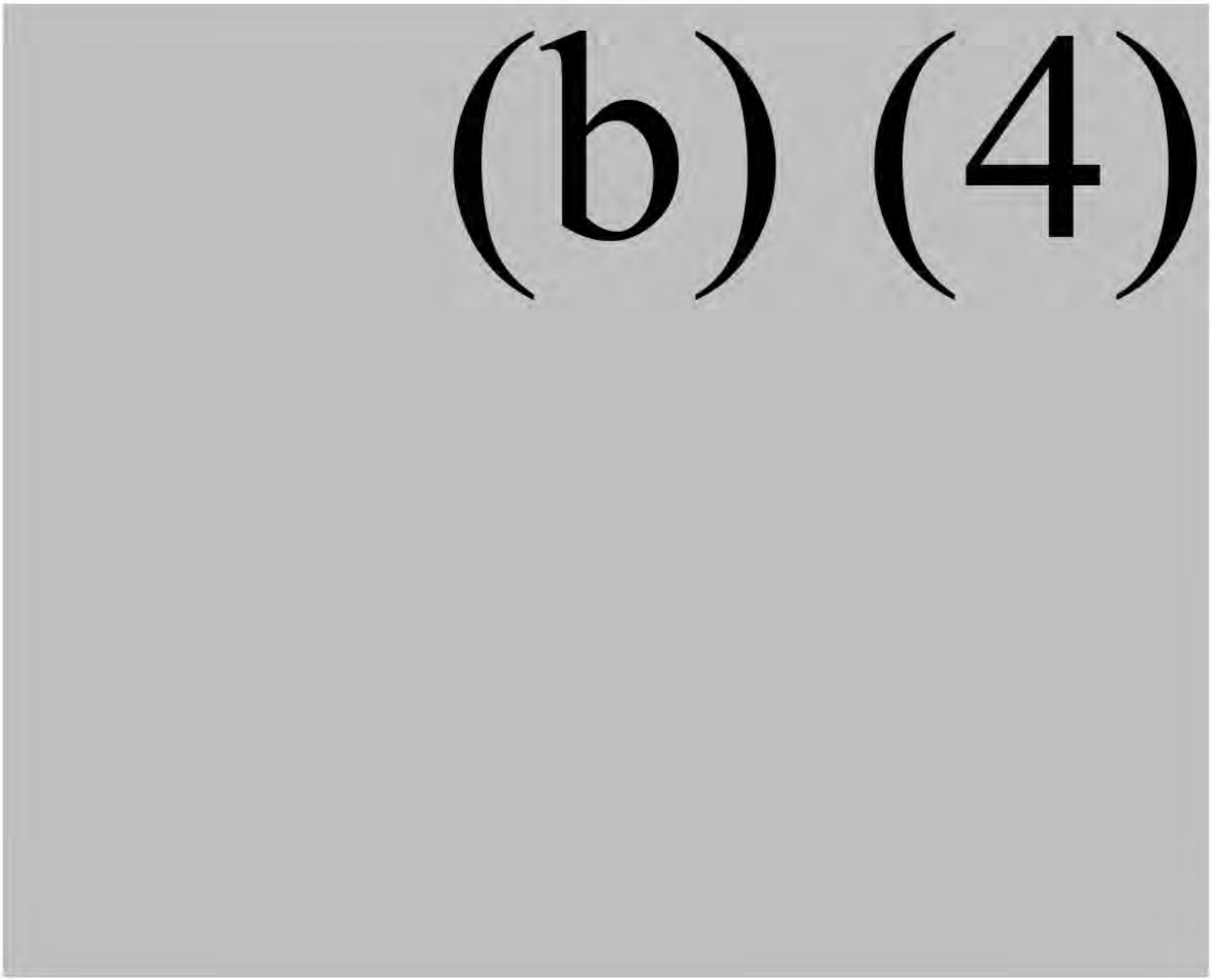
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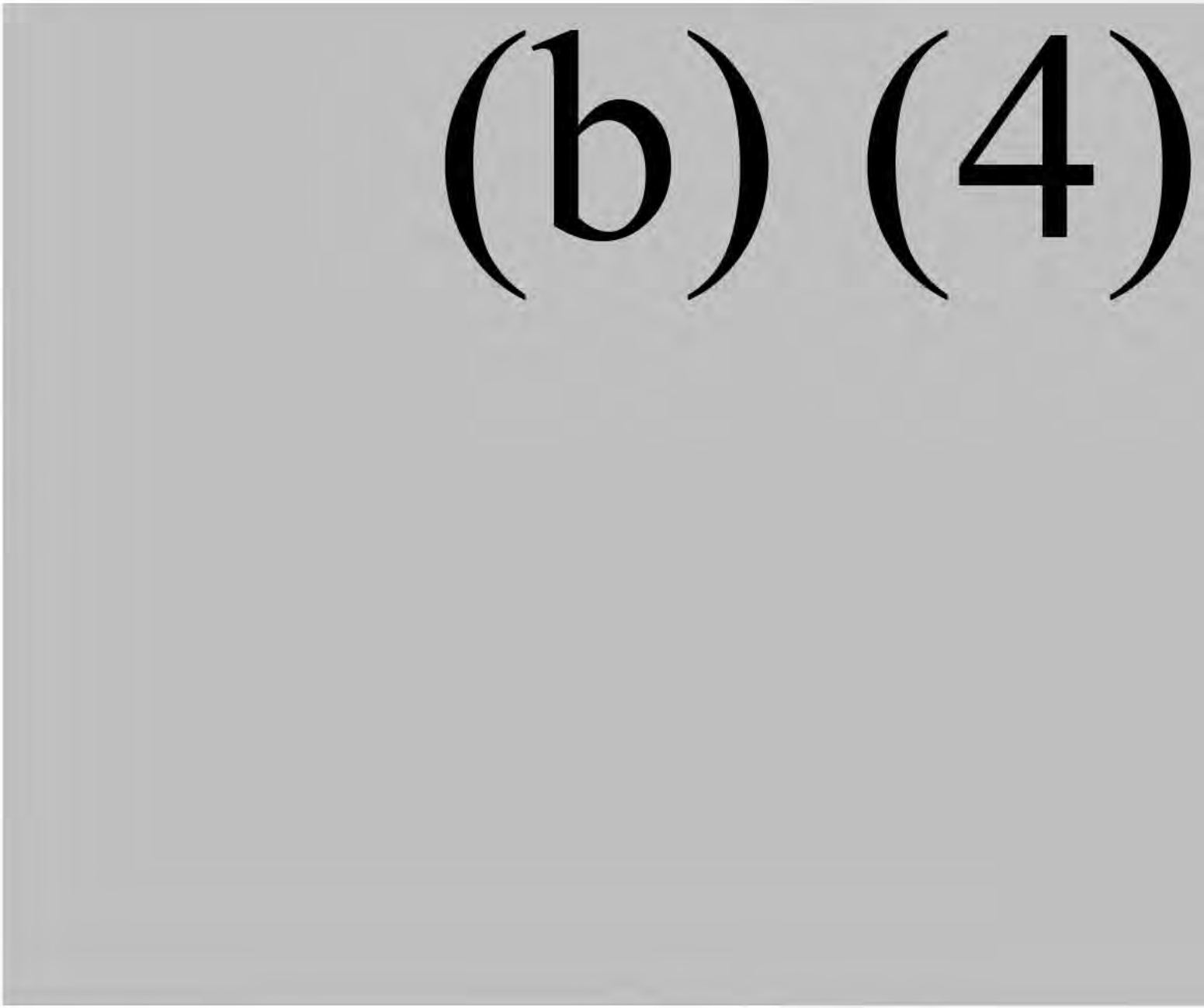
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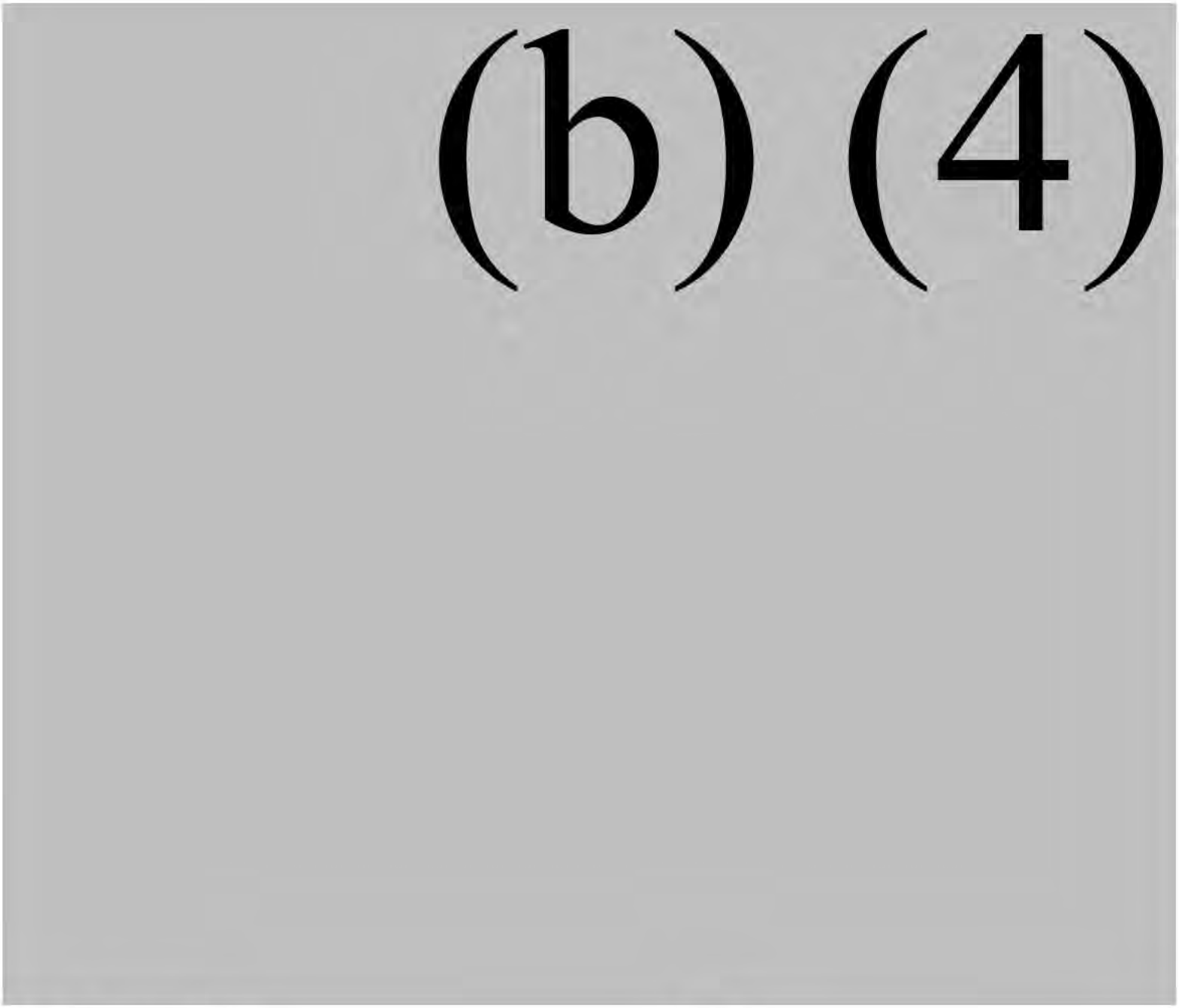
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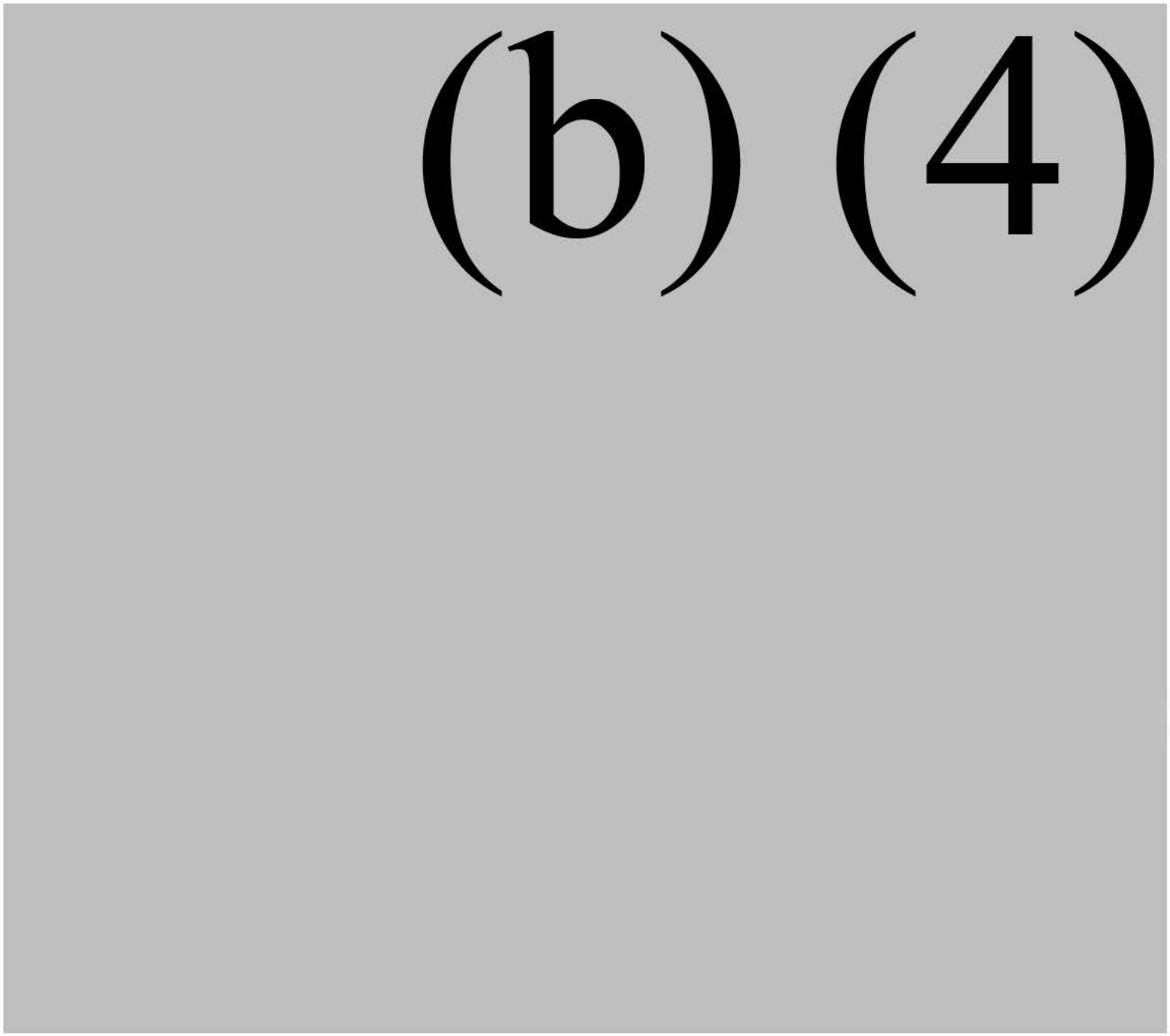
