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REPORT

ON

A REPEATED-DOSE (90 DAYS) ORAL TOXICITY STUDY

OF OCTOPIROX IN BEAGLE DOGS

Report No. 215/77

March 7, 1977

Vorsitzender des Aufsichtsrats: Karl Winnacker · Vorstand: Rolf Sammet, Vorsitzender; Kurt Lanz, stellv. Vorsitzender; Erhard Bouillon, Rudolf Frank, Enrique Hartung, Wolfgang Hilger, Willi Hoerkens, Josef Nowotny, Wolfgang von Pöinitz, Otto Ranft, Hans Reintges, Jürgen Schaalhausen, Hans Schlachter, Klaus Weissermel · Sitz der Gesellschaft: Frankfurt (M) · Handelsregister: Frankfurt (M) Abt. B Nr. 14500

Report on a repeated-dose (90 days) oral toxicity study of Octopirox in Beagle dogs

Summary:

In a 90-day toxicity study the anti-dandruff agent Octopirox (= H 72 6146 A) was administered in doses of 16.0, 40.0 or 100.0 mg per kg body weight, mixed with food, to groups of 4 male/4 female pure-bred English Beagle dogs from our own breeding. The dogs received the compound once daily for 90 days. A fourth group of 4 male/4 female Beagle dogs was not treated and served as control.

All dogs lived up to the scheduled end of the study.

In this study, oral treatment of dogs with Octopirox did not result in pathological changes.

Survey:

Compound:	Octopirox (= H 72 6146 A)
Category:	Anti-dandruff agent
Species:	English Beagle dog, breed: HOE:BEAK
No. of animals per group:	4 male/4 female
Route:	Oral, mixed with food
Dosage:	0, 16.0, 40.0, 100.0 mg/kg body weight
Duration of study:	90 days
No. of treatments:	90
Beginning of study:	August 10/11/12/13, 1976
Last treatment:	November 7/8/9/10, 1976
Killing:	November 8/9/10/11, 1976

Persons responsible:

Study director:	Dr. Brunk
Hematology:	Dr. Brunk/Dr.Schultes
Clinical chemistry:	Dr. Wicha/Dr. Hajdú
Histology:	Prof. Kief/Dr.Bähr
Head of department:	Prof. Kramer

Preliminary Remarks:

Compound: Octopirox (= H 72 6146 A), anti-dandruff agent, Batch E 002

Experimental animals: Pure-bred English Beagle dogs from our own breeding (breed HOE:BEAK). Age of male and female dogs at the beginning of the study: 10 months. Mean body weight of male dogs at the beginning of the study: 15.2 kg (14.6-17.6 kg). Mean body weight of female dogs at the beginning of the study: 14.0 kg (12.4 - 15.2 kg).

Groups and dosages: The doses administered in this study had been selected after exploratory studies.

Group I: 4 males, 4 females control, untreated

Group II: 4 males, 4 females 16.0 mg/kg

Group III: 4 males, 4 females 40.0 mg/kg

Group IV: 4 males, 4 females 100.0 mg/kg

Duration of study and route of administration: Octopirox was given daily (7 times a week) for 90 days, mixed with food, at the midday feeding. The control animals were not treated.

I. METHOD

1. Maintenance and Feeding:

The dogs were kept in individual boxes in climatized (18°C) kennels with open-air runs for the groups. They received a standard diet (Latz FF, mfr.: Latz Purina GmbH, for composition of feed see Appendix I) in daily portions of 850 g (males) or 650 g (females). In addition, each dog received an individual feeding of 150 g minced meat per day.

Water was provided ad libitum in automatic watering troughs.

Dogs which had not consumed all of their food two hours after feeding were recorded. The amount not consumed until the following morning was weighed.

2. Clinical Investigations:

2.1 Assessment of general state of health:

Daily.

2.2 Determination of body weight:

Once a week.

2.3 Behaviour:

aily observation.

2.4 Reflex response:

The flexor, patellar, anal, cutaneous, corneal, pupillary, blinking, placing (visual and tactile) and righting reflexes were examined prior to the first treatment, after 45 days and at the end of the study.

2.5 Eye examinations:

The eyes were examined by means of an Okulus hand slit lamp and a Kowa fundus camera RC2 (direct ophthalmoscopy) prior to the first treatment, after 45 days and at the end of the study.

In this assessment the examination of cornea, anterior chamber, iris/pupil,lens,vitreous body and fundus of the eye was included.

2.6 Examination of hearing:

Simple noise test for assessment of hearing, performed prior to the first treatment, after 45 days and at the end of the study.

2.7 Examination of teeth:

Prior to the first treatment, after 45 days and at the end of the study.

2.8 Examination of visible mucous membranes:

Prior to the first treatment, after 45 days and at the end of the study.

3. Laboratory tests:

For all tests, the blood samples were withdrawn from the vena cephalica antebrachii or from the vena saphena parva of the animals which had been fasted for 18 - 20 hours. For the determination of the coagulation time a marginal ear vein was punctured. With the exception of the last-mentioned parameter, all other hematological examinations were performed with EDTA blood.

3.1 Hematological examinations:

The blood samples were withdrawn prior to the beginning of the study (preliminary value), after 45 days (intermediate value) and at the end of the study (final value) and were then examined.

In these examinations the following parameters were determined:

erythrocytes leukocytes	Coulter Counter, model ZF	mil./mm^3 thous./mm^3
hemoglobin content	Counter (hemoglobinometer	g/100 ml blood
coagulation time	capillary method acc. to SCHALM (at 18°C)	min.
hematocrit	Coulter Counter, acc. to Hattersley	% of whole blood

BSR	Acc. to WINTROBE, uncorrected 1-hour value	mm/hour
reticulocyte count	brilliant cresyl blue staining acc.to BEGEMANN	% of erythrocytes
thrombocyte count	Coulter Counter, model ZF	100,000/mm^3 blood
Heinz bodies	nile blue chloride staining	
differential blood count	panoptic staining acc.to PAPPENHEIM	

3.2 Clinical chemistry examinations:

3.2.1 Serum analyses:

At the times of examination listed in 3.1, the following parameters were determined in all dogs:

calcium	Ca-Analyzer 940,Corning	mmol/l
sodium		mmol/l
potassium	with Autoanalyzer SMA 6/60	mmol/l
inorg.phosphorus	acc.to instructions by manufacturer	mmol/l
uric acid		umol/l
creatinine		umol/l
bilirubin,total		umol/l
chloride	chloride titrator, Aminco	mmol/l
urea-N	BUN Analyzer,Beckman,or bichromatic analyzer ABA-100,ABBOTT	mmol/l

3.2.2 Enzyme activities:

In all animals the following parameters were determined at the times of examination listed in 3.1:

SGOT	Bichromatic analyzer	U/l serum
SGPT	ABA-100, ABBOTT	U/l serum
alk.phosphatase		U/l serum

3.3 Urinalyses:

At the times of examination given in 3.1, the following parameters were determined in the pooled urine of each animal:

specific weight:	areometric method
pH value:	special indicator paper from Merck, Darmstadt
appearance and colour:	new methylene blue staining
protein :)	Combi-Uristix,
glucose:)	Ames Miles GmbH,Frankfurt
hemoglobin:)	
bilirubin:	Icotstix, Ames Miles GmbH, Frankfurt

4. Post Mortem Examinations:

The dogs were killed with an intravenous injection of 0.2 ml killing agent T 61-Hoechst (for composition see Appendix II) and were exsanguinated by opening of the carotid artery.
All animals (groups I - IV) were killed on the day after the last treatment.

4.1 Dissection:

Subsequently to the killing, the animals were dissected and examined macroscopiacally.

