#729

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August 24, 2017

Food and Drug Administration
Center for Food Safety & Applied Nutrition
Office of Food Additive Safety (HFS-255)
5001 Campus Drive
College Park, MD 20740-3835
Attention: Dr. Paulette Gaynor
Re: GRAS Notification—Galactooligosaccharides

Dear Dr. Gaynor:

GRAS Associates, LLC, acting as the agent for Neo Cremar, Co., Ltd. (South Korea), is submitting for FDA review Form 3667 and the enclosed CD, free of viruses, containing a GRAS notification for *Galactooligosaccharides (GOS)* produced by transgalactosylation of cow's milk and goat's milk lactose. Along with Neo Cremar's determination of safety, an Expert Panel of qualified persons was assembled to assess the composite safety information of the subject substance with the intended use as an ingredient in selected conventional foods, coffees, and teas at levels ranging from 0.3 to 11 grams galactooligosaccharides per serving. The attached documentation contains the specific information that addresses the safe human food uses for the subject notified substance as discussed in the GRAS guidance document.

If additional information or clarification is needed as you and your colleagues proceed with the review, please feel free to contact me via telephone or email.

We look forward to your feedback.

Sincerely,

(b) (6)

Katrina V. Emmel, Ph.D.
Senior Scientist/Associate
GRAS Associates, LLC
27499 Riverview Center Blvd., Suite 212
Bonita Springs, FL 34134
951-496-4178
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Enclosure: GRAS Notification for Neo Cremar - *Galactooligosaccharides*

GRAS ASSOCIATES, LLC

GRAS Notification

of

Galactooligosaccharides (GOS)

Food Usage Conditions for General Recognition of Safety

on behalf of

Neo Cremar, Co., Ltd.
Seoul, South Korea

8/24/17

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FOREWORD

At the request of Neo Cremar Co., Ltd. (hereinafter "Neo Cremar"), GRAS Associates, LLC ("GA") has undertaken an independent safety evaluation of Neo Cremar's galactooligosaccharides (GOS) preparations. The purpose of the evaluation is to ascertain whether the intended food uses of GOS as described in Part 3 are generally recognized as safe, i.e., GRAS, under the intended conditions of use. In addition, Neo Cremar has asked that GRAS Associates act as an agent for the submission of this GRAS notification.

Neo Cremar based its GRAS assessment on a large body of information that addressed the safety/toxicity of GOS, history of use of GOS and similar compounds, and compositional details, specifications, and method of preparation of the notified substance.

Safety/toxicity studies performed with animals and human clinical trials were noted to have value. The composite safety/toxicity studies, in concert with dietary exposure information, ultimately provide the specific scientific foundation for the GRAS conclusion.

In addition to the product specifications, chemical properties, manufacturing, and safety-related information, Neo Cremar provided consumption/exposure information, along with other related documentation. This was augmented with an independent search of the scientific and regulatory literature extending through July 17, 2017. A GRAS assessment based primarily on the composite safety information, i.e., based on scientific procedures, was undertaken by Neo Cremar in concert with an Expert Panel review by GRAS Associates. Those references that were deemed pertinent to the objective at hand are listed in Part 7.

PART 1. SIGNED STATEMENTS AND CERTIFICATION

A. Claim of Exclusion From the Requirement for Premarket Approval Pursuant to Proposed 21 CFR 170.36(c)(1)[1]

In accordance with the 21 CFR 170 Subpart E, regulations for GRAS notices, Neo Cremar Co., Ltd. is pleased to submit a notice that we have concluded that galactooligosaccharides (GOS) derived from lactose are Generally Recognized As Safe (GRAS), and therefore, are not subject to premarket approval, under the intended conditions of food use.

[1] See 81 FR 54960, 17 August 2016. Accessible at: https://www.gpo.gov/fdsys/pkg/FR-2016-08-17/pdf/2016-19164.pdf (Accessed 4/15/17).

This conclusion is based on scientific procedures as detailed herein and on the opinion of independent experts qualified by scientific training and expertise to evaluate the safety of GOS under the conditions of intended use in food and infant formula.

Signed:

(b) (6)

Agent for Neo Cremar

Steven Overgaard
President
GRAS Associates, LLC
27499 Riverview Center Blvd.
Suite 212
Bonita Springs, FL 34134

Date: 8/24/17

B. Name and Address of Responsible Party

Neo Cremar Co., Ltd.
A-714, Hyundai Knowledge Center 11,
Beobwon-ro 11-gil, Songpa-gu, Seoul,
05836, South Korea

As the Responsible Party, Neo Cremar Co., Ltd. ("Neo Cremar") accepts responsibility for the GRAS conclusion that has been made for its GOS preparations that will be marketed as standardized powder or liquid under the names Nature's GOS, Mother's OLIGO/Beauty OLIGO, or Goat OLIGO, as described in the notified substance safety evaluation; consequently, GOS preparations, which meet the conditions described herein, are not subject to premarket approval requirements for food ingredients.

C. Common Name and Identity of Notified Substance

The common name of the ingredient to be used on food labels is galactooligosaccharides (GOS).