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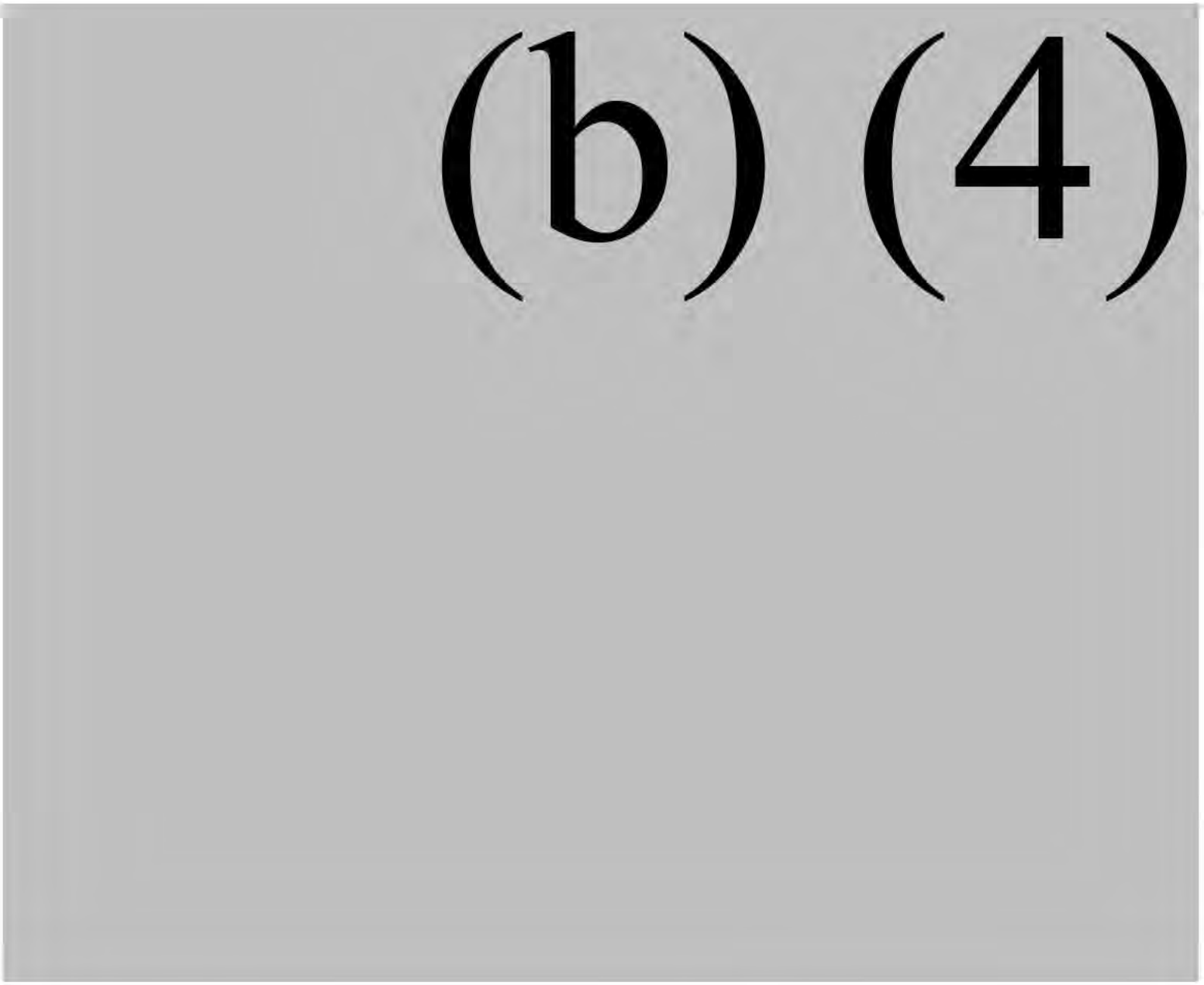
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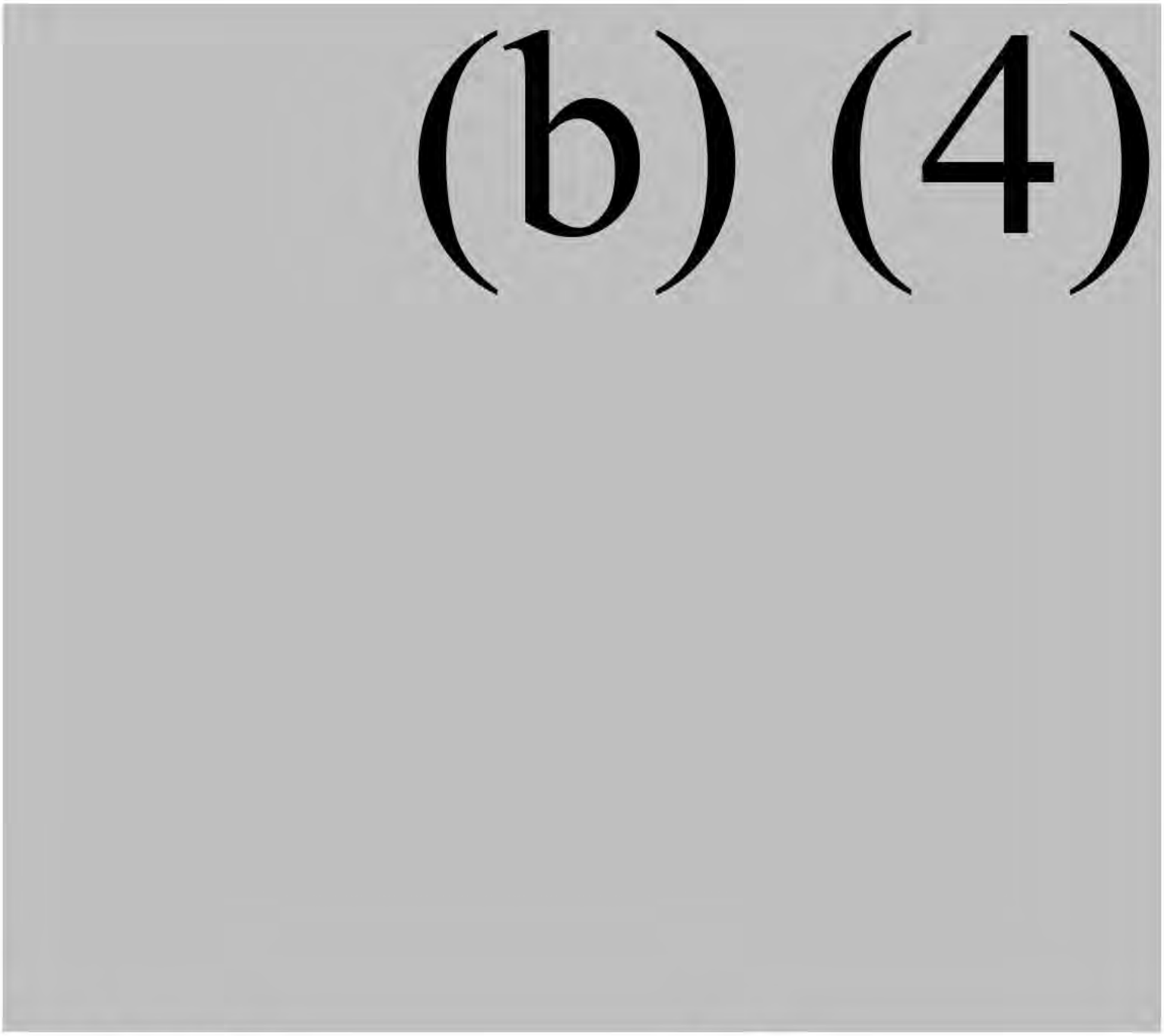
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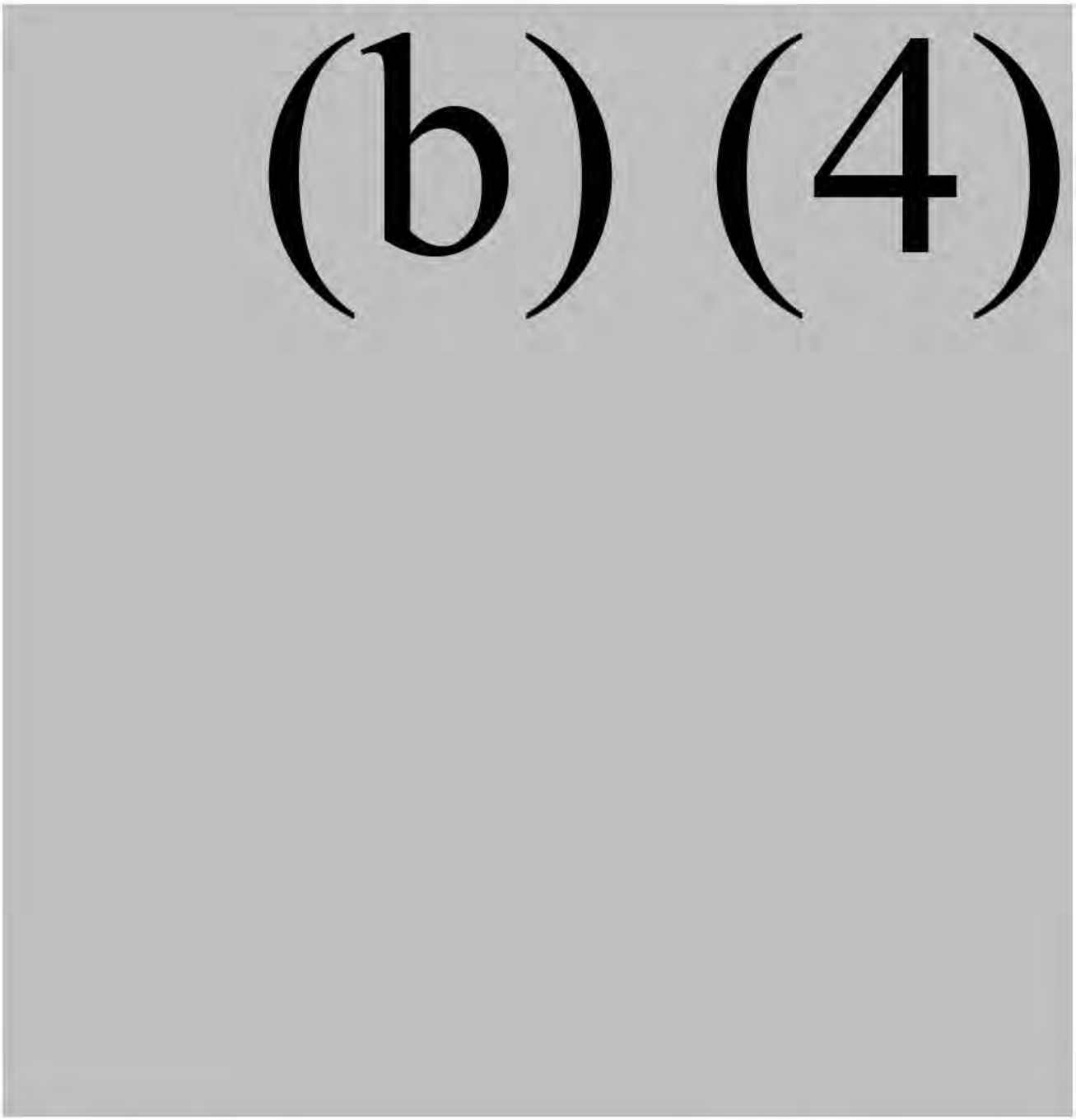
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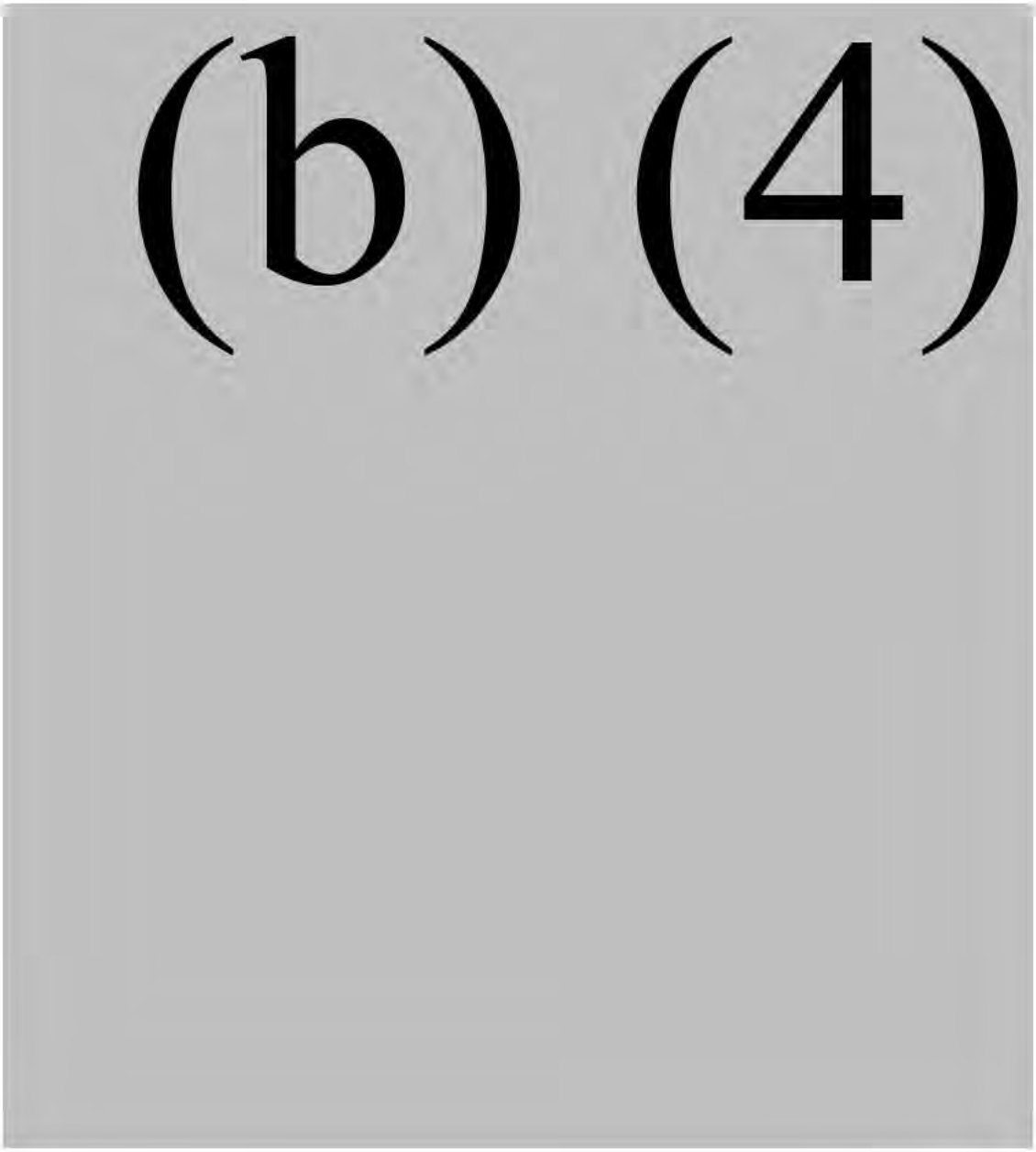