4.2 Organ weights:

The following organs were weighed:

heart	spleen	ovaries/testis
lungs	brain	adrenals
liver	pituitary	thyroid
kidneys	pancreas	

4.3 Histological examinations:

Sections of the following organs, or parts of organs were fixed in formalin and/or Carnoy's solution and were submitted to histological examination:

heart	pancreas	testis/ovaries
lungs	thymus	epididymis/uterus
liver	pituitary	prostate
kidneys	cerebrum	stomach
spleen	cerebellum	jejunum
adrenals	eye with optic nerve	colon
thyroid	urinary bladder	bone marrow (fixed in Schaffer's solution

II. RESULTS:

All dogs lived up to the scheduled end of the study.

1. Food consumption:

The amount of food offered was always consumed rapidly and completely.

2. Clinical findings:

2.1 General state of health:

The general state of health of the dogs was always good. Experiment-related disorders were not observed.

2.2 Body weight development: (Table and Figures 1 and 2)

The course of the body weight curves of treated dogs of all dosage groups corresponded largely to that of the control animals.

The nutritional state of all animals was very good.

Table: Body weight in kg

Dose Dog No.	Sex	Beginning of study	End of study	Difference
Controls				
698	♂	15.3	16.0	+ 0.7
699	♂	16.8	17.1	+ 0.3
700	♂	16.1	15.4	- 0.7
701	♂	17.6	17.1	- 0.5
714	♀	14.3	14.3	± 0
715	♀	13.5	13.6	+ 0.1
716	♀	14.7	13.2	- 1.5
717	♀	14.9	14.0	- 0.9
16.0 mg/kg				
702	♂	16.4	17.2	+ 0.8
703	♂	13.5	14.3	+ 0.8
704	♂	17.2	17.5	+ 0.3
705	♂	17.0	17.8	+ 0.8
718	♀	12.6	11.9	- 0.7
719	♀	12.4	12.7	+ 0.3
720	♀	14.6	13.4	- 1.2
721	♀	14.4	14.4	± 0
40.0 mg/kg				
706	♂	16.4	17.7	+ 1.3
707	♂	16.3	17.1	+ 0.8
708	♂	15.1	16.0	+ 0.9
709	♂	14.9	16.3	+ 1.4
722	♀	14.7	15.6	+ 0.9
723	♀	12.9	13.1	+ 0.2
724	♀	13.4	12.9	- 0.5
725	♀	14.6	14.1	- 0.5
100.0 mg/kg				
710	♂	15.9	16.7	+ 0.8
711	♂	15.9	16.6	+ 0.7
712	♂	16.0	15.7	- 0.3
713	♂	14.6	15.6	+ 0.1
726	♀	13.8	13.2	- 0.6
727	♀	14.1	14.2	+ 0.1
728	♀	13.4	13.1	- 0.3
729	♀	15.2	15.1	- 0.1

2.3 Behaviour:

N.A.D.

2.4 Reflex response:

N.A.D.

2.5 Eye findings:

N.A.D.

2.6 Hearing:

N.A.D.

2.7 Teeth:

N.A.D.

2.8 Visible mucous membranes:

N.A.D.

3. Laboratory findings:

3.1 Hematological findings:

The hematological examinations did not reveal any experiment-related changes.

3.2 Clinical chemistry findings:

3.2.1 Serum findings:

No experiment-related pathological values were measured.

3.2.2 Enzyme activities:

All values measured were within the physiological norm.

3.3 Urinalyses:

N.A.D.

4. Post Mortem Findings:

4.1 Macroscopic organ findings:
Experiment-related organ changes were not observed.

4.2 Organ weights:
Substance-induced changes were not demonstrable. One male dog (No. 713, 100 mg/kg) showed a testis weight which was lower than usual.

4.3 Microscopic organ findings: (report by Prof.Kief/ Dr. Bähr, Appendix III)
In this study, oral treatment with Octopirox did not lead to morphological demonstrable organ changes in dogs.

March 7, 1977

Pharmaceutical Research/Toxicology

of

HOECHST AG

signed:

Dr. Brunk
Clinical toxicology

Dr. Weigand
Industrial toxicology

Prof. Kramer
Head of department

Figure 1 : Body weight development in dogs after treatment with Octopirox
90-day oral toxicity study; species: English Beagle dog; 4 males per group