D. Conditions of Intended Use in Food

Neo Cremar intends to use galactooligosaccharides (GOS) as an ingredient in selected conventional foods, coffees, and teas at levels ranging from 0.3 to 11 grams GOS per serving, the same levels as other GOS products that have been determined to be GRAS and received "no questions" letters from the FDA (GRN 484, Clasado, 2013;

GRN 285, GTC Nutrition, 2009a; GRN 518, New Francisco, 2014; GRN 334, Yakult, 2010). Thus, the dietary exposure to Neo Cremar's GOS from the intended uses will not increase in the GOS-consuming population in the United States. The estimated mean and 90th percentile exposures to Neo Cremar's GOS from the intended uses in selected conventional foods are 12.2 and 25.3 grams per person per day (g/p/d) and in coffees and teas is 4.4 g/p/d for the total population.

Furthermore, Neo Cremar's galactooligosaccharides are intended for addition to term infant formula, and follow-on formula at a use level providing up to 7.8 grams of GOS per L of the reconstituted or ready to consume product as an alternative to oligosaccharides found in milk of lactating women. The same use of GOS and the resulting exposures from it have been estimated in a recent GRAS notice to FDA, submitted by Nestle Nutrition (GRN 620).

The serving levels reflect good manufacturing practices principles in that the quantities added to foods should not exceed the amounts reasonably required to accomplish its intended technical effect.

E. Basis for GRAS Conclusion

Pursuant to 21 CFR 170.30(a) and (b), Neo Cremar's GOS have been concluded to be GRAS on the basis of scientific procedures as discussed in the detailed description provided below.

GOS are not subject to premarket approval requirements of the FD&C Act based on Neo Cremar's conclusion that the substance is GRAS under the conditions of its intended food use.

Neo Cremar and GRAS Associates certify, to the best of our knowledge, that this GRAS notice is a complete, representative, and balanced assessment that includes all relevant information, both favorable and unfavorable, available and pertinent to the evaluation of safety and GRAS status of GOS.

F. Availability of Information

The data and information that serve as the basis for this GRAS Notice will be maintained at the offices of Neo Cremar, and will be made available during customary business hours, by:

Jaehwan Kim, CEO
Neo Cremar Co., Ltd.
A-714, Hyundai Knowledge Center 11
Beobwon-ro 11-gil, Songpa-gu, Seoul,
05836, South Korea

Tel: +82-2-401-4088
Fax: +82-2-401-4087

Should FDA have any questions or request additional information regarding this notice, Neo Cremar will supply these data and information.

Neo Cremar and GRAS Associates, LLC certify that no data or information contained herein are exempt from disclosure under the Freedom of Information Act (FOIA). No non-public, safety-related data were used by the Expert Panel to reach a GRAS conclusion.

PART 2. IDENTITY, METHOD OF MANUFACTURE, SPECIFICATIONS, AND PHYSICAL OR TECHNICAL EFFECT

A. Chemical Identity of Ingredient

GOS is derived from cow's milk or goat's milk lactose via a transgalactosylation catalyzed by β-galactosidase enzyme that has been determined to be safe, as discussed in Part 6.C.

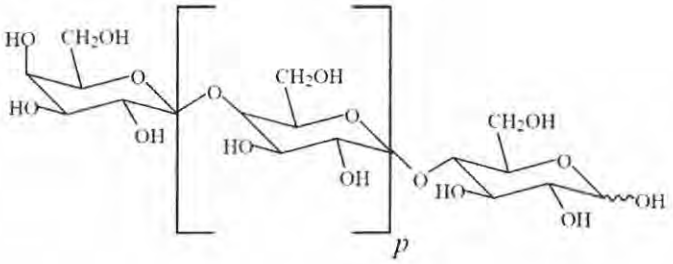
The common name of the substance of this notice is galactooligosaccharides (GOS), and the substance is also known as transgalactosylated oligosaccharide, transgalacto-oligosaccharide and oligogalactosyl-lactose. The terms transoligosaccharide (TOS) and trans-galacto-oligosaccharide (TGOS) are synonymously used for GOS. However, the term GOS is used most frequently, and is therefore used in this dossier.

The subject of this GRAS assessment will be marketed under the names Nature's GOS, Mother's OLIGO/Beauty OLIGO, and Goat OLIGO.

GOS is manufactured using a beta-galactosidase enzyme preparation derived from *Bacillus circulans* that mainly generates oligomers with beta-1,4 linkages. All GOS ingredients on the market have slightly different oligosaccharide profiles; however, trisaccharides with beta-1,3, beta-1,4, and beta-1,6 linkage configurations typically dominate the oligomer distribution in most GOS preparations. GOS consists of di- to octa-saccharides composed of 1-7 galactose units linked to a glucose molecule at the reducing end. The trisaccharide [O-beta-D-galactopyanosyl-(1-4)-O-beta-D-galactopyranosyl-(1-4)-beta-D-glucose] is the major saccharide among others found in GOS. The molecular weight of the individual oligosaccharides ranges from 342 (disaccharide) to 1,315 (octasaccharide) Daltons.

The chemical structure of GOS is shown in Figure 1. In the figure, p represents 0 to 6 sugar moieties.