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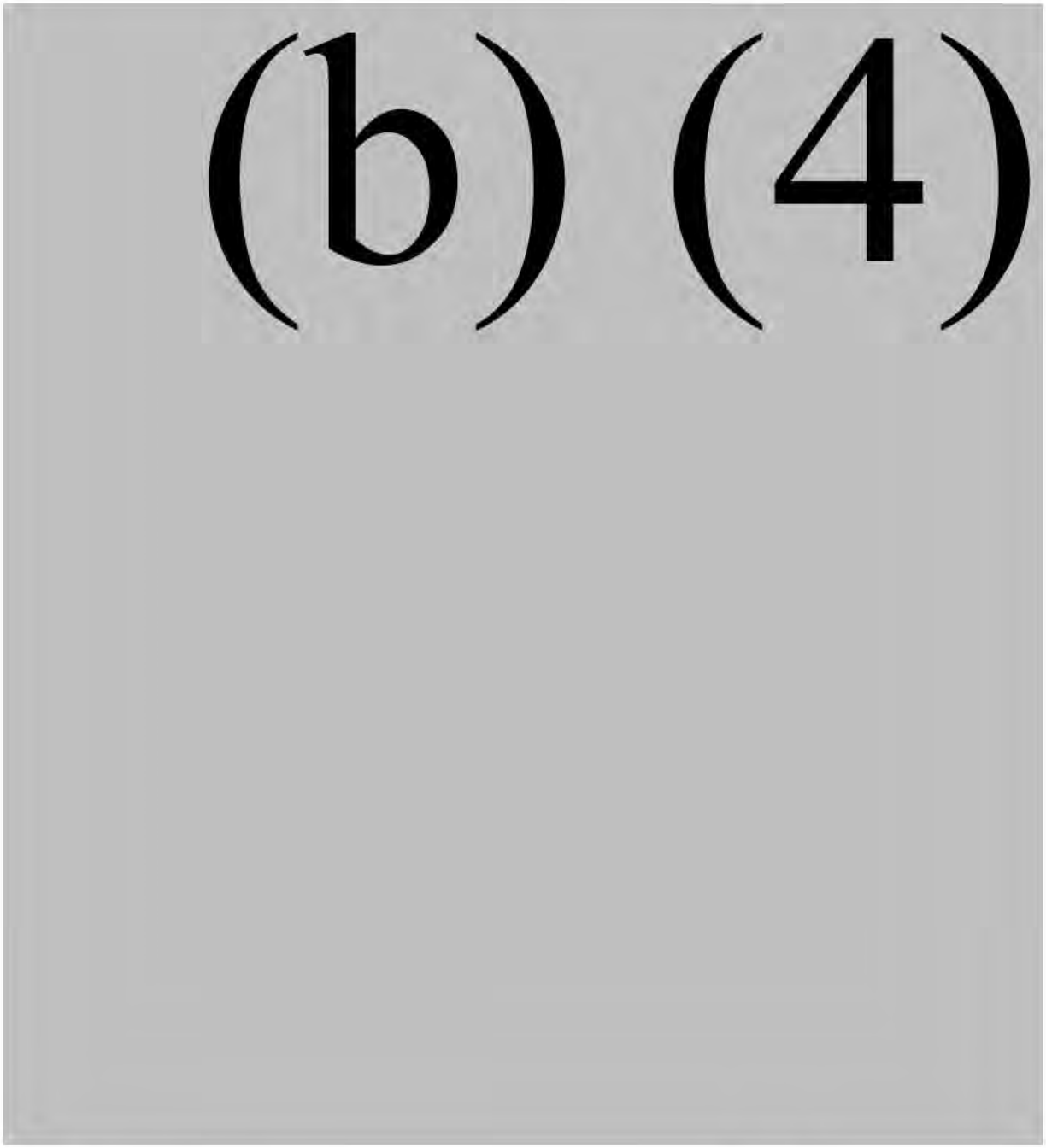
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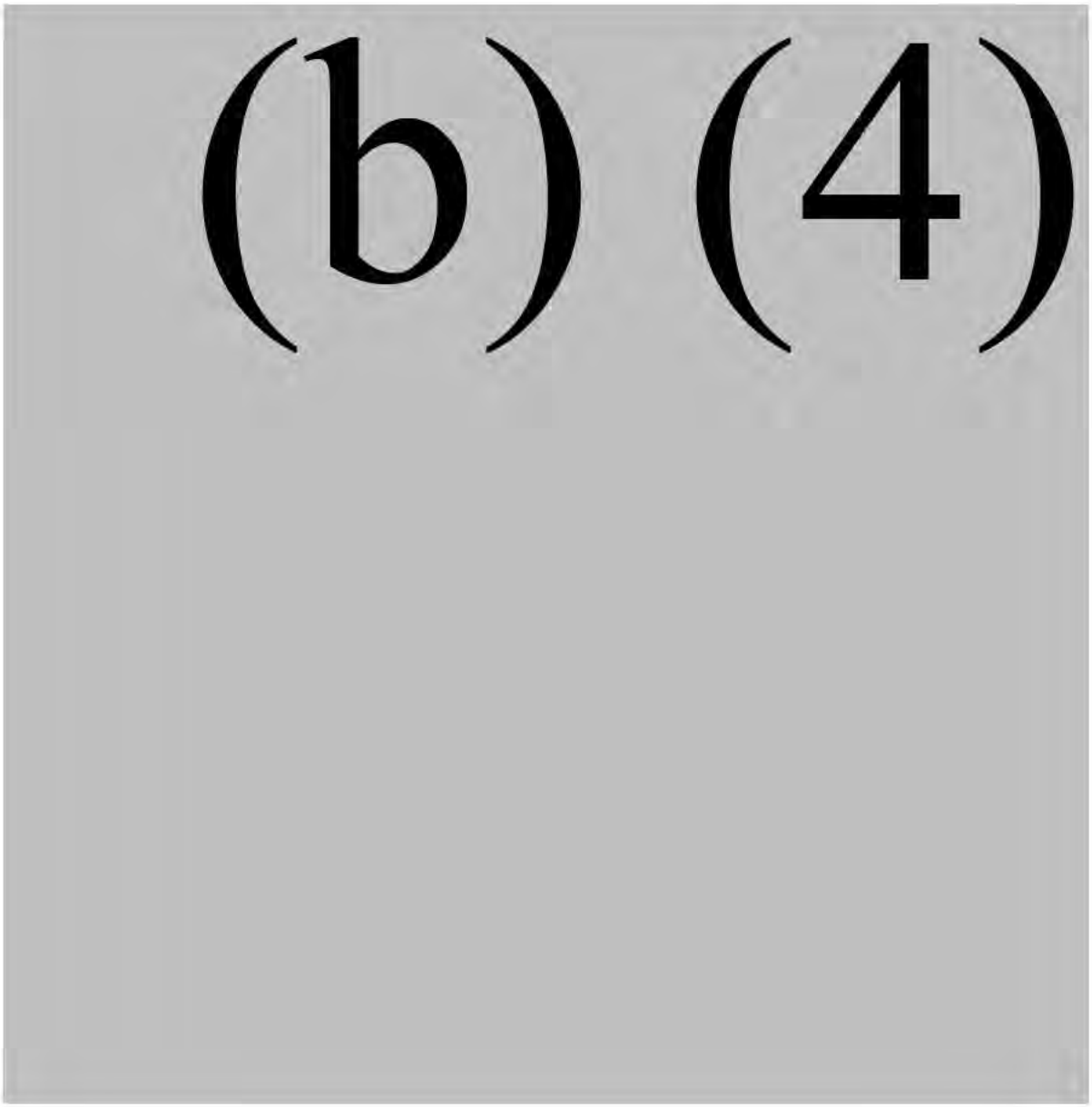
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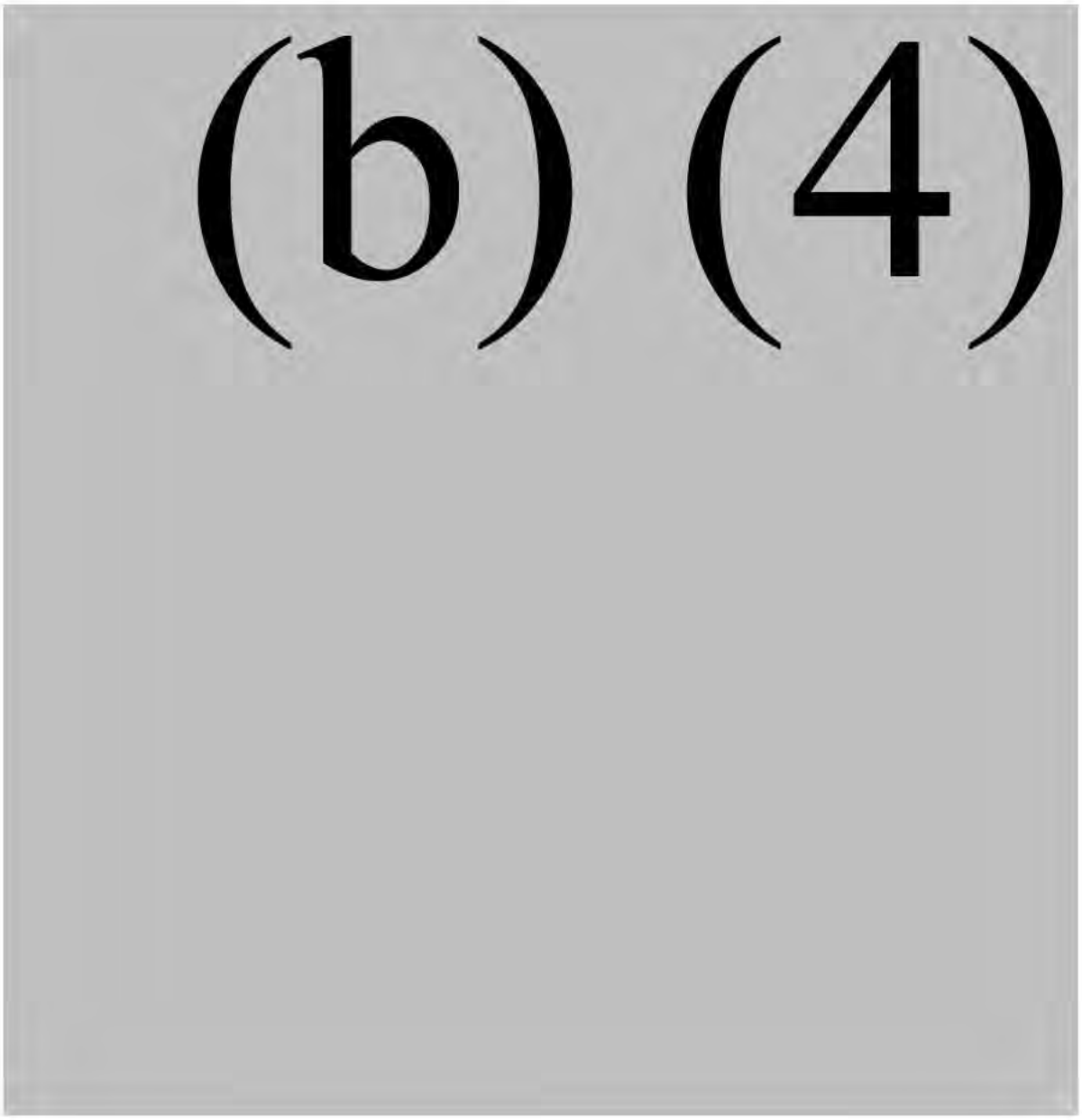
(b) (4)