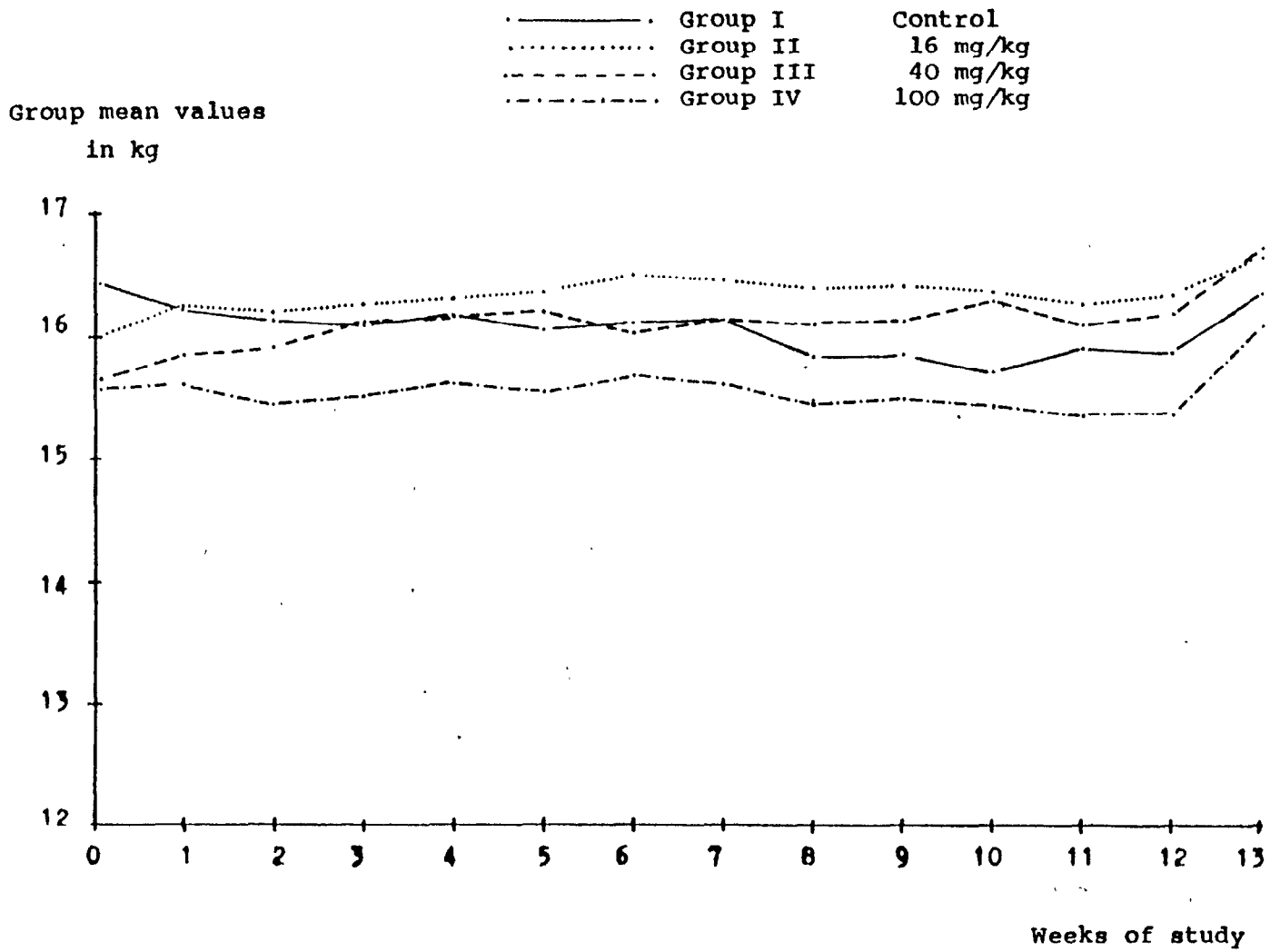

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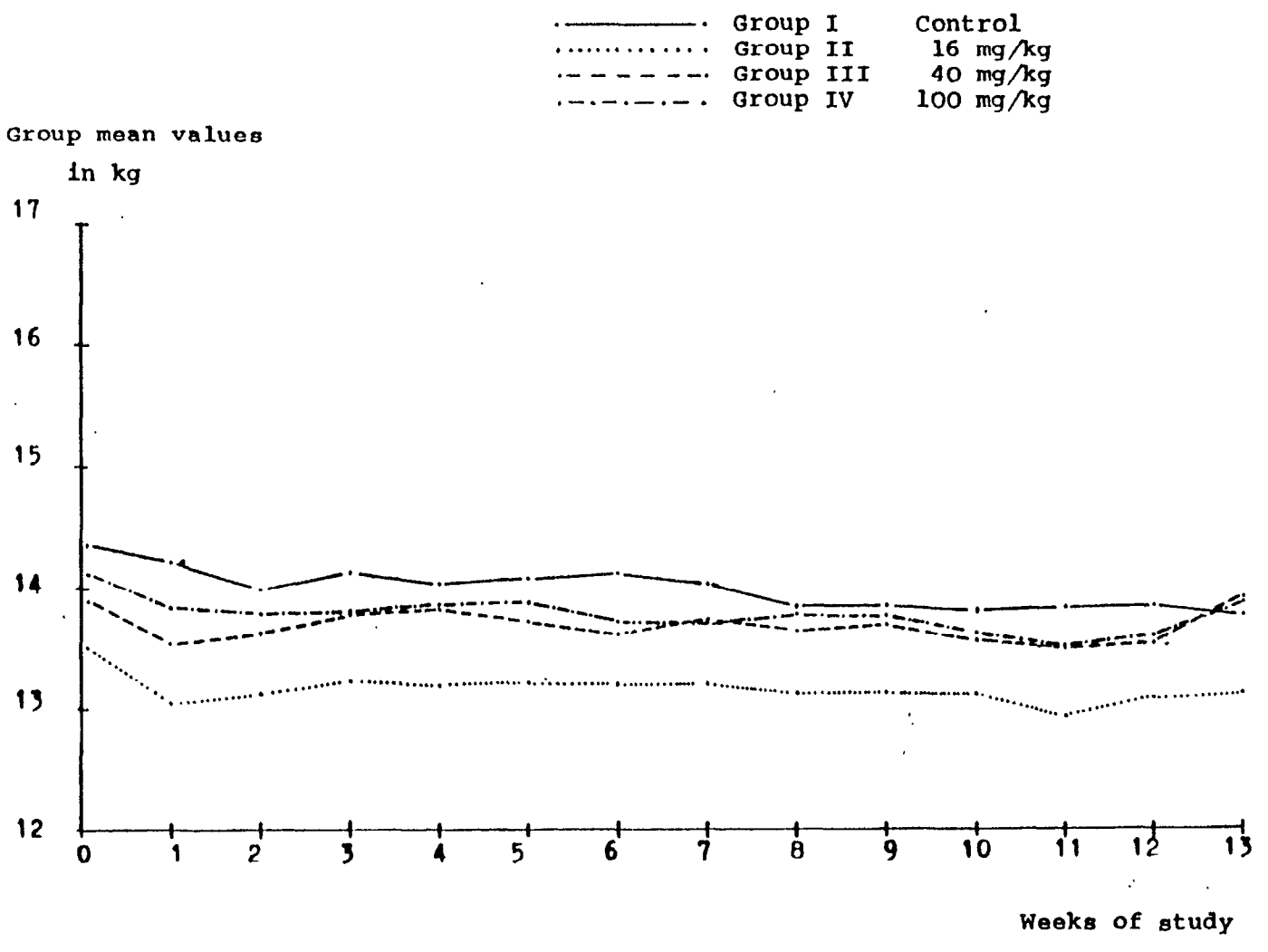
Figure 2: Body weight development in dogs after treatment with Octopirox
90-day oral toxicity study; species: English Beagle dog; 4 females per group



Hematological Findings

Compound: Octopirox

Dose :Control

Administration: untreated

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. %o	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
698	M	5.55	15.4	39	5	Ø	0	219	1	9.1	0	57	3	0	40	0
699	M	6.46	15.4	45	4	Ø	0	250	1	9.0	0	58	0	0	42	0
700	M	5.98	14.5	43	2	Ø	0	255	1	6.9	0	70	6	0	24	0
701	M	6.50	16.0	48	3	Ø	0	229	2	7.5	0	69	1	1	29	0
714	F	6.90	16.5	47	1	Ø	0	209	1	9.3	0	61	4	0	35	0
715	F	7.20	16.6	50	4	Ø	0	266	1	9.7	0	59	2	0	39	0
716	F	6.32	15.3	44	3	Ø	0	255	2	7.1	0	59	4	0	37	0
717	F	6.69	15.4	48	2	Ø	0	261	2	7.7	0	55	0	0	45	0

Hematological Findings

Compound: Octopirox

Dose 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. %	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
702	M	5.56	14.7	38	0	Ø	0	366	1	9.0	0	59	4	0	37	0
703	M	6.30	15.7	45	3	Ø	0	392	1	9.8	0	51	2	0	47	0
704	M	5.30	17.0	39	2	Ø	0	276	1	7.5	0	60	5	0	35	0
705	M	5.87	14.2	42	1	Ø	0	240	1	11.8	0	66	3	0	31	0
718	F	6.40	15.4	45	3	Ø	0	324	1	8.3	0	64	1	0	35	0
719	F	6.40	15.4	45	.0	Ø	0	318	1	7.2	0	64	1	0	35	0
720	F	6.63	16.0	46	1	Ø	0	318	1	8.6	0	70	1	0	29	0
721	F	6.51	15.3	44	2	Ø	0	329	1	11.2	0	56	0	0	44	0

Hematological Findings

Compound: Octopirox

Dose 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. %o	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
706	M	6.29	14.6	43	1	Ø	0	235	1	8.7	0	66	1	0	33	0
707	M	5.73	14.3	42	0	Ø	0	240	1	10.0	0	52	9	0	39	0
708	M	5.97	15.0	42	2	Ø	0	287	1	7.8	0	61	4	0	35	0
709	M	5.86	16.5	41	1	Ø	0	324	1	11.0	0	71	0	0	29	0
722	F	5.70	14.2	40	1	Ø	0	371	1	7.8	0	67	1	0	32	0
723	F	6.40	15.5	46	2	Ø	0	287	2	7.2	0	65	1	0	34	0
724	F	6.41	15.5	45	1	Ø	0	235	1	9.3	0	61	6	0	33	0
725	F	5.51	16.2	39	2	Ø	0	266	1	8.9	0	51	6	0	43	0

Hematological Findings

Compound: Octopirox

Dose 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. ‰	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
710	M	5.70	14.2	40	2	Ø	0	419	1	11.8	0	69	1	0	30	0
711	M	6.40	15.5	46	3	Ø	0	276	1	10.5	0	59	0	0	41	0
712	M	6.41	15.5	45	1	Ø	0	302	1	10.3	0	68	1	0	31	0
713	M	5.51	14.9	39	1	Ø	0	245	1	7.4	0	64	2	0	34	0
726	F	6.88	16.0	48	1	Ø	0	292	1	8.7	0	56	5	0	39	0
727	F	6.57	16.2	46	1	Ø	0	355	1	12.6	0	64	0	0	36	0
728	F	6.71	15.4	47	1	Ø	0	297	1	12.2	0	70	0	0	30	0
729	F	6.43	15.7	47	0	Ø	0	334	1	12.2	0	70	0	0	30	0