Figure 1. General Chemical Structure of GOS



B. Manufacturing Processes

Neo Cremar's GOS is produced by a contract manufacturer to Neo Cremar's specifications, as well as at Neo Cremar's own facility. Both facilities are ISO 22000 certified, and are Organic, and Halal Certified. Neo Cremar manufactures Nature's GOS series from organic cow's milk lactose in both liquid (Nature's GOS-L, Nature's GOS-CL) and powder (Nature's GOS-P) forms, as well as high-purity Mother's OLIGO series, which will also be marketed under the name Beauty OLIGO, in liquid (Mother's OLIGO-L and Mother's OLIGO-CL) and powder (Mother's OLIGO-P and Mother's OLIGO-CP) forms. Neo Cremar also manufactures Goat OLIGO-CL from goat's milk lactose.

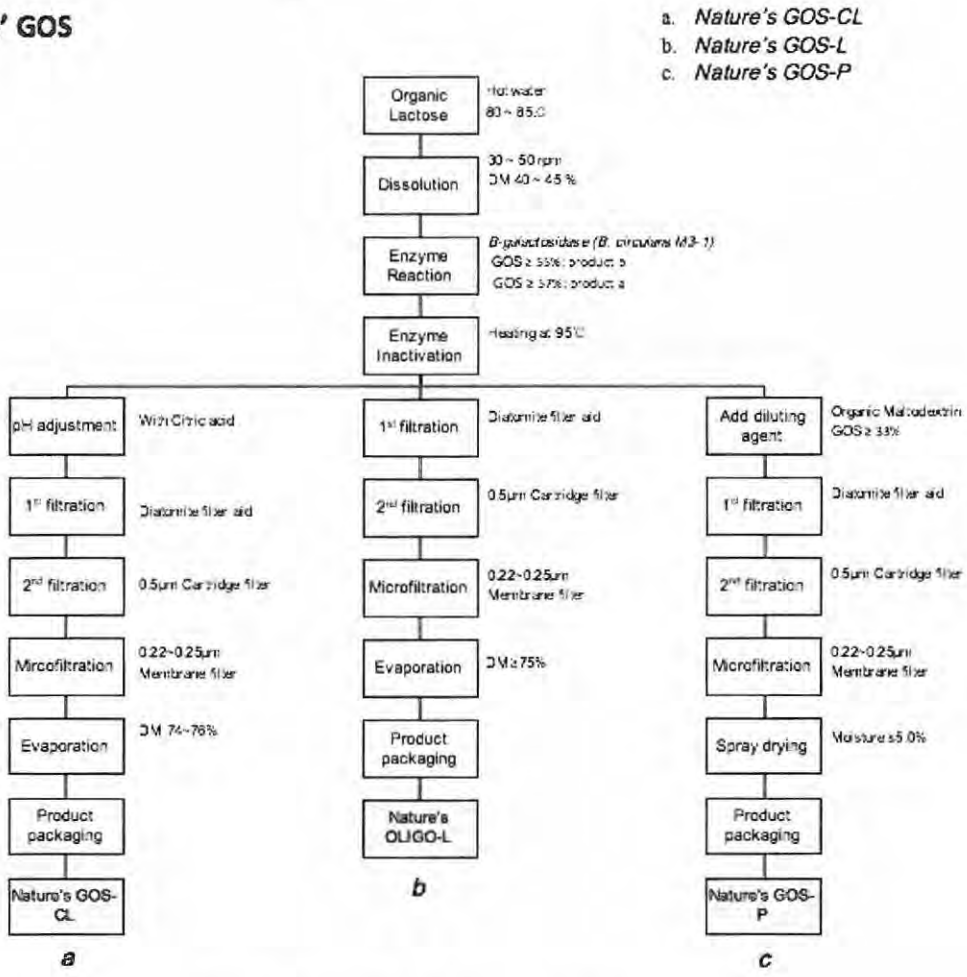
Neo Cremar's GOS preparations are manufactured through a multi-stage process from food grade cow's or goat's milk-derived lactose *via* a trans-galactosylation reaction catalyzed by a β-galactosidase enzyme obtained from a proprietary strain of the nontoxigenic non-pathogenic microorganism, *Bacillus circulans*, which is commonly used in food processing. The enzymatic reaction is performed by incubating β-galactosidase with a lactose solution. Lactose is dissolved in reverse osmosis (RO) water and a pH adjustment is performed. Then, β-galactosidase from *Bacillus circulans* is added to synthesize GOS. All reactions are terminated by heating at 95°C. This process results in the formation of a syrup containing at least 55% to 65% GOS. All finished products containing different levels of GOS (from 27% to 77%) are prepared from this syrup.

1. Nature's GOS Series Production

For the preparation of Nature's GOS series from organic cow's milk-derived lactose, following the termination of the enzymatic reaction, the syrup is either pH adjusted with citric acid prior to filtration, as is the case for Nature's GOS-CL, or directly filtered, as with Nature's GOS-L, in several steps through a diatomite filter aid and a 0.5 µm cartridge filter, and then microfiltered through a 0.22~0.25 µm membrane filter. The

filtered GOS liquid is evaporated, resulting in the formation of Nature's GOS-L or Nature's GOS-CL liquid preparations. For the preparation of Nature's GOS-P powder, the 55% GOS syrup is blended with maltodextrin, after which three filtration steps are performed. The resulting liquid mixture is evaporated, spray dried, and packaged. A manufacturing flow chart for these processes is provided in Figure 2.