(b) (4)

CONFIDENTIAL

FINAL STUDY PLAN

Algal Oil containing EPA and DHA (AOCED): A Gestation, Lactation and Growth Dietary Safety Study in Dogs/Puppies

Test Facility:

(b) (4)

(b) (4)

Sponsor:
DSM Nutritional Products AG
6480 Dobbin Road
Columbia, MD
USA 21045

Issue Date: July 5, 2017

GENERAL INFORMATION

Study Director	(b) (4), (b) (6)
Supporting Scientist	
Study Monitor and Sponsor's Representative	Irina Dahms, Ph.D., DABT Principal Scientist, Toxicology and Kinetics DSM Nutritional Products Phone: (443) 542-2388 E-mail: Irina.dahms@dsm.com

(b) (4) **Participating Managers**

Senior Director, Toxicology	(b) (4), (b) (6)
Director, Toxicology (Test Facility Management)	
Senior Director, Scientific Operations and Veterinary Services	
Associate Director, Toxicology	
Vice President, Operations	

(b) (4)

Director, Pathology Services	(b) (4), (b) (6)
Head, Veterinary Services	
Senior Director, Global Laboratory Operations	
Head, Statistics and Report Production	

(b) (4) **Participating Staff**

Statistics	(b) (4), (b) (6) Statistician

External Contributing Scientists

Consulting Toxicology Expert	(b) (4), (b) (6)
Clinical Pathology Data Interpretation	

Principal Investigators (Test Sites – Sponsor Designate)

Diet analysis

(b) (4)
DNP Dartmouth Canada
101 Research Drive,
Dartmouth, Nova Scotia
Canada B2Y 2J1
Phone: 902-480-3161
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Bioanalysis

(b) (4), (b) (6)

Interpretation of Bioanalysis Data

(b) (4), (b) (6)
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Tel: +41-61-815-87-71
E-mail: (b) (4), (b) (6)@dsm.com

Principal Investigators (Test Sites – Test Facility Designate)

Pretreatment and Prior to shipment Study Phase

(b) (4), (b) (6)

TARGETED STUDY SCHEDULE

Start of feeding control diet*:	Week of July 10, 2017
Experimental start (1st mating start*):	July 17, 2017
Start of dosing (1st mating*):	July 17, 2017
Animal Arrival**:	August 21, 2017
Littering start (GD*** 56):	Week of September 11, 2017
Weaning start (PPD*** 56):	Week of November 6, 2017
Last observation on F_0 females and F_1 animals not selected (up to 2 months post-partum):	Week of November 6, 2017
Last observation F_1 animals (34 weeks old):	Week of May 11, 2018
Experimental completion:	July 30, 2018
Draft report:	Week of August 13, 2018

* Performed at (b) (4).
** Confirmed 4- to 5-week pregnant (GD 29 to 35)
*** GD = Gestation Day, PPD = Post-Partum Day

The actual dates for start of treatment (experimental start), last observation and experimental completion will be presented in the study report.

COMPLIANCE STATEMENT

This study will be conducted according to the Standard Operating Procedures of (b) (4) The study will not comply with Good Laboratory Practice regulations.

OBJECTIVE

The objective of this study is to evaluate safety and bioavailability of Algal Oil containing EPA and DHA (AOCED) as a source of EPA and DHA when administered via diet to Beagle dogs starting at mating, throughout gestation, lactation, and growth (up to 34 weeks old).

EXPERIMENTAL DESIGN

The test and reference items will be administered as a diet as shown below:

Table 1: Study Design

Treatment Group [b]	Dosage Level (X of targeted dose)	Target Dosage Level (% of AOCED in the diet on DM basis)	Actual DHA+EPA content (% in the diet as it is)	DHA+EPA content (% in the diet on DM basis) ***	Number of Animals		
					F_0 Generation (dams)@	F_1 Generation (puppies) [a]	
					F	M(Spare)	F(Spare)
1. Control diet*	0	0	0.11%	0.12%	5	4(1)	4(1)
2. AOCED	½ X	0.75%	0.41%**	0.44%	5	4(1)	4(1)
3. AOCED	1X	1.5%	0.77% **	0.83%	5	4(1)	4(1)
4. AOCED	2X	3.0%	1.55%**	1.69%	5	4(1)	4(1)

* Group 1 animals will receive the control diet, which will be formulated to meet or exceed dog AAFCO nutrient profiles for growth and reproduction (0.05%). The DHA and EPA level (0.11%) is achieved by using the chicken by-product meal as one of the ingredients.

** In the diet offered to Groups 2 to 4 animals, the target DHA and EPA content will be the sum of DHA+EPA from AOCED (nominally 50% of Algal Oil is DHA+EPA) and from the chicken by-product meal (0.11%). Values presented as a sum of DHA and EPA (% Weight) per Certificate of Analysis.

*** Calculated based on dry matter basis (adjusted for moisture content).

[a] Two puppies per litter (1 male and 1 female), randomly selected, the spare will be randomly selected from any litter within each group.

[b] Since this study design include blinding to treatment groups, designations for individual animals will not be revealed during the conduct of the study and will only become available following the end of the data collection period and interpretation by the Study Director.

@ Six (6) females per group will be mated, as an attempt to have at least 5 females per group confirmed pregnant at GD 28. Only confirmed pregnant females (up to a maximum of 5/group, randomly selected) will be shipped to (b) (4).