Hematological Findings

Compound: Octopirox

Dose Control

Administration: untreated

Species: Beagle, English

Week: 45 days

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. ‰	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
698	M	6.67	15.9	48	0	Ø	0	266	2	8.7	1	50	5	0	43	1
699	M	6.10	14.4	43	1	Ø	0	160	1	6.8	0	54	3	0	43	0
700	M	5.87	15.0	41	0	Ø	0	266	2	5.5	0	53	5	0	42	0
701	M	6.51	15.5	44	0	Ø	0	169	4	5.8	0	62	5	0	33	0
714	F	5.42	13.4	36	1	Ø	0	250	1	6.3	0	56	7	0	37	0
715	F	6.42	14.6	44	0	Ø	0	250	3	7.5	0	59	1	0	40	0
716	F	6.32	14.5	42	1	Ø	0	276	1	9.0	0	65	5	0	30	0
717	F	6.63	15.3	46	1	Ø	0	224	1	7.2	0	51	0	0	49	0

Hematological Findings

Compound: Octopirox

Dose 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. ‰	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
702	M	6.62	15.1	43	1	Ø	0	302	4	8.1	0	57	1	0	42	0
703	M	6.39	16.7	42	2	Ø	0	324	2	8.1	0	58	0	0	42	0
704	M	6.11	15.6	41	2	Ø	0	309	2	6.7	0	53	4	0	43	0
705	M	7.26	16.9	54	0	Ø	0	245	3	10.8	0	62	5	1	32	0
718	F	5.71	13.7	41	0	Ø	0	266	5	8.6	0	53	0	0	47	0
719	F	6.48	15.2	43	.0	Ø	0	334	3	7.2	0	62	0	0	38	0
720	F	6.43	15.2	42	1	Ø	0	334	3	7.9	0	62	0	0	38	0
721	F	6.16	14.1	42	0	Ø	0	324	4	8.1	0	65	6	0	29	0

Hematological Findings

Compound: Octopirox

Dose 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. %o	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
706	M	6.67	14.0	42	0	Ø	0	235	2	7.5	0	57	3	0	40	0
707	M	5.91	14.6	40	1	Ø	0	297	1	7.2	1	68	5	0	26	0
708	M	6.26	14.8	41	2	Ø	0	209	3	7.1	0	56	1	0	43	0
709	M	6.29	14.8	42	0	Ø	0	329	2	9.3	0	56	2	0	42	0
722	F	5.97	13.9	44	0	Ø	0	292	4	7.3	0	67	0	0	33	0
723	F	6.22	14.5	42	0	Ø	0	271	4	5.7	0	70	4	0	26	0
724	F	5.96	14.8	40	0	Ø	0	209	1	7.7	0	70	1	0	29	0
725	F	6.83	15.5	47	0	Ø	0	214	3	7.6	0	51	5	0	44	0

Hematological Findings

Compound: Octopirox

Dose 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. %	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
710	M	5.88	13.7	39	1	Ø	0	318	2	7.7	0	68	0	0	32	0
711	M	5.98	13.8	40	1	Ø	0	287	3	8.7	0	69	1	0	30	0
712	M	5.73	13.9	39	0	Ø	0	235	2	6.7	0	61	0	0	39	0
713	M	5.63	12.9	38	0	Ø	0	224	2	6.8	0	54	5	0	41	0
726	F	6.40	14.9	44	1	Ø	0	224	3	7.2	0	60	5	0	35	0
727	F	6.22	15.1	41	0	Ø	0	339	5	6.8	0	58	4	0	38	0
728	F	5.81	14.3	38	1	Ø	0	261	5	8.1	0	70	0	0	30	0
729	F	6.03	12.7	41	0	Ø	0	224	4	7.4	0	59	1	0	40	0

Hematological Findings

Compound: Octopirox

Dose Control

Administration: untreated

Species: Beagle, English

Week: Final value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. ‰	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
698	M	6.08	15.6	43	0	Ø	0	214	1	9.5	0	49	7	1	43	0
699	M	7.13	16.7	47	0	Ø	0	214	1	9.1	0	52	5	0	43	0
700	M	6.60	16.6	44	0	Ø	0	203	2	7.9	0	58	3	0	39	0
701	M	6.69	16.3	45	1	Ø	0	198	3	6.4	0	61	5	0	34	0
714	F	6.32	15.5	43	3	Ø	0	214	1	8.6	0	58	9	0	33	0
715	F	6.66	15.2	45	4	Ø	0	287	1	9.0	0	58	2	0	40	0
716	F	6.60	15.7	44	0	Ø	0	219	1	7.5	0	61	3	0	36	0
717	F	6.77	15.4	46	3	Ø	0	245	1	6.7	0	61	0	0	39	0

Hematological Findings

Compound: Octopirox

Dose 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. ‰	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
702	M	6.79	16.9	47	2	Ø	0	219	2	7.9	0	50	3	0	47	0
703	M	7.62	18.0	51	1	Ø	0	350	1	10.5	0	56	5	0	39	0
704	M	6.40	15.5	43	1	Ø	0	172	2	13.3	0	70	3	0	27	0
705	M	6.96	16.2	46	1	Ø	0	266	2	9.3	0	64	4	0	32	0
718	F	5.80	14.0	39	0	Ø	0	266	1	10.0	0	64	1	0	35	0
719	F	5.99	15.0	41	1	Ø	0	313	2	9.5	0	71	0	0	29	0
720	F	6.28	14.6	41	2	Ø	0	318	2	7.6	0	58	2	0	39	1
721	F	8.51	19.7	59	3	Ø	0	297	1	10.5	0	53	2	0	45	0

Hematological Findings

Compound: Octopirox

Dose 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. %	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
706	M	7.20	15.8	47	2	Ø	0	152	1	9.0	0	56	9	0	35	0
707	M	7.02	16.4	49	0	Ø	0	245	1	8.9	0	55	9	0	36	0
708	M	7.07	16.8	47	1	Ø	0	162	2	9.8	0	54	5	0	41	0
709	M	7.73	17.4	52	1	Ø	0	392	2	10.1	0	59	0	0	41	0
722	F	6.12	13.9	41	0	Ø	0	245	1	7.1	0	67	8	0	25	0
723	F	5.77	13.7	41	2	Ø	0	261	1	6.8	0	66	0	0	34	0
724	F	6.71	15.9	46	1	Ø	0	203	1	7.8	0	63	4	0	33	0
725	F	7.41	16.8	49	1	Ø	0	219	1	8.8	0	64	5	0	31	0

Hematological Findings

Compound: Octopirox

Dose 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	RBC 10^6	HB g%	PCV %	Retic. %o	Heinz B	Sed. Rate mm/h	Platelets 10^3	Coag. T. min.	WBC 10^3	Neutro Band %	Neutro Segm. %	Eos %	Baso %	Lympho %	Mono %
710	M	6.88	16.3	46	0	Ø	0	276	1	8.6	0	65	4	0	31	0
711	M	6.62	15.3	45	2	Ø	0	271	1	9.2	0	68	3	0	29	0
712	M	6.58	15.7	44	1	Ø	0	229	1	8.1	0	63	4	0	32	1
713	M	6.53	14.9	43	1	Ø	0	209	1	7.0	0	65	9	0	25	1
726	F	7.21	16.2	48	2	Ø	0	209	1	6.8	0	60	3	0	37	0
727	F	6.93	16.2	46	9	Ø	0	345	1	10.2	0	67	3	0	30	0
728	F	6.71	15.4	45	3	Ø	0	255	1	8.9	0	66	0	0	34	0
729	F	6.47	15.3	43	4	Ø	0	240	2	6.9	0	61	6	0	33	0

Clinical Chemistry

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
698	M	150	4.5	1.55	40	4.0	92	2.6	99	5.7	5.7
699	M	150	4.4	1.56	42	3.5	85	2.8	103	3.6	5.3
700	M	151	4.7	1.50	36	4.0	81	2.6	104	3.6	5.9
701	M	152	4.6	1.45	38	4.0	94	2.7	107	4.8	5.9
714	F	148	4.2	1.35	34	4.5	80	2.7	108	4.2	5.9
715	F	152	4.4	1.46	36	4.5	83	2.7	102	4.1	5.8
716	F	152	4.3	1.52	36	5.5	82	2.7	104	3.5	5.4
717	F	152	4.4	1.65	38	4.5	85	2.8	103	4.4	5.2