Figure 2. Manufacturing Process of Nature's GOS Preparations



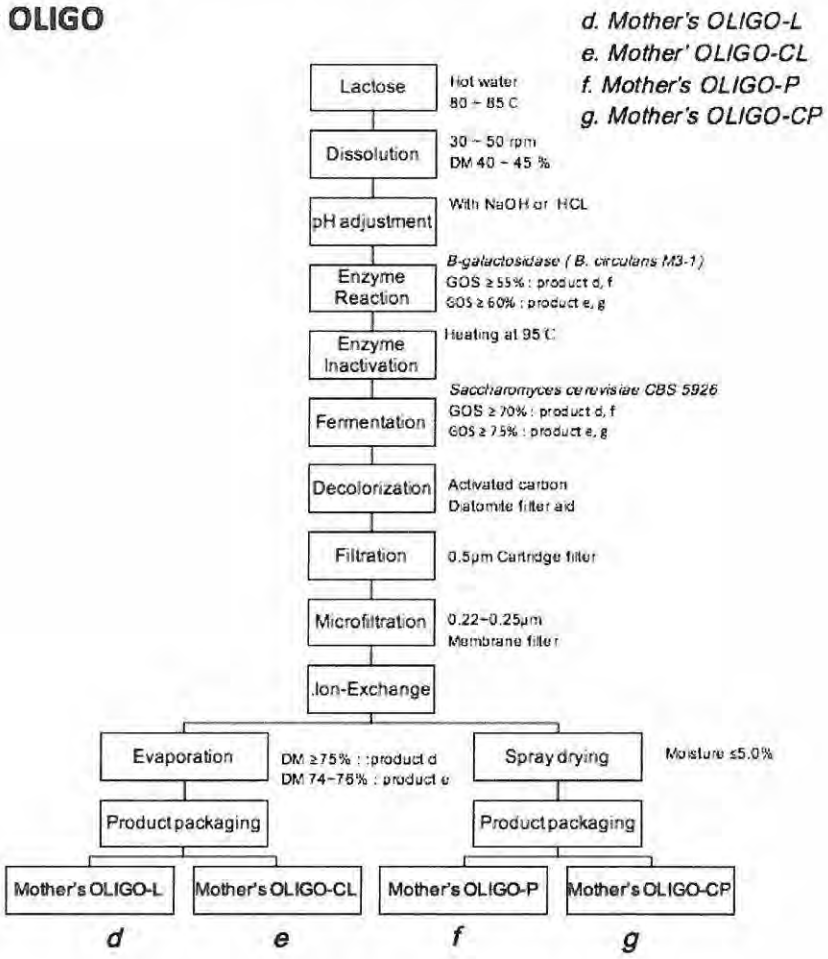
DM = Dry Matter; DE = Dextrose equivalent

2. Mother's/Beauty OLIGO Series Production

For the preparation of high purity Mother's/Beauty OLIGO series from cow's milk lactose, the GOS content is further increased through fermentation by adding yeast to the 55-60% GOS syrup that was produced by enzymatic hydrolysis with β-galactosidase. The yeast is derived from a non-toxigenic non-pathogenic microorganism, *Saccharomyces cerevisiae*, commonly used in food processing. The

syrup resulting from the fermentation is treated with activated carbon for decolorization and filtered in several steps. Ion exchange chromatography is utilized for further purification. The pooled fractions are either evaporated, resulting in Mother's/Beauty OLIGO-L or Mother's/Beauty OLIGO-CL liquid, or dried with a spray dryer into a powder (Mother's/Beauty OLIGO-P or Mother's/Beauty OLIGO-CP). A flow chart of the production process is provided in Figure 3.

Figure 3. Manufacturing Process of Mother's/Beauty OLIGO Preparations



DM = Dry Matter

3. Goat OLIGO-CL Series Production

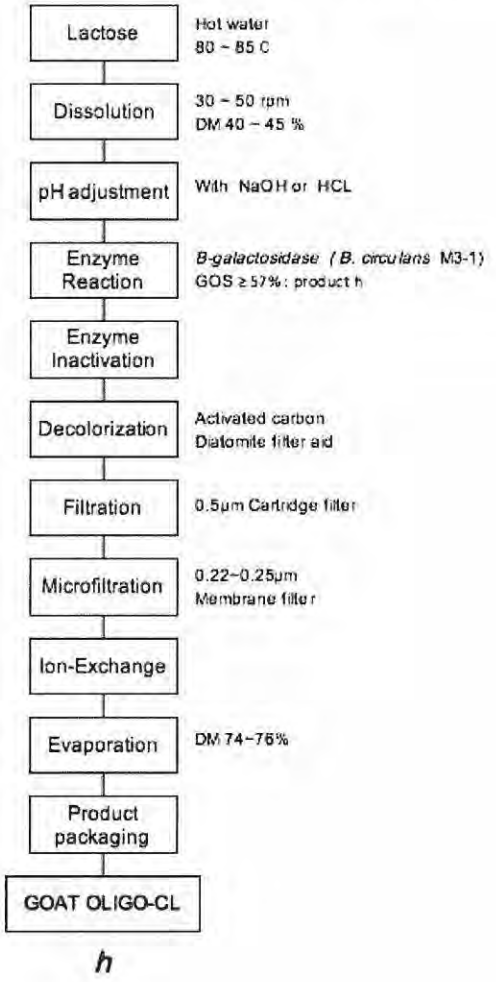
Goat OLIGO-CL is manufactured from goat's milk lactose in a similar production process as is used for the cow's milk lactose-derived oligosaccharides. The enzymatic reaction is terminated by heating, and the syrup is filtered in several steps through a diatomite filter aid, and a 0.5 μm cartridge filter, and is then microfiltered through a

0.22~0.25 μm membrane filter. The purified GOS is evaporated, resulting in the production of Goat OLIGO-CL. A flow chart of the production process is provided in Figure 4.