M: male; F: female

Test Methods and/or Guidelines

This study was designed with reference to the following test methods and/or guidelines:

- CVM Guidance for Industry 56: Protocol Development Guideline for Clinical Effectiveness and Target Animal Safety Trials

- CVM Guidance 221: Recommendations for Preparation and submission of Animal Food additive petitions
- VICH GL43 (CVM GFI #185): Guidance for Industry. Target Animal Safety for Veterinary Pharmaceutical Products
- AAFCO Dog Food Gestation/Lacation and Growth Feeding Protocols

Justification for Dose Levels

Dose levels were selected by the Sponsor based on available marketing data. The recommended dose level (1X) was defined as the dose which provides the actual maximum dose of EPA and DHA currently available on the market worldwide. The survey of labels of dog food products was conducted by the DSM marketing team in December 2016. The high dose as a 2x multiple of the use dose was agreed upon with the CVM staff at the presubmission conference in June 2016. The ½ dose will provide information on dose-response relations of test item-related findings, if any.

Reason for Choice of Route of Administration

The dietary route is the intended route of administration of the test item in dogs.

Justification for Selection of the Test System

The dog (*Canis familiaris)* has been selected by the Sponsor to satisfy the regulatory requirements for safety testing in the selected species.

The current state of scientific knowledge and the applicable guidelines cited previously in this study plan do not provide acceptable alternatives, in vitro or otherwise, to the use of live animals to accomplish the purpose of this study. The development of knowledge necessary for the improvement of the health and well-being of other animals requires in vivo experimentation with a wide variety of animal species. Whole animals are essential in research and testing because they best reflect the dynamic interactions between the various cells, tissues, and organs comprising the dog body.

The dog was selected for use in this study by the Sponsor since the dog is the target animal for the investigated feed ingredient.

Justification for Numbers of Animals Selected

The number of animals used on the study is considered the minimum required to achieve the study objectives, based on regulatory requirements, statistical power and/or availability of historical data and are within IACUC and CVM approved guidelines. The Sponsor, by his or her signature, attests that the activities specified in this study plan do not unnecessarily duplicate any previous experiment.

TEST ITEM INFORMATION

Test Item Action Feed ingredient and a source of omega-3 fatty acids (EPA and DHA)

Characterization of Test Item, Test Item Diets and Control Diet

Test Item

Identity:	Algal Oil containing EPA and DHA
Alternative name:	AOCED
Batch/Lot No.:	(b) (4)
Correction Factor:	None
Storage conditions:	Room temperature
Expiry Date:	To be documented via study plan amendment

High Dose Diet**

Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	3.0%
Actual DHA+EPA content in diet (as it is):	1.55%
DHA+EPA content (on a dry matter basis):	1.69%
Storage conditions:	Room temperature
Best before:	October 14, 2018

Mid Dose Diet**

Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	1.5%
Actual DHA+EPA content in diet (as it is):	0.77%
DHA+EPA content (on a dry matter basis):	0.83%
Storage conditions:	Room temperature
Best Before:	October 14, 2018

Low Dose Diet**

Batch/Lot No.*:	Not applicable
Target AOCED content in diet (on a dry matter basis):	0.75%
Actual DHA+EPA content in diet (as it is):	0.41%
DHA+EPA content (on a dry matter basis):	0.44%
Storage conditions:	Room temperature
Best Before:	October 14, 2018

Control Diet**

Batch/Lot No.*:	Not applicable
Actual DHA+EPA content (as it is):	0.11%
Storage conditions:	Room temperature
Best Before:	October 14, 2018

*The diets were produced once for the entire study duration; therefore, lot numbers were not assigned.
**The diet identity and coding are not presented in this study plan in order to preserve blinding. A separate study document, with access restricted to unblinded personel, will be issued to document it.

Documentation characterizing AOCED, the test diets and the reference diet (control) will be supplied by the Sponsor for inclusion in the study report.

Upon receipt at (b) (4), diets will be stored in a temperature controlled room (humidity not controlled/monitored), separated from any other diets.

Upon receipt at (b) (4) diets will be stored in a room where other diets are stored. The room will only be controlled for temperature, but both the temperature and humidity will be monitored (daily).

Preparation of Dietary Admixtures

Extruded dry diets (one each for control, low, mid, and high concentrations of AOCED) will be provided by the Sponsor as ready-to-use.

The control diet will fulfill the 2016 AAFCO Dog Food Nutrient Profiles, which include recommendations for inclusion of EPA+DHA for puppies.

Stability of Test Item

Documentation of AOCED stability over the period of the study will be provided by the Sponsor.

Analysis of Diets

Representative samples (approximately 500 g, in duplicate) of each manufactured batch of each formulation will be taken from one bag used on Day 1 (at (b) (4)), from the first day of dosing at (b) (4) (day of animal arrival), at two months intervals throughout the study, and at the end of treatment. If a batch is used for less or equal than two months, then samples will be taken at the beginning and at the end of the use period.

Additional samples may be collected and/or analyzed as necessary at the request of the Study Director (documented via study plan amendment).

The samples will be kept at room temperature.

(b) (4)

One set of the duplicate samples will be shipped at room temperature to the Sponsor-designated laboratory, for analysis:

(b) (4), (b) (6)
Analytics Laboratory
DNP Dartmouth Canada
101 Research Drive,
Dartmouth, Nova Scotia
Canada B2Y 2J1
Phone: 902-480-3161
E-mail: (b) (4), (b) (6)@dsm.com

Following confirmation of safe and intact receipt of the first set of samples, the second set of samples may be shipped at room temperature to the Sponsor-designated laboratory, if required. If not required for analysis, the second set of samples will be kept at (b) (4) pending discard. The second set of samples collected at (b) (4) if not required for analysis, will be shipped to (b) (4) where it will be kept pending discard.

The analysis will be performed by the analytical laboratory to verify the DHA and EPA contents (DSM Nutritional Products (b) (4) and PV values (CDR FoodLabFat Analyzer for Measuring Peroxide Value – equivalent to AOCS Cd 8-53 reapproved 1997) in all diets. The acceptance criteria for the formulation will be ±15% of nominal.

Any analytical samples not employed in the primary analysis or required following completion of the primary analysis will be discarded prior to issuance of the final report (but after finalization of the Analysis Report).

Archive Sampling and Disposition of Diets

An adequate sample (minimum of 1 g) of each lot of each diet will be collected (at (b) (4)) and stored in the archives of (b) (4) under the same storage conditions used during the study.

After completion of the study, any sealed bags of diet remaining at (b) (4) will be destroyed (incinerated), or will be returned to the Sponsor prior to finalization. Similarly, any individual amount of food remaining daily (at (b) (4) (b) (4) will be retained for incineration at intervals or at completion of the study.

Any diets remaining at (b) (4) at shipment of animals will be discarded.

Administration of Diets

As the Sponsor will provide the diets already coded, each animal's actual treatment designation will be unknown to staff performing dosing or data collection.

As animals will be housed in different rooms (at (b) (4) due to the space restrictions), treatment will be done in a separate designated room. Treatment of the animals will be by each housing room (applicable to (b) (4) only), by ascending animal number (see Animal Assignment and Blinding Procedure).

At (b) (4), animals will be housed in separate pens from animals not assigned to the study, starting approximately 1 to 2 weeks (3-14 days) prior to Day 1, to receive the reference/control diet.

F_0 (at (b) (4)): During the acclimation/pre-treatment period, the females will receive (b) (4) standard diet for breeders up until approximately 1 to 2 weeks prior to Day 1 (3-14 days) when they will receive the reference/control diet (approximately 400 g of food per day). Daily oral dietary administration to dams (approximately 600 g of food per day) will start on the day of the first successful mating* and will continue until shipment to the Test Facility. If appetence issues are observed, warm water can be added to the diet.

** Females will be mated 2 or 3 times, with one day of rest between each mating. Successful mating will be described as observation of the tie. Males used for mating will be proven breeders of at least 12 months of age and confirmed healthy (health record of both sires and dams will be provided to the Study Director – only the health record of dams will be reported, health records of sires will be retained on file).*

F_0 (at (b) (4): Daily oral dietary administration to dams will continue immediately after arrival and throughout gestation and lactation (approximately 15 weeks in total). Dams will receive approximately 600 g of food per day from arrival to parturition, and 900 g per day from parturition until weaning. More food can be added during the day if needed, but additional quantities will be measured/recorded. If appetence issues are observed, 100 mL of warm reverse osmosis water can be added to the diet.

F_1: Starting at 5 weeks of age and until weaning, puppies will be provided with a feeding pan. During that period, the daily food intake will be calculated for the dam plus its litter (i.e.: dam's bowl, plus feeding pan) since the dam will also have access to the feeding pan (approximately 300 g).
As of weaning, puppies selected for the study will continue on their mothers' respective diets (approximately 400 g per day/dog for a 6-8 hours daily feeding period) for the additional 6 months until they reach 34 weeks of age. Puppies will remain pair-housed for feeding during the first two weeks post-weaning to confirm ability to properly thrive, and will then be individually housed for feeding for the remainder of the study. If appetence issues are observed, 100 mL of warm reverse osmosis water can be added to the diet. Similarly,

puppies not selected to continue on the study will continue on their mothers' respective diets until release from the study (approximately 2 weeks after weaning).

The remaining puppies will be released from the study once ability to thrive of all randomly selected puppies is confirmed (transferred to (b) (4) dog colony where they will receive the standard commercially available diet).

TEST SYSTEM

Species:	Dog (*Canis familiaris*)
Strain:	Beagle
Source:	(b) (4)
Total animal No. on study*:	24 females
Target age range:	1.5 to 3 years old at start of treatment (assumed GD 0)
Target body weight range:	9 to 12 kg at start of treatment (assumed GD 0)

* Six (6) females per group will be mated, as an attempt to have at least 5 females per group confirmed pregnant at GD 28. Only confirmed pregnant females (up to a maximum of 5/group, randomly selected) will be shipped to (b) (4) (confirmed 4- to 5-week pregnant (GD 29 to 35).

The actual age and body weight ranges at the start of treatment will be presented in the study report. Bitches must be in at least their second heat period when they are mated and at least one year of age.

Health Status

Animals will be vaccinated and dewormed a (b) (4) standard program) prior to dosing start, and free of infectious diseases which could complicate the interpretation of the study results.

Following arrival, all animals will be subject to a health assessment (including weight measurement). The evaluation will be performed in accordance with the standard operating procedures by technical staff. The results of the evaluations (including body weight) will be reviewed by the Clinical Veterinarian to confirm that animals are healthy and were not affected by transportation.

Puppies will be vaccinated, dewormed and examined at (b) (4) as per SOPs (data retained on file).

Identification

Each dam will arrive from the supplier individually identified by means of a tattoo. Each dam will be assigned an animal number to be used (as described in the following table and in the Animal Assignment and Blinding Procedure section).

(b) (4)

Group	Animal Numbers*
	Females
1	1501, 1502, 1503, 1504, 1505, 1506
2	2501, 2502, 2503, 2504, 2505, 2506
3	3501, 3502, 3503, 3504, 3505, 3506
4	4501, 4502, 4503, 4504, 4505, 4506

* Number of animals at assignment. The identification of animals received at (b) (4) will vary since (b) (4) will only ship confirmed pregnant females (up to a maximum of 5/group).

The first number corresponds to the respective dose group while the second number identifies the gender of the animal (numbers 5 to 9 will be used for females). The third and fourth number identifies the animal's rank per gender within each group.

The puppies (F_1) will be identified as per relevant (b) (4) SOPs (i.e.: paper collar on PPD 0, then microchip from PPD 1).

For the second generation, the utilization of animal number with 3 numbers can be used. Animal identification will be interpreted using example below (animal 1501).

i.e.: First generation (F_0) = 1501 for Dam
Second generation (F_1) = 151 or 101 for Puppies

Housing

Animals will be assigned to cages/pens in order of ascending animal mating number (for blinding).

Dams (F_0) will be housed individually in pens (at (b) (4)) or in European cages (at (b) (4)) (dimensions: approximately 3 by 6 feet for pens and approximately 5 by 6 feet for European cages) equipped with an automatic watering system due to the nature of this study which does not permit group housing (i.e.: pregnant animals, dams with litter) and study requirements (i.e.: diet study).

Approximately 2 weeks prior to parturition, a nesting box will be offered to each dam. In addition, a litter pan will be given to the puppies from weaning until they reach approximately 3 to 4 months of age.