Clinical Chemistry

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
702	M	152	4.5	1.65	34	4.5	85	2.7	105	4.5	5.6
703	M	153	4.7	1.42	30	5.0	90	2.7	105	5.2	5.9
704	M	153	4.9	1.43	32	4.5	80	2.8	102	5.0	5.8
705	M	151	4.8	1.62	34	4.5	85	2.7	107	3.3	5.9
718	F	152	4.6	1.43	38	4.5	87	2.7	106	5.1	5.7
719	F	152	4.6	1.48	36	4.5	86	2.7	102	4.2	6.2
720	F	152	4.7	1.48	32	4.0	88	2.4	104	6.3	5.6
721	F	150	4.7	1.75	36	5.5	101	2.7	103	5.5	5.8

Clinical Chemistry

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
706	M	151	4.5	1.54	34	4.0	82	2.8	106	4.6	5.6
707	M	151	4.7	1.42	40	5.5	82	2.6	102	4.2	4.7
708	M	152	4.8	1.44	36	4.0	92	2.7	107	4.7	6.3
709	M	152	4.7	1.32	30	4.0	92	2.7	100	3.8	6.0
722	F	147	4.7	1.54	38	5.0	90	2.7	106	4.9	4.9
723	F	149	4.7	1.52	40	4.0	92	2.8	100	4.6	5.2
724	F	148	4.6	1.53	38	5.0	92	2.7	106	3.9	5.0
725	F	150	4.9	1.65	40	4.5	100	2.7	108	7.5	4.6

Clinical Chemistry

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary Value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
710	M	153	5.1	1.48	34	4.0	80	2.6	107	4.0	6.0
711	M	152	5.2	1.42	32	4.5	80	2.8	101	5.0	6.0
712	M	153	4.5	1.47	38	4.0	86	2.7	102	4.1	6.0
713	M	152	4.9	1.70	36	4.0	82	2.7	105	4.9	5.8
726	F	151	4.9	1.75	40	6.5	110	2.8	101	7.6	5.2
727	F	148	4.5	1.50	36	4.5	80	2.6	104	4.3	5.2
728	F	152	5.0	1.54	42	4.5	92	2.7	103	3.9	5.0
729	F	151	4.8	1.58	40	5.0	86	2.6	105	4.1	4.9

Clinical Chemistry

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
698	M	147	4.7	1.30	30	4.0	78	2.6	109	6.9	5.2
699	M	152	4.7	1.32	32	4.5	92	2.6	104	5.9	4.7
700	M	154	4.6	1.48	34	5.5	85	2.5	108	4.9	4.6
701	M	152	4.8	1.46	30	4.0	87	2.5	109	6.5	4.4
714	F	153	4.5	1.32	32	3.5	86	2.6	105	6.3	4.4
715	F	152	4.3	1.50	36	5.0	86	2.5	102	6.5	4.7
716	F	152	4.8	1.45	30	4.5	108	2.4	112	4.5	5.0
717	F	150	4.6	1.45	34	5.0	106	2.6	113	6.1	4.8

Clinical Chemistry

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
702	M	150	4.6	1.38	34	5.0	88	2.5	113	7.1	5.2
703	M	148	4.7	1.42	36	5.5	90	2.5	113	7.8	4.8
704	M	151	4.8	1.43	40	5.0	90	2.5	110	5.4	5.0
705	M	152	4.8	1.53	36	5.5	85	2.6	114	5.8	4.6
718	F	154	4.5	1.52	42	6.0	90	2.6	101	7.9	4.8
719	F	152	4.7	1.52	32	6.5	85	2.6	103	6.0	4.9
720	F	153	4.8	1.47	38	5.5	90	2.5	106	5.5	4.7
721	F	153	4.8	1.43	34	4.5	94	2.5	105	4.4	5.2

Clinical Chemistry

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
706	M	155	4.8	1.45	32	4.5	96	2.5	109	6.1	4.7
707	M	152	4.8	1.43	34	5.5	103	2.5	106	7.0	4.8
708	M	153	5.0	1.51	34	5.0	108	2.5	114	6.4	5.1
709	M	151	5.0	1.46	32	4.0	103	2.6	106	5.7	4.6
722	F	152	4.6	1.43	40	4.5	93	2.5	115	6.2	4.8
723	F	153	4.7	1.62	38	5.5	92	2.5	109	7.5	4.4
724	F	153	4.4	1.60	34	6.0	90	2.4	110	5.4	4.9
725	F	152	4.4	1.47	32	5.0	88	2.6	111	6.0	4.7

Clinical Chemistry

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
710	M	152	4.4	1.60	36	5.0	90	2.6	112	4.8	5.3
711	M	152	4.7	1.68	34	6.0	101	2.6	108	5.6	5.0
712	M	151	4.8	1.59	34	5.0	102	2.6	110	5.4	4.9
713	M	152	4.6	1.48	34	5.0	120	2.5	107	7.2	5.1
726	F	153	4.6	1.51	32	5.0	116	2.5	108	6.1	5.4
727	F	154	5.0	1.62	38	5.5	88	2.5	106	5.4	5.2
728	F	153	5.0	1.54	40	5.0	91	2.4	108	5.4	5.0
729	F	152	4.8	1.53	34	5.0	83	2.5	109	5.4	4.9

Clinical Chemistry

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Final value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
698	M	150	4.7	1.53	32	4.5	124	2.5	104	7.3	4.2
699	M	148	4.8	1.72	38	4.0	105	2.7	104	5.9	5.0
700	M	148	4.8	1.70	40	5.5	95	2.5	100	5.7	4.0
701	M	150	4.7	1.30	40	5.5	105	2.6	109	7.3	4.4
714	F	149	4.7	1.44	32	4.0	98	2.6	103	5.1	4.0
715	F	149	4.7	1.32	28	3.5	96	2.7	104	5.7	4.3
716	F	148	4.7	1.59	28	4.0	85	2.5	104	5.2	4.2
717	F	148	4.6	1.31	32	4.0	100	2.6	105	6.0	4.8

Clinical Chemistry

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
702	M	149	4.8	1.63	34	4.0	110	2.7	104	7.2	4.4
703	M	148	4.9	1.60	30	5.0	120	2.7	102	10.6	4.3
704	M	147	4.8	1.45	40	4.0	102	2.5	103	5.6	4.2
705	M	147	4.9	1.35	32	3.5	92	2.5	112	5.0	4.0
718	F	148	5.2	1.47	34	4.0	85	2.7	109	6.7	4.1
719	F	148	4.3	1.72	40	5.0	82	2.7	103	5.2	4.8
720	F	147	4.5	1.15	44	4.0	87	2.5	107	4.1	4.5
721	F	149	4.5	1.58	34	4.0	108	2.7	108	5.5	6.1

Clinical Chemistry

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
706	M	148	4.7	1.22	28	4.5	107	2.7	103	6.8	4.6
707	M	148	4.6	1.12	28	4.0	103	2.6	101	7.0	4.4
708	M	147	4.8	1.53	28	4.5	110	2.8	108	7.0	5.0
709	M	145	4.8	1.23	30	3.0	109	2.6	107	6.2	4.6
722	F	148	4.3	1.12	34	3.5	92	2.6	110	6.3	4.4
723	F	147	4.3	1.45	32	3.5	101	2.5	101	7.7	4.6
724	F	146	4.2	1.41	40	4.5	92	2.6	103	6.1	4.7
725	F	147	4.5	1.10	38	5.5	95	2.6	109	4.9	4.1

Clinical Chemistry

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Sodium mM/l	Potassium mM/l	Inorg. Phosphorus mM/l	Uric Acid uM/l	Bilirubin (total) uM/l	Creatinine uM/l	Calcium mM/l	Chloride mM/l	BUN mM/l	Glucose mM/l
710	M	150	4.9	1.77	34	4.0	93	2.7	101	4.2	4.8
711	M	149	4.7	1.69	26	3.5	103	2.6	113	4.9	4.9
712	M	149	4.7	1.98	28	3.5	91	2.6	104	4.6	4.7
713	M	150	4.2	1.76	26	5.0	103	2.5	101	7.5	4.7
726	F	150	4.3	2.05	38	4.0	111	2.5	102	6.9	4.1
727	F	149	4.3	2.12	34	3.5	82	2.6	104	4.0	4.8
728	F	148	4.3	1.76	42	3.5	83	2.5	105	4.8	4.4
729	F	150	4.5	1.80	32	3.5	82	2.4	102	4.4	4.7