Figure 4. Manufacturing Process of Goat OLIGO-CL

- **GOAT OLIGO-CL**

h. GOAT OLIGO-CL



DM = Dry Matter

All raw materials used in the manufacturing process comply with Food Chemicals Codex (FCC) 10th Edition specifications. All filters and resins comply with 21 CFR 173 specifications. Specifications and supporting documentation for the raw materials and processing aids are provided Appendix 1.

C. Product Specifications

1. Specifications for Neo Cremar's Cow's Milk Lactose-Derived GOS Preparations and Supporting Methods

Neo Cremar has established specifications for its organic and non-organic cow's milk lactose-derived GOS ingredients, and analyses of 3 non-consecutive lots of each preparation demonstrate that each Nature's GOS and Mother's/Beauty OLIGO product is consistently manufactured to comply with established specifications. The specification parameters comprise physical appearance, purity, and GOS distribution, as well as limits for potential chemical and microbiological impurities and contaminants. These specifications are similar to those presented in previous GOS GRAS notifications (Clasado, 2013; 2014; Friesland Foods Domo, 2007; GTC Nutrition, 2009a; b; International Dairy Ingredients, 2013; Nestle Nutrition, 2016; New Francisco, 2014; 2015; Yakult, 2010).

Table 1. Specifications for Neo Cremar's Nature's GOS-L Preparation

Physical and Chemical Parameters	Nature's GOS-L Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Appearance Form & Color	Yellow syrup	Pass	Pass	Pass
Assay (DM)	More than 55.0% GOS	63.46%	62.88%	61.48%
Dry Matter	More than 75.0%	76.5%	76.66%	76.4%
Sulfated Ash	Less than 0.3%	0.20%	0.22%	0.19%
Nitrogen	Less than 0.1%	ND	ND	ND
Nitrite	Less than 2.0 ppm	ND	ND	ND
pH (10% solution)	4.0-7.0	6.23	6.22	5.95
Viscosity (25°C)	1,000 ~ 5,000 cPs	1,468	1,387	1,432
Lead	Less than 1.0 ppm	ND	ND	ND
Arsenic	Less than 0.1 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0008 ppm	0.0009 ppm	0.0008 ppm
Mercury	Less than 0.1 ppm	0.004 ppm	0.004 ppm	0.006 ppm
Total Plate Count	Less than 3,000 cfu/g	50 cfu/g	50 cfu/g	50 cfu/g

Physical and Chemical Parameters	Nature's GOS-L Specifications	Results of Batch Numbers		
		[redacted]	[redacted]	[redacted]
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

ND = not detected; DM= Dry matter

Table 2. Specifications for Neo Cremar's Nature's GOS-CL Preparation

Physical and Chemical Parameters	Nature's GOS-CL Specifications	Results of Batch Numbers		
		[redacted]	[redacted]	[redacted]
Appearance Form & Color	Yellow syrup	Pass	Pass	Pass
Assay (DM)	More than 57.0% GOS	62.1%	62.0%	61.9%
Dry Matter	74.0-76.0%	75.3%	75.8%	75.2%
Lactose (DM)	Less than 23.0%	18.08%	18.02%	18.01%
Glucose (DM)	Less than 22.0%	18.98%	19.12%	19.21%
Galactose (DM)	More than 0.8%	0.82%	0.83%	0.87%
Sulfated Ash	Less than 0.3%	0.2%	0.21%	0.21%
Nitrogen	Less than 0.1%	ND	ND	0.001%
Nitrite	Less than 2.0 ppm	ND	ND	ND
pH	3.2-3.8	3.53	3.57	3.72
Viscosity (25°C)	1,000 ~ 5,000 cPs	1,478	1,495	1,423
Arsenic	Less than 0.1 ppm	ND	ND	ND
Lead	Less than 1.0 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0014 ppm	0.0018 ppm	0.0014 ppm

Physical and Chemical Parameters	Nature's GOS-CL Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Mercury	Less than 0.1 ppm	0.009 ppm	0.01 ppm	0.009 ppm
Total Plate Count	Less than 3,000 cfu/g	30 cfu/g	50 cfu/g	50 cfu/g
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

ND = not detected; DM = dry matter

Table 3. Specifications for Neo Cremar's Nature's GOS-P Preparation

Physical and Chemical Parameters	Nature's GOS-P Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Appearance Form & Color	White to yellow powder	Pass	Pass	Pass
Assay (DM)	More than 33.0% GOS	33.5%	34.1%	34.3%
Moisture	Less than 5.0%	3.45%	3.42%	3.36%
Sulfated Ash	Less than 0.3%	0.11%	0.12%	0.11%
Nitrogen	Less than 0.1%	0.001%	0.001%	ND
Nitrate	Less than 50 ppm	23.2 ppm	24.8 ppm	26.3 ppm
Nitrite	Less than 0.5 ppm	ND	ND	ND
pH (10% solution)	3.0 – 6.0	4.2	4.71	4.32
Lead	Less than 1.0 ppm	ND	ND	ND
Arsenic	Less than 0.1 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0007 ppm	0.0006 ppm	0.0008 ppm