After weaning, puppies selected to continue on the study (F_1) will be pair housed in stainless steel dog cages (dimensions: approximately 3 by 3 feet) equipped with an automatic watering system, but will be separated during the 6-8 hour daily feeding period (separation starting at the third week post-weaning), to acquire individual food consumption data (i.e.: diet study). If possible, one male and one female will be housed together in each group to harmonize the food consumption values between cages during the first two weeks post-weaning. Throughout the weaning process and after weaning, dams will be individually housed in stainless steel dog cages (dimensions: approximately 3 by 3 feet) equipped with an automatic

watering system. Puppies not selected to continue on the study will remain in European cages until their release from the study (approximately 2 weeks after weaning).

All pens/cages will be clearly labeled with cage cards, indicating the study number, animal tattoo number, blinded animal assignment number, sex and replicate.

Due to space restrictions, at (b) (4), animals will be housed in different rooms, but all rooms will be of the same type, within the same building, and will have the same environmental controls, water sources, and daily routines for care and cleaning. Every room will include animals from each treatment group (designated by unblinded technical staff not involved in data collection), such that the rooms will be balanced for sex (applicable to puppies only), and treatment. Within each room (at (b) (4)), animals will be assigned to cages by ascending animal arrival number (*e.g.*, in clockwise placement around the room) in order to maintain the study blind. Approximately 1 week after weaning, selected pups will be consolidated into a single room.

At (b) (4), animals will be assigned to pens by ascending animal mating number (e.g., in rows of ascending blinded animal assignement number) in order to maintain the study blind.

Room Environment

At (b) (4) a commercial breeder facility, the temperature, humidity and air changes per hour are not controlled (set) but the temperature is monitored (once a day). The light dark cycle is set to 14 hours light/10 hours dark.

At (b) (4), the animal room environment will be set to maintain a relative humidity of 50 ± 20%; a light dark cycle of 12 hours light/12 hours dark, except during Study Plan-designated procedures; and 10 - 15 air changes per hour. The room temperature will be set to maintain 21 ± 3°C from arrival until approximately 2 weeks prior to parturition when it will be increased to maintain 24 ± 3°C until at least PPD 42. From PPD 43 (of the youngest litter) until the end of the study, the temperature will be returned to 21 ± 3°C.

At (b) (4), the temperature and relative humidity will be monitored continuously. Room environmental conditions will be reported to the Study Director, and excursions from the prescribed ranges will be included in the study report. Records will be kept on file at (b) (4).

Facility diagram, building orientation, ventilation and lighting procedures will be provided to CVM (as an Appendix to the report). The housing rooms at (b) (4) will measure 14 by 33 feet.

Diet/Water

Throughout the pretreatment period until approximately 1 week prior to mating, animals will receive (b) (4) ` standard diet. For approximately 1 to 2 weeks (3-14 day) prior to Day 1 (day of first successful mating), the females will receive the reference/control diet, except during designated procedures. During the treatment period, animals in each group will be provided access to the Sponsor-provided dietary mixtures (one specific for each group – See Administration of Diets section for details).

No treats will be provided to the dams. A very small amount of treats will be provided to the puppies as part of the animal enrichment program. The provision of the treats will be approved by the Study Director prior to being given.

Municipal tap water (which has been exposed to ultraviolet light and purified by reverse osmosis, at (b) (4) only) will be provided to the animals *ad libitum*, via automatic water system or via water bottles, if required. A bowl of water will also be placed in the cage until weaning. Periodic analyses of the municipal tap water (purified water) will be performed by a (b) (4) designated facility and the results are retained on file at (b) (4) . Identified contaminants, if any, in the water will be assessed for concentrations that could interfere with the objectives of the study. Similarly, at (b) (4) periodic analyses of the municipal tap water will be performed and the results will be provided to the Study Director (retained on file).

Acclimation/Socialization

While at the breeding facility, animals will be socialized per (b) (4) ` relevant standard procedures (retained at (b) (4) to ensure they are relaxed and calm when handled by caretakers in a laboratory setting.

There will be no acclimation period upon arrival at the Test Facility, as daily oral dietary administration started at (b) (4) is to be continued immediately after arrival. Nevertheless, the activities in the animal housing room(s) will be minimized for the 7 days following arrival to accustom the animals to the laboratory environment.

Dams will be socialized by the key technicians (no more than 4) at least twice weekly throughout the gestation period starting 7 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. Only the key technicians are allowed to take the puppies out of the cage.

Secondary technicians (no more than 6) will socialize with the dams at least once weekly during the gestation period starting 7 days following arrival at the Test Facility and will stop as soon as signs of parturition are observed. The secondary technicians are only allowed to manipulate the puppies if a key technician has taken them out of the cage first.

Puppies will also be socialized per SOP (submission technique).

Animal Assignment and Blinding Procedure

The animal assignment will be performed at (b) (4). The order of the animal number assignement was randomly determined. In order to preserve the blinding, the table describing the assignment of animals based on timing of mating confirmation will be maintained in a separate document, with access restricted to unblinded personel.

(b) (4) will test for pregnancy approximately 28 days after mating. If all 6 dams within a group are confirmed pregnant, 1 dam will be randomly selected using a dice and will be released from the study, so that a maximum of 5 pregnant dams per group will be shipped to (b) (4). The dams will be shipped to (b) (4) in one shipment.

One or two puppy/sex/litter will be randomly retained for the F_1 assessments (See Weaning section for details). Additional puppies/sex/litter may be selected if less than 4 litters/group are obtained.

During the in-life portion of the study, each animal's treatment designation will be unknown to the staff who will be blinded.

The animal cage cards will only display the study number, animal sex, the blinded animal identification numbers (i.e., mating number) and the animal tattoo number.

Blinding in the study will be applied to the identity of the test item or reference item (control) assigned to each experimental dose group (i.e., Group 1 through Group 4). As the animal arrival numbers (e.g., 1, 2, etc.) will be maintained in Provantis for the in-life portion of the study, there will be no indicator of the animal assignment to treatment groups in Provantis until the study will be unblinded. Note that the Provantis system will only be used at (b) (4), not at (b) (4) where all data capture will be performed manually.

Personnel involved in the in-life data collection will be blinded to the experimental groups. However, the Study Director, the Principal Investigator (at (b) (4)), the Clinical Pathologist, the pharmacy staff and the departmental team leaders will not be blinded. These unblinded personnel will not participate in direct evaluation of the animals/data collection. This relaxation in requirement will be necessary in order to permit adequate monitoring and quality checks during the course of the study. For ethical reasons, the Veterinarian staff will not be blinded, since access to an animal's identification and treatment type could be required in order to assess the correct interventions that are needed and to properly fulfill animal care requirements.

Animal Replacement

Any dam considered unsuitable for use on study may be excluded prior to assignment (day of 1st mating). There will be no replacement of dams after initiation of treatment.

(b) (4)

Any dam confirmed not pregnant on GD 28 will not be shipped to (b) (4)

Any puppy (F_1) considered unsuitable for use on study may be excluded at selection (PPD 56). There will be no replacement of puppies after the first two weeks of weaning (once ability to thrive is confirmed).

Fluid Replacement

Fluid replacement (0.9% sodium chloride USP administered subcutaneously or Lactate Ringers administered intravenously) may be performed as required based on blood sample volumes collected during the study. The volume of fluid to be administered will be documented in the study data.

Animal Care Compliance

Procedures involving the care and use of animals in this study will be reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) prior to conduct. During the study, the care and use of animals will be conducted in accordance with the principles outlined in the current Guidelines published by the Canadian Council on Animal Care and the Guide for the Care and Use of Laboratory Animals, an NRC publication and/or USDA regulations. (b) (4) ca facility is accredited by the Canadian Council on Animal Care and AAALAC. Per the Canadian Council on Animal Care guidelines, this study is considered as a category of invasiveness B. The portion of the study to be performed at (b) (4) is considered a category C for USDA Pain and Distress classification.

As a study in the field of regulated research, this study is expected to significantly contribute to medical advancement and improving the quality of animal life through animal use based on the intended purpose of the test item.

IN-LIFE OBSERVATIONS

Signed and dated records of activities relating to the day-to-day running and maintenance of the study within the animal room as well as the activities relating to the observations and examinations outlined in this Study Plan will be recorded. Observations will be made and data collections will be performed by blinded trained technicians (i.e., without knowledge of the treatment groups for individual animals). During the course of the study, additional evaluations to those described below and/or scheduled and considered necessary by the Study Director and the Veterinarian, as applicable, to assess health status will be conducted and duly documented in the study file and included in the study report.

Mortality

Mortality checks will be recorded concomitantly with the cage-side observations (see below), during all phases of the study.

Animals in unrelievable pain or distress will be euthanized at the discretion of the Study Director or based on the clinical judgment of the Clinical Veterinarian in consultation with the Study Director and the Sponsor, if possible. Euthanasia endpoints are described in facility Standard Operation Procedures.

For animals euthanized for humane reason, a blood sample (unfasted) will be collected for clinical pathology investigations, when possible.

Animals pre-terminally euthanized or found dead will be processed as detailed in the Terminal Procedures section.

Clinical Observations

Animals will be observed on multiple occasions for clinical signs that may indicate ill health or other changes; observations are planned to be made at the cage-side, and during scheduled detailed clinical examinations, but additional clinical observations may be conducted if warranted to properly monitor animals health condition. Clinical observations will be conducted by blinded trained technicians and per facility SOPs (or SSPs at (b) (4)) and this study plan; the occasions are described in further detail below. Clinical findings may be referred to the Clinical Veterinarian.

Clinical signs (ill health, behavioral changes, etc.) will be recorded on all animals twice daily throughout the study. The nature of these observations will include evaluation of general appearance, activity, and other indicators of changes in animal health and behavior, including fur condition, gait and mobility. Litter checks will be performed once daily (concurrently with a clinical sign activity) until PPD 56.

A detailed clinical examination (DCE) will be performed on each animal at least on the day of estrous and on the day of treatment initiation and once within the week prior to shipment (at (b) (4) , concurrently with body weight measurements), and monthly thereafter (at (b) (4)). A DCE will also be performed on the day prior to release from the study.

Detailed clinical examinations will be conducted per facility SOPs (or SSPs at (b) (4) , which describe that during the detailed clinical examination, animals will be observed while in the cage for behavior, general appearance, coordination, etc., and then will be removed from the cage for close evaluation of general condition of the whole body including (but not limited to) head, thoracic, and abdominal areas through examination and palpation. Body temperature, heart rate and respiratory rate (counts per minute) will also be evaluated.

For puppies, height and head circumference will also be measured weekly starting on PPD 7.

In addition, a detailed examination will also be performed on all puppies selected to continue on the study (F_1) by blinded technical staff once a month from weaning thereafter, including within 3 days prior to release from the study. This evaluation will be conducted per facility SOPs which include assessment of the general body condition, autonomic and central nervous system, somatomotor activity, gait, skin/fur condition, lymph nodes, eyes, mucus membranes, respiration, behavior, circulatory system, state of hydration, and lungs, bladder, reproductive system and gastrointestinal auscultation and/or palpation. Particular attention should be directed to observations of central nervous system signs (seizures, tremors, salivation), vomiting and diarrhea. Additional observations may be performed as deemed necessary.

Animals whose health condition warrants further evaluation will be examined. Initiation of medical treatments, as recommended, will begin only following authorization (with the exception of pre-approved treatments) by the Study Director (in consultation with the Sponsor, if possible). Whenever possible, the Sponsor will be consulted prior to administration of systemic therapeutic drugs (i.e. other than topical). In the event that medical intervention is necessary, all medications and treatments, and reason for administration will be recorded and included in the study report.

Body Weights

Body weights will be recorded for all dams at least on the day of estrous and on the day of treatment initiation (at (b) (4), concurrently with DCE), and weekly thereafter.

Puppies will be weighed on PPD 0, 4, 7, 10, 14, 17, 21, etc. until weaning, and weekly thereafter.