Clinical Chemistry

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
698	M	11	25	123
699	M	11	20	103
700	M	8	32	146
701	M	8	32	140
714	F	8	22	116
715	F	11	31	94
716	F	7	23	125
717	F	9	27	107

Clinical Chemistry

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
702	M	8	15	151
703	M	10	24	143
704	M	10	30	137
705	M	10	30	187
718	F	12	24	139
719	F	10	27	115
720	F	11	32	121
721	F	6	17	108

Clinical Chemistry

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
706	M	9	21	119
707	M	10	30	116
708	M	10	24	114
709	M	9	18	134
722	F	8	16	105
723	F	10	18	82
724	F	19	59	114
725	F	11	42	97

Clinical Chemistry

Compound: Octopirox

Dose: 100 mg/kg

Administration:oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
710	M	11	21	119
711	M	9	25	120
712	M	10	20	119
713	M	11	22	140
726	F	7	23	85
727	F	12	30	104
728	F	9	41	131
729	F	7	16	73

Clinical Chemistry

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: 45 days

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
698	M	12	23	91
699	M	14	20	75
700	M	8	25	113
701	M	9	36	93
714	F	9	21	72
715	F	9	18	58
716	F	12	23	79
717	F	9	23	83

Clinical Chemistry

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
702	M	12	39	110
703	M	12	33	114
704	M	14	37	98
705	M	11	27	105
718	F	16	30	99
719	F	12	30	89
720	F	15	26	95
721	F	7	21	82

Clinical Chemistry

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
706	M	11	26	83
707	M	11	61	78
708	M	13	29	99
709	M	13	21	109
722	F	12	17	81
723	F	10	16	55
724	F	13	36	83
725	F	11	38	72

Clinical Chemistry

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
710	M	14	26	104
711	M	9	21	111
712	M	12	23	98
713	M	11	29	143
726	F	12	32	112
727	F	13	25	109
728	F	9	32	165
729	F	8	17	81

Clinical Chemistry

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Final value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
698	M	12	35	82
699	M	11	21	73
700	M	12	34	127
701	M	13	51	82
714	F	12	24	69
715	F	12	30	59
716	F	10	18	77
717	F	13	38	77

Clinical Chemistry

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
702	M	15	25	90
703	M	15	23	97
704	M	14	23	105
705	M	15	39	106
718	F	16	22	86
719	F	13	25	84
720	F	19	26	94
721	F	15	35	105

Clinical Chemistry

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
706	M	15	25	72
707	M	14	45	66
708	M	15	32	92
709	M	13	25	101
722	F	11	20	77
723	F	13	19	61
724	F	13	31	99
725	F	12	28	63

Clinical Chemistry

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	GOT U/l	GPT U/l	Alk. Phos. U/l
710	M	11	24	99
711	M	10	19	106
712	M	10	35	88
713	M	7	25	154
726	F	10	22	98
727	F	13	33	117
728	F	13	44	135
729	F	10	18	74

Urinalysis

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
698	M	slightly turbid	yellow	1.045	6.6	20, 30, 50, 90
699	M	slightly turbid	yellow	1.030	6.2	10, 20, 30, 50, 90
700	M	slightly turbid	yellow	1.032	6.6	20, 30, 50, 90
701	M	clear	yellow	1.032	6.4	20, 30, 50, 90
714	F	clear	yellow	1.032	6.6	30, 36, 72, 73, 90
715	F	clear	bright yellow	1.026	6.4	10, 20, 36, 72
716	F	clear	yellow	1.030	6.2	20, 30, 90
717	F	slightly turbid	yellow	1.036	6.2	10, 20, 30, 90

Urinalysis

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
698	M	Ø	Ø	Ø	Ø	
699	M	Ø	Ø	Ø	Ø	
700	M	Ø	Ø	Ø	Ø	
701	M	Ø	Ø	Ø	Ø	
714	F	Ø	Ø	Ø	Ø	
715	F	Ø	Ø	Ø	Ø	
716	F	Ø	Ø	Ø	Ø	
717	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
702	M	clear	yellow	1.042	6.6	20, 30, 50, 70, 72, 90
703	M	clear	yellow	1.029	6.7	20, 50, 70, 73, 90
704	M	turbid	yellow	1.040	6.4	10, 20, 30, 72, 73, 90
705	M	slightly turbid	yellow	1.033	6.7	21, 30, 50, 70, 72, 90
718	F	clear	yellow	1.034	5.4	21, 30, 72, 73, 90
719	F	clear	yellow	1.043	6.7	10, 20, 30, 72, 90
720	F	clear	yellow	1.041	5.4	20, 30, 36, 90
721	F	slightly turbid	yellow	1.038	6.4	20, 30, 72, 90

Urinalysis

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
702	M	Ø	Ø	Ø	Ø	
703	M	Ø	Ø	Ø	Ø	
704	M	Ø	Ø	Ø	Ø	
705	M	Ø	Ø	Ø	Ø	
718	F	Ø	Ø	Ø	Ø	
719	F	Ø	Ø	Ø	Ø	
720	F	Ø	Ø	Ø	Ø	
721	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
706	M	slightly turbid	yellow	1.036	6.4	21, 30, 50, 70, 72, 73, 90
707	M	slightly turbid	yellow	1.048	6.4	20, 30, 50, 72, 90
708	M	clear	yellow	1.052	8.2	20, 30, 51, 70
709	M	slightly turbid	yellow	1.046	6.4	10, 21, 30, 50, 70, 90
722	F	slightly turbid	yellow	1.045	6.7	30, 36, 70
723	F	slightly turbid	yellow	1.045	6.4	20, 72, 73, 90
724	F	clear	yellow	1.036	7.0	10, 20, 30, 72, 90
725	F	slightly turbid	yellow	1.046	6.2	20, 30, 72, 73, 91

Urinalysis

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
706	M	Ø	Ø	Ø	Ø	
707	M	Ø	Ø	Ø	Ø	
708	M	Ø	Ø	Ø	Ø	
709	M	Ø	Ø	Ø	Ø	
722	F	Ø	Ø	Ø	Ø	
723	F	Ø	Ø	Ø	Ø	
724	F	Ø	Ø	Ø	Ø	
725	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
710	M	clear	yellow	1.034	6.6	20, 30, 50, 70, 72, 90
711	M	slightly turbid	yellow	1.043	6.4	20, 30, 70, 72, 90
712	M	slightly turbid	yellow	1.037	6.2	10, 20, 32, 50, 90
713	M	slightly turbid	yellow	1.051	6.4	10, 20, 30, 72, 90
726	F	clear	yellow	1.034	5.8	20, 30, 90
727	F	clear	yellow	1.055	6.4	21, 30, 70
728	F	clear	yellow	1.045	6.4	10, 30, 36, 90
729	F	slightly turbid	yellow	1.044	6.7	20, 31, 70, 72, 73, 90

Urinalysis

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Preliminary value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
710	M	Ø	Ø	Ø	Ø	
711	M	Ø	Ø	Ø	Ø	
712	M	Ø	Ø	Ø	Ø	
713	M	Ø	Ø	Ø	Ø	
726	F	Ø	Ø	Ø	Ø	
727	F	Ø	Ø	Ø	Ø	
728	F	Ø	Ø	Ø	Ø	
729	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
698	M	clear	yellow	1.049	6.4	10, 20, 30, 50, 70, 72, 90
699	M	slightly turbid	yellow	1.050	6.2	20, 30, 50, 72, 90
700	M	slightly turbid	yellow	1.050	6.2	10, 20, 30, 50, 70, 72, 90
701	M	slightly turbid	yellow	1.049	5.4	10, 20, 50, 72
714	F	clear	yellow	1.040	6.4	20, 30, 70, 72, 90
715	F	clear	bright yellow	1.035	5.8	20, 31, 70, 72, 90
716	F	clear	yellow	1.048	7.0	20, 30, 72, 90
717	F	clear	yellow	1.051	6.7	10, 20, 30, 70, 72, 90