Physical and Chemical Parameters	Nature's GOS-P Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Mercury	Less than 0.1 ppm	0.004 ppm	0.002 ppm	0.001 ppm
Total Plate Count	Less than 1,000 cfu/g	10 cfu/g	20 cfu/g	10 cfu/g
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

ND = not detected; DM = dry matter

Table 4. Specifications for Neo Cremar's Mother's OLIGO-L[a] Preparation

Physical and Chemical Parameters	Mother's OLIGO-L Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Appearance Form & Color	Clear to yellow syrup	Pass	Pass	Pass
Assay (DM)	More than 70.0% GOS	71.62%	72.43%	72.64%
Dry Matter	More than 75.0%	76.36%	76.69%	76.78%
Sulfated Ash	Less than 0.3%	0.14%	0.15%	0.14%
Nitrogen	Less than 0.1%	0.05%	0.06%	0.05%
Nitrite	Less than 2.0 ppm	ND	ND	ND
pH (10% solution)	4.0-7.0	6.21	6.30	6.12
Viscosity (25°C)	1,000-5,000 cPs	1,882 cPs	1,869 cPs	1,879 cPs
Lead	Less than 1.0 ppm	ND	ND	ND
Arsenic	Less than 0.1 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0028 ppm	0.0028 ppm	0.0029 ppm

Physical and Chemical Parameters	Mother's OLIGO-L Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Mercury	Less than 0.1 ppm	0.006 ppm	0.007 ppm	0.008 ppm
Total Plate Count	Less than 3,000 cfu/g	30 cfu/g	50 cfu/g	50 cfu/g
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

[a] Mother's OLIGO-L will also be marketed as Beauty OLIGO-L
ND = not detected; DM = dry matter

Table 5. Specifications for Neo Cremar's Mother's OLIGO-CL[a] Preparation

Physical and Chemical Parameters	Mother's OLIGO-CL Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Appearance Form & Color	Clear to yellow syrup	Pass	Pass	Pass
Assay (DM)	More than 75.0% GOS	77.16%	77.23%	77.19%
Dry Matter	74.0-76.0%	75.4%	75.8%	75.9%
Lactose (DM)	Less than 23.0%	17.57%	17.3%	17.46%
Glucose (DM)	Less than 5.0%	1.86%	1.87%	1.88%
Galactose (DM)	More than 0.8%	3.41%	3.60%	3.53%
Sulfated Ash	Less than 0.3%	0.21%	0.20%	0.21%
Nitrogen	Less than 0.1%	ND	ND	0.001%
Nitrite	Less than 2.0 ppm	ND	ND	ND
pH	3.2-3.8	3.21	3.48	3.52
Viscosity (25°C)	1,000-5,000 cPs	1,427 cPs	1,486 cPs	1,476 cPs

Physical and Chemical Parameters	Mother's OLIGO-CL Specifications	Results of Batch Numbers		
		(b)(4)	(b)(4)	(b)(4)
Lead	Less than 1.0 ppm	ND	ND	ND
Arsenic	Less than 0.1 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0038 ppm	0.0038 ppm	0.0039 ppm
Mercury	Less than 0.1 ppm	0.006 ppm	0.007 ppm	0.006 ppm
Total Plate Count	Less than 3,000 cfu/g	30 cfu/g	30 cfu/g	40 cfu/g
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

[a] Mother's OLIGO-CL will also be marketed as Beauty OLIGO-CL
ND = not detected; DM = dry matter

Table 6. Specifications for Neo Cremar's Mother's OLIGO-P[a] Preparation

Physical and Chemical Parameters	Mother's OLIGO-P Specifications	Results of Batch Numbers		
		(b)(4)	(b)(4)	(b)(4)
Appearance Form & Color	White to yellow powder	Pass	Pass	Pass
Assay (DM)	More than 70.0% GOS	71.4%	72.54%	71.14%
Moisture	Less than 5.0%	4.20%	3.20%	3.30%
Sulfated Ash	Less than 0.3%	0.16%	0.15%	0.16%
Nitrogen	Less than 0.1%	ND	ND	0.01%
Nitrate	Less than 50 ppm	19.8 ppm	19.8 ppm	20.1 ppm
Nitrite	Less than 0.5 ppm	ND	ND	ND
pH (10% solution)	4.0-7.0	6.08	6.07	6.27

Physical and Chemical Parameters	Mother's OLIGO-P Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Lead	Less than 1.0 ppm	ND	ND	ND
Arsenic	Less than 0.1 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0005 ppm	0.0006 ppm	0.0005 ppm
Mercury	Less than 0.1 ppm	0.007 ppm	0.008 ppm	0.008 ppm
Total Plate Count	Less than 1,000 cfu/g	10 cfu/g	10 cfu/g	20 cfu/g
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

[a] Mother's OLIGO-P will also be marketed as Beauty OLIGO-P
ND = not detected; DM = dry matter