A body weight measurement will also be performed on dams and puppies on the day prior to release from the study.

Food Consumption

Individual food intake will be measured on all animals at least daily (except on days of food deprivation) throughout the study, starting at initiation of feeding the reference/control diet (3-14 days prior to treatment start). In addition to the daily food consumption, achieved intakes will be calculated on a weekly basis (calculations performed at (b) (4) (b) (4).

The average of daily individual achieved intake of the test item in mg/kg/body weight per week will be calculated for both generations based on daily food consumption using the following formulas:

(b) (4)

- On dams from Day 1 until puppies are 5 weeks of age (without feeding pan)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

- On dams with puppies, from 5 weeks of age until weaning (with feeding pan, including puppies body weight), and for the first two weeks post-weaning (2 puppies/cage)

$$\frac{\text{Dietary concentration (mg/kg/cage) x food consumption (kg)}}{\text{Start-week body weight (kg/cage)}}$$

- On selected puppies, from the 3rd week post-weaning (1 puppy/cage)

$$\frac{\text{Dietary concentration (mg/kg) x food consumption (kg)}}{\text{Start-week body weight (kg)}}$$

For reporting purposes weekly average of daily food consumption and achieved intakes will be presented.

Parturition Observations

Dams will be observed for parturition at least 3 times a day starting from GD 55 until GD 71 (as applicable), as per standard operating procedures. Body temperature will be measured twice daily (12 hours ± 1 hour apart) starting on GD 55 until the first signs of parturition are observed. Body temperature will also be measured daily from GD 52-54 for baseline acquisition. The time of onset and completion of delivery will be recorded for each animal whenever possible. The day parturition is completed will be termed as PPD 0. Any signs of difficulty in parturition will be recorded.

Litter Size

Following the littering, the number of live, dead and malformed puppies at birth of F_1 puppies will be recorded daily from PPD 0 until weaning on PPD 56. Gross abnormalties, if any, will be recorded.

External Sex Determination Puppies (F_1 generation)

The number of male and female puppies in each litter will be determined as per (b) (4) by visually judging the anogenital distance and/or presence of a vulva or penis.

Standardization of Litter (Culling)

If a dam has more than 6 puppies, on PPD 1, the litter will be randomly adjusted to 6 puppies.

(b) (4)

On PPD 4, the size of each litter may be adjusted by eliminating extra puppies by random selection to yield, as closely as possible, 4 puppies/litter (with at least 1 male and 1 female puppy where the number of puppies allows).

The culled puppies will be randomly selected and no criteria (e.g.: body weights or similar) used for selection, and they will be euthanized (intracardiac injection of sodium pentobarbital solution – 240 mg/mL – dose volume based on the SOP, unless the animal`s body weight is less than 0.5 kg, in which case the dose volume will be 0.6 mL).

The puppies will be identified as per relevant (b) (4) standard operating procedures.

Weaning

The puppies will be weaned on PPD 56 and separated from the dams. One puppy/sex/litter will be randomly retained for the F_1 assessments.

In case of fewer than 4 litters obtained per group, two males and two females from the same litter can be selected for the same treatment group. Puppies not selected will be released from the study.

Starting on PPD 49, the daily period of separation of the puppies from their mother will be introduced. It will gradually increase until complete separation on PPD 56. At all time while separated from their mother during gradual weaning process, the puppies will have access to a bowl of electrolytes solution.

Clinical Pathology

Clinical pathology evaluations (hematology and clinical chemistry) will be performed on all dams (F_0) once during pretreatment (at (b) (4)) and at weaning.

In addition, on all puppies continued on the study (F_1), coagulation and urinalysis will be performed during Weeks 13 and 34; while hematology and clinical chemistry evaluation will be performed at weaning and every two months thereafter for the 4 total times during the growth phase.

Blood samples will be collected from the jugular vein (the cephalic vein may be used if required). Food will be removed overnight prior to blood collections (required for clinical chemistry). Urine will be collected overnight (targeted 10 hours ± 1 hour) from individually housed (in stainless steel dog cages) animals that will be deprived of food and water. The urine collection period may be extended in the event a sufficient urine sample volume is not collected within the time frame permitted.

Repeat for hematology and/or coagulation can be repeated with or without food and/or water deprivation if permissible sampling frequency and blood volume are not exceeded.

a) **Hematology**

The following parameters will be measured on blood samples collected into tubes containing K_3-EDTA as anticoagulant. The target volume of blood collected for each sample will be 1.3 mL at (b) (4) and 3 mL at (b) (4).

Cell morphology *
Hematocrit
Hemoglobin
Mean corpuscular volume
Mean corpuscular hemoglobin
Mean corpuscular hemoglobin concentration
Platelet count
Red blood cell count
Red cell distribution width
Reticulocyte counts (absolute and relative)
White blood cell count (WBC)
WBC differential (absolute and relative)

* Manual reading of smears for morphology check only carried out as necessary, in accordance with (b) (4) standard operating procedures. At (b) (4), if manual reading of smears for morphology check is required, it will be performed by (b) (4) (b) (4)).

b) **Coagulation**

The following parameters will be measured on blood samples collected into tubes containing citrate as anticoagulant. The target volume of blood collected for each sample will be 1.0 mL.

Sample Appearance (when abnormal)
Activated partial thromboplastin time
Fibrinogen
Prothrombin time

c) **Clinical Chemistry**

The following parameters will be measured on blood samples collected into tubes containing clotting activator gel. The target volume of blood collected for each sample will be 1.1 mL at (b) (4) and 4 mL at (b) (4). At (b) (4) the obtained serum will be separated into two aliquots. One aliquots will be shipped to (b) (4) designated laboratory (b) (4)) for analysis of the parameters with an '*' below. The other aliquot will be analyzed at (b) (4) for the remaining parameters.

Sample Appearance (when abnormal)
A/G ratio (calculated)
Alanine aminotransferase
Albumin
Alkaline phosphatase
Amylase
Aspartate aminotransferase
Bile acids (total)
Bilirubin (total)
Total Calcium
Chloride
Cholesterol (total)
Creatinine
Creatine kinase
Gamma glutamyltransferase (GGT)
Globulin (calculated)
Glucose
Lactate dehydrogenase (LDH)*
Magnesium
Phosphorus (inorganic)
Potassium
Sodium
Total protein
Triglycerides*
Urea

d) **Urinalysis**

Minimum volume of approximately 1.0 mL. The following parameters will be measured on urine samples:

Bilirubin
Blood
Color and appearance
Glucose
Ketones
Leukocytes
Microscopic analysis (sediments)
Nitrites
pH
Protein
Specific gravity
Urobilinogen
Volume

Buccal mucosal bleeding time

Buccal mucosal bleeding time will be measured on all puppies continued on the study (F_1) during Week 34, on the same day (+/- 1 day) as the clinical pathology occasion (coagulation).

Bioanalysis

Blood samples (a target of 3 mL each) will be collected from dams during the pretreatment period for a baseline (at (b) (4) urces), after 4 to 5 weeks of treatment (at (b) (4)) and at weaning (at (b) (4)). Blood samples (a target of 2 mL each) will also be collected from all selected weaned puppies (F_1) at weaning and during Weeks 13 and 34, at approximately the same time on each occasion.

Each blood sample will be collected by jugular venipuncture (or any other vein may be used if required) into tubes containing K_2-EDTA (alternatively, K_3-EDTA can also be used, but the tube type should be consistent throughout the study) as anticoagulant and kept on wet ice pending centrifugation. Samples will be centrifuged at 1500 g RCF for targeted 10 minutes. Centrifugation will be refrigerated (set to +4°C) at (b) (4) , but not at (b) (4) where it will be performed at room temperature.

Excursions from the target volume will be documented in the raw data. In the event samples must be re-centrifuged, the times of sample processing will be documented. Plasma will be transferred into 2 separate tubes, placed on dry ice pending storage in a freezer set to maintain -70°C until shipment. One set of samples will be shipped on dry ice, to the Sponsor-designated laboratory for analysis at the following address:

(b) (4), (b) (6)

(b) (4)

Samples should be shipped by FedEx overnight on dry ice. An email should be sent to (b) (4), (b) (6) alerting him of the shipment. An electronic list of samples should be included in the e-mail and with the shipment.

Following confirmation of safe and intact receipt of the first set of samples, the second set of the duplicate samples may be shipped to the Sponsor-designated laboratory on dry ice or may be discarded at the request of the Sponsor.

Samples will be analyzed using a validated assay (b) (4) for measurement of DHA and EPA plasma concentrations.

Remaining Sample Disposal Policy Statement

All remaining unanalyzed biological samples (if any) will be discarded prior to finalization, unless specifically instructed otherwise in writing, by the Sponsor. In the event the Sponsor requests, in writing, prolonged storage time of the above material it will be documented via a study plan amendment (at additional cost).

TERMINAL PROCEDURES

At weaning (for dams) or two weeks after weaning (for puppies), all dams and all puppies not selected for the growth phase of the study (once ability to thrive of selected puppies is confirmed, i.e. 2 weeks post-weaning) will be transferred to the (b) (4) animal colony. Similarly, at the completion of the study, all surviving selected puppies will be transferred to the (b) (4) animal colony.

Dams found dead or euthanized for humane reasons will be processed as per relevant standard operating procedures. Necropsy of the dams will consist of an external macroscopic examination, including identification of all clinically recorded lesions, as well as a detailed internal examination and the reprodutive tract dissected out, the ovaries removed and corpora lutea counted, and processed as per standard operating procedures. Grossly abnormal tissues will be retained for possible future histopathology.

Similarly, any puppies found dead or euthanized for humane reasons will be processed as per relevant standard operating procedures. Necropsy of the puppies will consist of an external macroscopic examination, including identification of all clinically recorded lesions, as well as a detailed internal examination, and processed as per standard operating procedures. Grossly abnormal tissues will be retained for possible future histopathology.

In order to avoid autolytic changes, the macroscopic examination of the carcass will be conducted, as soon as possible, on all animals which die or are euthanized prematurely. Should an animal be found dead or euthanized outside regular working hours, necropsy will be completed as soon as possible after the time of death. Pending necropsy, the carcass will be stored in a refrigerator (set to 2-8°C).

(b) (4)

Photographs of individual macroscopic or microscopic findings may be taken at the discretion of the attending Pathologist and/or the Study Director for illustrative purposes only. Photographs (if any) will not routinely be reported but will be kept in the study file. Photographs may be reported at the discretion of the Sponsor or Study Pathologist, at additional cost.

Histopathology

No histopathological preparation or evaluation will be performed (except at the request of the Sponsor and at additional cost).

DATA HANDLING AND REPORTING

Data Capture

The following data capture systems may be used during the conduct of this study. Version numbers of the systems will be specified in the study report.

In-life data collection	Provantis (at (b) (4), none at (b) (4))
Pathology (if any)	Provantis (at (b) (4), none at (b) (4))
Clinical pathology	Provantis (at (b) (4)), CEDRIC ((b) (4)' custom-designed animal management database)
Analytical Chemistry	Agilent OpenLab CDS, version C.01.07
Bioanalytical	Shimadzu Lab Solutions, version 5.81
Statistical analysis	SAS (at (b) (4))
Room environment	Siemens Insight (at (b) (4), none at (b) (4))

Various parameters, not mandated by the Study Plan, will be automatically measured and recorded by the instrumentation(s), but will not be reported.

Manual or computerized recording (in-life data collection and pathology, if any) in accordance with the standard operating procedures may be used to ensure data capture as necessary. At (b) (4), most data will be manually collected and subsequently entered in Provantis (by (b) (4)) for reporting purposes.

All data collected at (b) (4) will be transferred to (b) (4) prior to and/or at shipment of the animals.

A quality check of the raw data will be performed prior to unblinding of the animal identification information.

Data Analysis

The statistical analysis approach for this study was designed with reference to Guidance for Industry #226: Target Animal Safety Data Presentation and Statistical Analysis. The statistical reporting will be done in compliance with the Guidance for Industry #197: "Documenting Statistical Analysis Programs and Data Files".