Urinalysis Compound: Octopirox Dose: Control

Administration: untreated

Species: Beagle, English Week: 45 days

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
698	M	Ø	Ø	Ø	Ø	
699	M	Ø	Ø	Ø	Ø	
700	M	Ø	Ø	Ø	Ø	
701	M	Ø	Ø	Ø	Ø	
714	F	Ø	Ø	Ø	Ø	
715	F	Ø	Ø	Ø	Ø	
716	F	Ø	Ø	Ø	Ø	
717	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
702	M	clear	yellow	1.053	7.0	10, 20, 30, 50, 70, 72, 73, 90
703	M	clear	yellow	1.028	6.2	10, 20, 30, 50, 70, 72, 90
704	M	slightly turbid	yellow	1.054	6.2	10, 20, 30, 50, 70, 72, 90
705	M	clear	yellow	1.052	6.4	10, 20, 30, 70, 72, 73, 90
718	F	clear	yellow	1.046	5.8	20, 30, 72
719	F	clear	yellow	1.056	6.7	10, 20, 30, 72, 90
720	F	slightly turbid	yellow	1.065	6.2	20, 30, 70, 90
721	D	slightly turbid	yellow	1.047	5.8	20, 30, 72, 90

Urinalysis

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
702	M	Ø	Ø	Ø	Ø	
703	M	Ø	Ø	Ø	Ø	
704	M	Ø	Ø	Ø	Ø	
705	M	Ø	Ø	Ø	Ø	
718	F	Ø	Ø	Ø	Ø	
719	F	Ø	Ø	Ø	Ø	
720	F	Ø	Ø	Ø	Ø	
721	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
706	M	clear	yellow	1.047	6.7	20, 30, 50, 72, 90
707	M	slightly turbid	yellow	1.041	5.8	20, 30, 90
708	M	clear	yellow	1.048	6.7	20, 30, 50, 70, 72, 90
709	M	clear	yellow	1.058	6.7	10, 20, 30, 70, 72, 90
722	F	clear	yellow	1.047	6.4	10, 20, 30, 72, 90
723	F	clear	yellow	1.049	6.7	10, 20, 30, 70, 72, 90
724	F	clear	yellow	1.045	6.4	10, 21, 31, 72, 90
725	F	clear	yellow	1.038	7.0	20, 30, 72, 90

Urinalysis

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
706	M	Ø	Ø	Ø	Ø	
707	M	Ø	Ø	Ø	Ø	
708	M	Ø	Ø	Ø	Ø	
709	M	Ø	Ø	Ø	Ø	
722	F	Ø	Ø	Ø	Ø	
723	F	Ø	Ø	Ø	Ø	
724	F	Ø	Ø	Ø	Ø	
725	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
710	M	slightly turbid	yellow	1.044	6.2	20, 30, 70, 72, 73, 90
711	M	clear	yellow	1.054	6.4	10, 20, 30, 50, 70, 72, 90
712	M	clear	bright yellow	1.059	6.7	20, 30, 50, 70, 72, 90
713	M	clear	yellow	1.047	6.2	20, 30, 72, 90
726	F	clear	yellow	1.038	6.4	20, 30, 72, 90
727	F	clear	yellow	1.035	5.8	10, 20, 30, 70, 72, 73, 90
728	F	clear	yellow	1.052	6.4	30, 36, 72
729	F	slightly turbid	bright yellow	1.040	5.8	20, 30, 70, 72, 73, 90

Urinalysis

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: 45 days

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
710	M	Ø	Ø	Ø	Ø	
711	M	Ø	Ø	Ø	Ø	
712	M	Ø	Ø	Ø	Ø	
713	M	Ø	Ø	Ø	Ø	
726	F	Ø	Ø	Ø	Ø	
727	F	Ø	Ø	Ø	Ø	
728	F	Ø	Ø	Ø	Ø	
729	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Final value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
698	M	slightly turbid	yellow	1.054	6.2	10, 20, 30, 50, 70, 72, 90
699	M	turbid	yellow	1.050	6.7	10, 20, 30, 50, 70, 91
700	M	slightly turbid	yellow	1.049	6.4	20, 30, 50, 70, 72, 90
701	M	slightly turbid	yellow	1.042	5.8	10, 20, 30, 36, 50, 72, 90
714	F	slightly turbid	yellow	1.049	6.7	10, 20, 30, 70, 72, 91
715	F	clear	yellow	1.051	6.2	20, 30, 72, 90
716	F	slightly turbid	yellow	1.051	6.4	10, 20, 30, 70, 72, 90
717	F	clear	yellow	1.052	6.4	10, 20, 30, 70, 90

Urinalysis

Compound: Octopirox

Dose: Control

Administration: untreated

Species: Beagle, English

Week: Final value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
698	M	Ø	Ø	Ø	Ø	
699	M	Ø	Ø	Ø	Ø	
700	M	Ø	Ø	Ø	Ø	
701	M	Ø	Ø	Ø	Ø	
714	F	Ø	Ø	Ø	Ø	
715	F	Ø	Ø	Ø	Ø	
716	F	Ø	Ø	Ø	Ø	
717	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
702	M	slightly turbid	yellow	1.050	7.6	20, 30, 50, 70, 72, 90
703	M	slightly turbid	yellow	1.038	5.8	10, 20, 30, 50, 70, 72, 90
704	M	slightly turbid	yellow	1.040	5.8	20, 30, 50, 72, 73, 90
705	M	slightly turbid	yellow	1.048	6.2	10, 20, 30, 36, 72, 90
718	F	clear	bright yellow	1.029	5.8	10, 20, 31, 36, 72, 73, 90
719	F	clear	bright yellow	1.032	6.2	10, 20, 72, 73, 90
720	F	slightly turbid	yellow	1.051	5.8	10, 20, 30, 70, 73, 90
721	F	slightly turbid	yellow	1.051	6.4	10, 30, 70, 72, 90

Urinalysis

Compound: Octopirox

Dose: 16 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
702	M	Ø	Ø	Ø	Ø	
703	M	Ø	Ø	Ø	Ø	
704	M	Ø	Ø	Ø	Ø	
705	M	Ø	Ø	Ø	Ø	
718	F	Ø	Ø	Ø	Ø	
719	F	Ø	Ø	Ø	Ø	
720	F	Ø	Ø	Ø	Ø	
721	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
706	M	slightly turbid	yellow	1.043	6.7	10, 30, 50, 70, 73, 91
707	M	turbid	yellow	1.042	5.8	30, 50, 72, 73, 90
708	M	slightly turbid	yellow	1.045	6.7	20, 30, 50, 70, 72, 73, 90
709	M	clear	yellow	1.046	6.7	10, 20, 30, 50, 70, 72, 90
722	F	slightly turbid	yellow	1.048	6.4	20, 30, 72, 90
723	F	turbid	yellow	1.045	6.7	10, 20, 30, 70, 72, 73, 90
724	F	slightly turbid	yellow	1.048	6.7	11, 30, 36, 70, 72, 90
725	F	slightly turbid	yellow	1.046	6.4	10, 20, 31, 70, 72, 90

Urinalysis

Compound: Octopirox

Dose: 40 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
706	M	Ø	Ø	Ø	Ø	
707	M	Ø	Ø	Ø	Ø	
708	M	Ø	Ø	Ø	Ø	
708	M	Ø	Ø	Ø	Ø	
722	F	Ø	Ø	Ø	Ø	
723	F	Ø	Ø	Ø	Ø	
724	F	Ø	Ø	+	Ø	
725	F	Ø	Ø	Ø	Ø	