Table 7. Specifications for Neo Cremar's Mother's OLIGO-CP[a] Preparation

Physical and Chemical Parameters	Mother's OLIGO-CP Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Appearance Form & Color	White to light yellow powder	Pass	Pass	Pass
Assay (DM)	More than 75.0% GOS	77.12%	77.53%	76.75%
Moisture	Less than 5.0%	3.3%	3.2%	3.1%
Lactose (DM)	Less than 23.0%	17.71%	17.34%	18.01%
Glucose (DM)	Less than 5.0%	1.86%	1.89%	1.95%
Galactose (DM)	More than 0.8%	3.31%	3.24%	3.29%
Sulfated Ash	Less than 0.3%	0.11%	0.12%	0.11%
Nitrogen	Less than 0.1%	ND	ND	0.001%

Physical and Chemical Parameters	Mother's OLIGO-CP Specifications	Results of Batch Numbers		
		[redacted]	[redacted]	[redacted]
Nitrate	Less than 50 ppm	24.6 ppm	25.8 ppm	24.7 ppm
Nitrite	Less than 0.5 ppm	ND	ND	ND
pH (10% solution)	3.0-6.0	4.67	4.55	4.62
Lead	Less than 1.0 ppm	ND	ND	ND
Arsenic	Less than 0.1 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0006 ppm	0.0007 ppm	0.0006 ppm
Mercury	Less than 0.1 ppm	0.005 ppm	0.007 ppm	0.005 ppm
Total Plate Count	Less than 1,000 cfu/g	10 cfu/g	20 cfu/g	10 cfu/g
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

[a] Mother's OLIGO-CP will also be marketed as Beauty OLIGO-CP
ND = not detected; DM = dry matter

Neo Cremar analyzes its GOS preparations by high performance liquid chromatography (HPLC) following the AOAC 2001.02 method (Determination of TGOS). In addition to the presentation of key specifications found in Table 1-Table 7, certificates of analysis for three representative lots of each GOS preparation are provided in Appendix 2. The chromatograms for a representative lot of each GOS preparation are provided in Appendix 3. The collection of these reports demonstrates that the substance is well characterized and meets the established purity criteria.

2. Specifications for Neo Cremar's Goat's Milk Lactose-Derived GOS Preparations and Supporting Methods

Neo Cremar has established specifications for its goat's milk lactose-derived GOS ingredients, and analyses of 3 non-consecutive lots demonstrate that Goat OLIGO-CL is

consistently manufactured to comply with established specifications. The specification parameters comprise physical appearance, purity, and GOS distribution, as well as limits for potential chemical and microbiological impurities and contaminants. These specifications are comparable to those established for cow's milk lactose-derived GOS preparations, as described in Part 2.C.1.

Table 8. Specifications for Neo Cremar's Goat OLIGO-CL Preparation

Physical and Chemical Parameters	Goat OLIGO-CL Specifications	Results of Batch Numbers		
		(b) (4)	(b) (4)	(b) (4)
Appearance Form & Color	Clear to yellow syrup	Pass	Pass	Pass
Assay (DM)	More than 57% GOS	59.4%	59.2%	59.3%
Dry Matter	74-76.0%	75.8%	75.3%	75.2%
Lactose (DM)	Less than 23.0%	17.29%	20.14%	18.8%
Glucose (DM)	Less than 22.0%	21.53%	18.72%	20.6%
Galactose (DM)	More than 0.8%	1.83%	1.98%	1.92%
Sulfated Ash	Less than 0.3%	0.05%	0.05%	0.05%
Nitrogen	Less than 0.1%	0.008%	0.008%	0.008%
Nitrite	Less than 2.0 ppm	ND	ND	ND
pH	3.2-3.8	3.55	3.66	3.57
Viscosity (25°C)	1,000-5,000 cPs	1,212 cPs	1,527 cPs	1,463 cPs
Lead	Less than 1.0 ppm	ND	ND	ND
Arsenic	Less than 0.1 ppm	ND	ND	ND
Cadmium	Less than 0.06 ppm	0.0012 ppm	0.0015 ppm	0.0013 ppm
Mercury	Less than 0.1 ppm	0.009 ppm	0.01 ppm	0.009 ppm
Total Plate Count	Less than 3,000 cfu/g	30 cfu/g	50 cfu/g	50 cfu/g
Yeast and Mold	Less than 50 cfu/g	Negative	Negative	Negative
E. coli	Negative in 25 g	Negative	Negative	Negative
Coliform (mpn/g)	Negative in 25 g	Negative	Negative	Negative

Physical and Chemical Parameters	Goat OLIGO-CL Specifications	Results of Batch Numbers		
		[redacted]	[redacted]	[redacted]
Salmonella spp.	Negative in 75 g	Negative	Negative	Negative
Staphylococcus aureus	Negative in 75 g	Negative	Negative	Negative
Enterobacter sakazakii	Negative in 300 g	Negative	Negative	Negative

ND = not detected; DM = dry matter

Neo Cremar analyzes its Goat OLIGO-CL preparation by HPLC. In addition to the presentation of key specifications found in Table 8, certificates of analysis for three representative lots of Goat OLIGO-CL are provided in Appendix 4. The chromatogram for a representative lot of Goat OLIGO-CL is provided in Appendix 5. The collection of these reports demonstrates that the substance is well characterized and meets the established purity criteria.

D. Physical or Technical Effect

GOS are intended to be added to term infant formula and follow-on formula, and in a variety of conventional foods, as dietary sources of non-digestible oligosaccharides.