Data recorded at unscheduled occasions will be reported on an individual basis but will not be included in the analysis described below.

Whenever a continuous variable is measured on more than one pup per litter, an average per litter and sex will be computed, reported and the statistical analysis will be performed using the average per litter and sex.

Continuous variables specified in the study plan and collected during the conduct of the study will be subjected to calculation of group means, standard deviations, minimum and maximum values and will be reported by group and sex on each occasion. The calculation of group descriptive statistics will also be presented by group on combined occasions and/or combined sexes when a non significant occasion and\or sex interaction with the treatment effect is detected by the respective statistical analysis.

Categorical and dichotomous data specified in the study plan and obtained during the conduct of the study will be reported as individual results and, if deemed appropriate for interpretation, as group incidences by group on occasion and combined occasions for each sex and combined sexes.

The individual food consumption will be reported and analyzed as weekly average of daily food intake and as weekly average of achieved food intake.

To keep the statistical model as simple as possible and, considering that the inclusion of data from both sexes and across time in the same analysis would increase the power of the analysis, considering the group and the sex are the most relevant factors of interest and considering the the inclusion of more factors may over parameterize the statistical model, only the group, the sex and the time effects will be considered as fixed factors in the statistical models.

Statistical analysis will be independantly performed for the three periods: gestation, pre and post weaning.

To get a data distribution more closely to a normal one, data transformation may be used before doing the statistical comparisons when the data distribution is clearly skewed, e.g. for percentages approaching 0% or 100%.

One-Way ANOVA/ANCOVA

A one-way analysis of variance (ANOVA) will be performed for the following datasets:

- average of pre-treatment individual results of body weights F0;
- average of pre-treatment individual results of food and water consumption F0;
- mean day per litter and sex of positive development of vaginal opening and preputial separation;
- percentage live pups by litter, percentage malformed pups per litter at PPD0.
- clinical pathology parameters of F0

Two-Way Repeated Measures ANOVA/ANCOVA

A **two-way repeated measures** analysis of variance (ANOVA) will be performed for the following datasets:

- body weight changes for F0 during gestation;
- post-start of treatment results of food consumption F0 pre-weaning

A **two-way repeated** measures analysis of covariance (**ANCOVA**) will be performed for the following datasets:

- post-start of treatment results of body weights F0 during gestation
- post-start of treatment results of food consumption F0 during gestation

Three-Way Repeated Measures ANOVA/ANCOVA

A **three-way repeated measures** analysis of variance (ANOVA) will be performed for the following datasets:

- body weight and body weight change for F1 post-weaning
- food consumption, achieved food intake F1 post-weaning
- numerical clinical pathology data for F1
- buccal mucosal bleeding time for F1

A **three-way nested repeated measures** analysis of variance (ANOVA) will be performed for the following datasets (pups nested within litter):

- body weight and body weight change for F1 pre-weaning

Statistical methods

One-Way ANOVA/ANCOVA

The following statistical group comparison will not include groups with less than three observations or with zero variance.

For each data set with more than two groups to compare, a one-way analysis of variance (ANOVA) will be performed with group as fixed effect. When significant differences among the group means are indicated by the ANOVA overall *F*-test ($p \leq 0.10$), a *t*-test will be used to perform the group mean comparisons between the control diet group and each test item treated group.

For datasets with only two groups to compare (including the control diet group), a two-sample *t*-test will replace the one-way ANOVA *F*-test.

Two-Way Repeated Measures ANOVA/ANCOVA

Whenever possible, the pre-treatment results (i.e. prior to first treatment) will be used as covariate. The average of pre-treatment results will be used as covariate if there is more than one result.

The fixed effects in the model will be the group, the time and their interaction with the animal as subject and, when applicable, the pre-treatment as covariate. For the pre-weaning period, subject will be the pup nested within litter. The repeated measures analysis of variance will be performed using each of the following four covariance structures: the first-order autoregressive (AR(1)), the heterogeneous first-order autoregressive (ARH(1)), the compound symmetry (CS) and the heterogeneous (CSH) in order to determine which one would best express the pattern of measurement correlations across time. A common covariance matrix for all groups will be used. The Kenward and Roger's (or the alternative Satterthwaite's) method will be used when computing the denominator degrees of freedom for the tests involving the fixed effects. If the final Hessian is not positive definite or computational limitation/convergence problems are encountered while fitting a model, the model will not be considered in the following steps. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) will be selected.

If the retained two-way repeated measures ANOVA/ANCOVA indicates that the group-by-time interaction is significant ($p \leq 0.10$), the group effect will be assessed within each time point using *F*-test on least-squares means. If there is no significant group-by-time interaction ($p \leq 0.10$), then the group effect will be assessed across pooled time points using the *F*-test from the retained three-way repeated measure ANOVA/ANCOVA.

When the group effect is significant ($p \leq 0.10$), *t*-test on least-squares means will be performed to compare control diet group with each of the test item treated groups. The pairwise group comparisons will be assessed at an alpha level of 0.10. Significant differences from group mean comparisons will be reported as $p \leq 0.10$, $p \leq 0.05$, $p \leq 0.01$, where *p* represents the *t*-test probability. Least-square means related to the pairwise group comparisons will be presented with *p*-values.

Three-Way Repeated Measures ANOVA/ANCOVA

Whenever possible, the pre-treatment results (i.e. prior to first treatment) will be used as covariate. The average of pre-treatment results will be used as covariate if there is more than one result.

The fixed effects in the model will be the group, the sex, the time and their two-way and three-way interactions with the animal as subject and, when applicable, the pre-treatment as covariate. For the pre-weaning period, subject will be the pup nested within litter. The repeated measures analysis of variance will be performed using each of the following six covariance structures: the spatial power (SP(POW)), the spatial anisotropic power (SP(POWA)), the first-order autoregressive (AR(1)), the heterogeneous first-order autoregressive (ARH(1)), the compound symmetry (CS) and the heterogeneous (CSH) in order to determine which one would best express the pattern of measurement correlations across time. A common covariance matrix for all group-sex levels will be used. The Kenward and Roger's (or the alternative Satterthwaite's) method will be used when computing the denominator degrees of freedom for the tests involving the fixed effects. If the final Hessian is not positive definite or computational limitation/convergence problems are encountered while fitting a model, the model will not be considered in the following steps. Among the successfully fitted covariance structures, the one having the lowest corrected Akaike's Information Criterion (AICC) will be selected.

If the retained three-way repeated measures ANOVA/ANCOVA indicates that the group-by-sex-by-time interaction is significant ($p \leq 0.05$), the group effect will be assessed within each sex-time combination using F-test on least-squares means. If there is no significant group-by-sex-by-time interaction ($p > 0.05$), then the group-by-sex and the group-by-time interactions will be assessed using the F-test from the retained three-way repeated measure ANOVA/ANCOVA.

If the group-by-sex interaction is significant ($p \leq 0.10$), the group effect will be assessed within each sex using F-test on least-squares means. If the group-by-time interaction is significant ($p \leq 0.10$), the group effect will be assessed within each time using F-test on least-squares means. If both group-by-sex and group-by-time interactions are not significant ($p > 0.10$), then the group effect will be assessed on pooled sexes and pooled time points using the F-test i.e. the main group effect from the retained three-way repeated measure ANOVA/ANCOVA.

When the group effect is significant ($p \leq 0.10$), t-test on least-squares means will be performed to compare control diet group with each of the test item treated groups. The pairwise group comparisons will be assessed at an alpha level of 0.10. Significant differences from group mean comparisons will be reported as $p \leq 0.10$, $p \leq 0.05$, $p \leq 0.01$, where p represents the t-test probability. Least-square means related to the pairwise group comparisons will be presented with p-values.

Profile plots

For continuous variables measured repeatedly, the individual and group mean variations across time will be presented in graphs.

Reporting

Study updates will be provided to the Sponsor on a biweekly basis, or as required during the study.

A draft report will be submitted electronically to the Sponsor. Should external contributing reports be unavailable for inclusion in the initial draft of the report, the draft report will be issued on schedule, unless otherwise directed by the Sponsor. Following Sponsor (and/or Sponsor designate) review, appropriate modifications will be made to the draft report and a revised version (Word) of the draft report will be issued for review. Following agreement to the final content of the report by the Sponsor and (b) (4), the report will be finalized and one electronic copy (PDF and Word format) of the final version of the report will be issued and sent to the Sponsor.

The raw data and the statistical analysis will be provided in compliance with GFI #197 to facilitate the submission of the dossier to CVM.

(b) (4) expects that the draft report will be commented upon by the Sponsor and finalized within 6 months of issuance. Should the Sponsor fail to contact (b) (4) to make alternate arrangements, within the above referenced period, (b) (4) will consider that the draft report is acceptable and proceed with the finalization of the report. If such a case occurs, the Sponsor will be notified in writing at least 30 days prior to finalization of the report.

Archives

The following study materials (including but not limited to) generated during this study will be retained a (b) (4) and/or subcontracted archive facility for a period of 5 years after the signature of the study report by the Study Director:

Study Plan and Study Plan Amendments (if any)
Receiving and shipping records
Records of room maintenance and environmental data
Records of test system and animal care
Records of day to day activities
Final Report
Test material and formulation records
Records of laboratory analysis
Records of histopathology (if any) and clinical pathology
Statistical analysis
Appropriate samples and specimens (if any)

(b) (4)

(b) (4) agrees to give the Sponsor sufficient advance notification of any intended disposal of such materials after the 5-year holding period, to allow the Sponsor to secure alternative storage facilities.

All study material generated by the (b) (4), and (b) (4)) will be retained in the archives of (b) (4) .

All study material generated by (b) (4) will be transferred to (b) (4) for archiving.

Communication

Any untoward changes occurring during the conduct of the study will be communicated to the Sponsor by phone, e-mail, or facsimile, and discussed. All mutually-agreed changes to the Study Plan or study conduct will be duly documented in the form of a Study Plan amendment and signed by the signatories of the Study Plan (as appropriate). Any additional costs associated with these changes will be communicated to the Sponsor.

If the Sponsor cannot be reached immediately or if there is insufficient time to contact the Sponsor, the Study Director will take all steps necessary to ensure continuity and viability of the study and/or the general well-being of the animals. If such action is taken, the Study Director will notify the Sponsor as soon as possible.

Copies of any Study Plan amendments will be sent to the Sponsor, whose formal approval will be indicated by the return of one signed copy to (b) (4) .

Regulatory

Although this is a non-GLP study, the Quality Assurance Program of (b) (4) may undertake and document inspections and audits of critical aspects of the study during its conduct. The results of all the study audits will be reported to the Study Director. The Sponsor study monitor or authorized designate(s) may inspect this study during regular working hours for quality assurance purposes and copy any study-related original data.

Multisite

For any portion of the study conducted by a subcontractor (i.e.: (b) (4)), the Study Director will ensure that a qualified Principal Investigator will be identified by the site conducting that portion of the study, prior to the start of the study phase analysis.

For any portions of the study conducted by a test site (i.e.: analytical, bioanalytical), a sub-report will be provided by the Principal Investigator to the Study Director for inclusion in the study report.

Standard Operating Procedures

All activities of this study will be performed according to standard operating procedures (SOPs) and/or Study Specific Procedures (SSPs), which will be maintained on-file at (b) (4) and at the location of any subcontracting laboratories.

Government Inspection

(b) (4) agrees to notify the Sponsor promptly of any government inquiry or proposed inspections with respect to this study. The Sponsor shall have the right to participate in (b) (4) response to the inquiry, when time permits.

(b) (4)

(b) (4), (b) (6)

(b) (4), (b) (6)

July 05, 2017.
Date

(b) (4)

Approved by:

(b) (4), (b) (6)

July 05, 2017
Date

July 05, 2017
Date

Reviewed by:

(b) (4), (b) (6)

July 05, 2017
Date

Approved on behalf of the Sponsor by:

(b) (6)

Irina Dahms, Ph.D., DABT
DSM Nutritional Products AG

July 6, 2017
Date