Urinalysis

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Appearance	Color	Spec. Grav.	pH	Sediment
710	M	turbid	yellow	1.050	6.2	10, 20, 30, 50, 72, 73, 90
711	M	clear	yellow	1.033	5.8	10, 20, 30, 50, 72, 90
712	M	slightly turbid	yellow	1.052	6.7	20, 30, 50, 70, 72, 90
713	M	clear	yellow	1.042	6.4	20, 30, 50, 72, 90
726	F	slightly turbid	yellow	1.044	6.7	10, 20, 30, 70, 72, 90
727	F	slightly turbid	yellow	1.049	5.8	10, 20, 30, 72, 73, 91
728	F	slightly turbid	yellow	1.052	5.8	10, 30, 72, 90
729	F	slightly turbid	yellow	1.052	7.0	20, 30, 70, 72, 90

Urinalysis

Compound: Octopirox

Dose: 100 mg/kg

Administration: oral in food

Species: Beagle, English

Week: Final value

Animal No.	Sex	Protein	Glucose	Hemoglobin	Bilirubin	Ketone Bodies
710	M	Ø	Ø	Ø	Ø	
	M	Ø	Ø	Ø	Ø	
	M	Ø	Ø	Ø	Ø	
	M	Ø	Ø	Ø	Ø	
	F	Ø	Ø	Ø	Ø	
	F	Ø	Ø	Ø	Ø	
	F	Ø	Ø	Ø	Ø	
	F	Ø	Ø	Ø	Ø	

Body weight, Organ weight

Compound: Octopirox

Dose: Control

in g

Administration: untreated

Species: Beagle, English

Animal No.	Sex	Body wt.	Heart	Lungs	Liver	Kidneys	Spleen	Brain	Pancreas	Testicles/ Ovary	Adrenals	Pituitary	Thyroid
698	M	15980	115.0	117.0	389.0	46.0	35.0	89.0	36.0	17.0	0.799	0.045	1.228
699	M	17060	137.0	130.0	423.0	57.0	50.0	99.0	32.0	21.0	1.099	0.089	0.959
700	M	15410	134.0	135.0	490.0	58.0	37.0	92.0	25.0	20.0	1.082	0.115	1.299
701	M	17090	142.0	142.0	541.0	60.0	61.0	92.0	34.0	25.0	1.200	0.135	1.149
714	F	14250	111.0	122.0	400.0	50.0	43.0	95.0	27.0	0.963	1.011	0.088	0.761
715	F	13550	97.0	103.0	359.0	53.0	36.0	86.0	28.0	0.834	0.973	0.079	0.666
716	F	13240	114.0	112.0	420.0	54.0	55.0	92.0	29.0	1.295	1.013	0.090	0.792
717	F	14000	120.0	122.0	378.0	54.0	50.0	86.0	32.0	0.990	1.216	0.107	0.644

Body weight, Organ weight

Compound: Octopirox

Dose: 16 mg/kg

in g

Administration: oral in food

Species: Beagle, English

Animal No.	Sex	Body wt.	Heart	Lungs	Liver	Kidneys	Spleen	Brain	Pancreas	Testicles/ Ovary	Adrenals	Pituitary	Thyroid
702	M	17180	132.0	149.0	399.0	55.0	42.0	89.0	30.0	25.0	0.732	0.085	0.996
703	M	14280	119.0	132.0	422.0	54.0	31.0	87.0	30.0	21.0	1.128	0.089	1.062
704	M	17530	156.0	152.0	467.0	54.0	45.0	87.0	32.0	19.0	0.795	0.099	1.483
705	M	17770	139.0	147.0	528.0	60.0	42.0	96.0	33.0	20.0	0.989	0.099	1.146
718	F	11860	100.0	120.0	413.0	47.0	25.0	85.0	31.0	1.705	0.944	0.099	0.586
719	F	12740	105.0	114.0	390.0	56.0	33.0	76.0	24.0	0.941	1.057	0.105	0.899
720	F	13430	107.0	113.0	406.0	53.0	41.0	83.0	37.0	0.999	1.071	0.096	0.765
721	F	14430	111.0	112.0	360.0	50.0	35.0	76.0	32.0	0.768	1.352	0.099	1.163

Body weight, Organ weight

Compound: Octopirox

Dose: 40 mg/kg

in g

Administration: oral in food

Species: Beagle, English

Animal No.	Sex	Body wt.	Heart	Lungs	Liver	Kidneys	Spleen	Brain	Pancreas	Testicles/ Ovary	Adrenals	Pituitary	Thyroid
706	M	17650	121.0	127.0	467.0	57.0	65.0*	94.0	29.0	19.0	1.143	0.078	0.769
707	M	17120	142.0	145.0	478.0	62.0	33.0	97.0	38.0	24.0	1.237	0.086	1.070
708	M	16000	119.0	137.0	439.0	42.0	37.0	90.0	32.0	22.0	1.157	0.099	1.040
709	M	16280	126.0	135.0	428.0	58.0	39.0	83.0	31.0	21.0	1.199	0.113	0.983
722	F	15620	112.0	137.0	407.0	58.0	87.0*	87.0	29.0	1.415	1.042	0.109	0.939
723	F	13050	87.0	107.0	347.0	56.0	80.0*	82.0	28.0	1.064	0.999	0.097	0.641
724	F	12940	107.0	117.0	386.0	56.0	42.0	89.0	32.0	1.762	1.172	0.129	0.788
725	F	14100	119.0	130.0	462.0	54.0	46.0	88.0	29.0	1.141	1.127	0.087	1.143

*congestion

Body weight, Organ weight

Compound: Octopirox

Dose: 100 mg/kg

in g

Administration: oral in food

Species: Beagle, English

Animal No.	Sex	Body wt.	Heart	Lungs	Liver	Kidneys	Spleen	Brain	Pancreas	Testicles/ Ovary	Adrenals	Pituitary	Thyroid
710	M	16700	137.0	140.0	508.0	69.0	41.0	88.0	30.0	22.0	1.074	0.105	0.827
711	M	16620	126.0	141.0	554.0	62.0	42.0	78.0	41.0	23.0	1.009	0.075	0.741
712	M	15650	133.0	130.0	491.0	63.0	34.0	89.0	27.0	20.0	0.999	0.090	1.374
713	M	15580	115.0	130.0	425.0	53.0	36.0	94.0	34.0	11.0	1.027	0.066	1.427
726	F	13210	111.0	113.0	453.0	45.0	34.0	76.0	28.0	0.928	1.169	0.068	1.004
727	F	14150	121.0	122.0	424.0	61.0	29.0	84.0	35.0	0.862	1.158	0.097	1.053
728	F	13070	111.0	118.0	371.0	53.0	64.0*	85.0	25.0	0.844	1.208	0.123	0.775
729	F	15070	126.0	146.0	392.0	47.0	36.0	79.0	30.0	0.936	1.099	0.095	0.800

*congestion

Composition of the prepared food Latz FF

Manufacturer:	Latz Purina GmbH 5350 Euskirchen Federal Republic of Germany

Composition:	55.5 %	Cereals
	14.4 %	Animal protein fodder
	14.0 %	Oil cake
	7.4 %	Fat
	3.2 %	Mineral fodder
	2.5 %	Dried vegetables
	1.0 %	Whey powder
	1.0 %	Yeasts
	1.0 %	Vitamin pre-mix
	100.0 %	

Vitamin A	24,000 I.U. per kg
Vitamin D_3	2,000 I.U. per kg
Vitamin E	24 mg per kg

Content of critical constituents:

21.0 %	Raw protein
11.0 %	Raw fat
1.0 %	Calcium
0.7 %	Phosphorus

PREPARATION FOR KILLING ANIMALS

T-61 HOECHST®

Composition (per 1 ml)

200 mg	N-[2-(m-methoxyphenyl)-2-ethylbutyl-(1)]-γ--hydroxybutyramide
50 mg	4,4'-methylene-bis-(cyclohexyltrimethylammonium iodide)
5 mg	4'-butylaminobenzoyl-2-dimethylaminoethanol hydrochloride