E. Stability Data on Galactooligosaccharides

The stability of GOS has been well-documented in the literature and in previous GRAS notifications. GOS are generally reported to be stable under high temperature and acidic conditions.

With respect to GOS syrup, Sangwan et al. (2011) states:

> "GOS syrup is very stable under low pH conditions. Storage at low pH will not degrade GOS…[t]hey are stable to pH 2 at 37°C for several months…The presence of β-type linkages makes them resistant to high temperature in acidic medium. They remain unchanged after treatment at 160°C for 10 min at neutral pH and after treatment at 120°C for 10 min at a pH of 3 [and] for 10 min at a pH of 2."

In a study of GOS formed during the production of yogurt with β-galactosidase enzyme, Vénica et al. (2015) reported no changes in the content of GOS over the refrigerated storage period in different yogurt matrices. The authors noted that GOS stability could be decreased in yogurts of different cultures or with enzymes functioning under different pH conditions.

Stability data presented in previously submitted GRNs can be summarized, as follows:

- A liquid GOS preparation was reported to be stable at pH values ranging from 3-7 and high temperature conditions (80-120°C). A soft drink model system was also used to demonstrate stability under pre-pasteurization, post-pasteurization, and storage at 7 days, 3 months, and 6 months (GRN 236; Friesland Foods Domo, 2007).

- A 6-month stability study was conducted on powdered GOS stored at 30°C and 80% relative humidity (RH). It was reported that the GOS was shelf-stable for at least 6 months. Solutions of 5% GOS, at pH values ranging from 3-7, were also reported to be stable (GRNs 285 and 286; GTC Nutrition, 2009a; b).

- A GOS syrup was reported to be stable over a period of 18 months; however, a "slight" decrease in pH and a darkening of color was observed over time. These observations were attributed to the presence of monosaccharides. Under elevated temperature (up to 55°C) and low pH (2 or 3) conditions, the GOS syrup was reported to be stable (GRN 334; Yakult, 2010).

- A GOS syrup was reported to be stable under accelerated (30°C and 65% RH or 40°C and 75% RH) and real-time storage conditions (25°C and 60% RH) over a period of 6 months. A darkening of the syrup, and corresponding increase in caramel taste, was observed, and was more distinct in the samples stored at 40°C and 75% RH. These observations are not a safety concern, and the GOS content was not significantly altered over time.

  Samples of GOS powder were reported to be stable at 25°C over the course of 24 months.

  GOS in a fruit juice matrix with a pH of 4.5, stored at room temperature, was reported to be stable over the course of 6 months. In addition, GOS solutions at pH values ranging from 5-7 and temperatures from 80-120°C were observed to be stable over the course of 30 minutes, whereas some hydrolysis of galacto-oligosaccharides were observed in solutions with pH values ranging from 3-4 under high temperature conditions (GRN 484; Clasado, 2013).

- Disintegration of GOS has been reported at temperatures exceeding 110°C; however, no supporting data was provided (GRN 489; International Dairy Ingredients, 2013).

2. Stability Data for Neo Cremar's Galactooligosaccharides Preparation

Neo Cremar is currently conducting a 24-month shelf-stability study on its GOS preparations. Samples of each GOS preparation are stored under ambient conditions over the course of the study, and are tested for assay, moisture, and microbiological parameters at 0, 6, 12, 18, and 24 months.

Summary tables (Table 9-Table 16) of the available shelf-stability data are presented for each GOS preparation below.

Table 9. Nature's GOS-L Shelf-Stability Data

Parameter	Date / Spec.	NCOG20160406					NCOG20160511					NCOG20160601				
		2016.04.06	2016.10.07	2017.04.05			2016.05.11	2016.11.12	2017.05.11			2016.06.01	2016.12.02	2017.06.01		
Appearance	Yellow syrup	Passed	Passed	Passed			Passed	Passed	Passed			Passed	Passed	Passed		
Dry matter (%)	≥75%	76.81	76.9	77.2			77.17	77.2	77.9			77.2	77.8	78.3		
GOS (%)	≥55%	57.54	56.32	56.5			57.56	57.7	57.1			57.14	56.8	56.8		
Total Mesophilic bacteria	500CFU/g	10	N.D	20			10	20	20			10	N.D	30		
Total Enterobacteriaceae	Neg/10g	N.D	N.D	N.D			N.D	N.D	N.D			N.D	N.D	N.D		
Yeast and Molds	50CFU/g	N.D	N.D	N.D			N.D	N.D	N.D			N.D	N.D	N.D		
Bacillus cereus	Neg/g	N.D	N.D	N.D			N.D	N.D	N.D			N.D	N.D	N.D		

ND = not detected

Table 10. Nature's GOS-CL Shelf-Stability Data

Parameter	Date / Spec.	OGCL20170116					OGCL20170120					OGCL20170123				
		2017. 01.16					2017. 01.20					2017. 01.23				
Appearance	Yellow syrup	Passed					Passed					Passed				
Dry matter (%)	≥75%	75.3					75.8					75.2				
GOS (%)	≥57%	62.1					62.0					61.9				
Total Mesophilic bacteria	500CFU/g	30					50					50				
Total Enterobacteriaceae	Neg/10g	N.D					N.D					N.D				
Yeast and Molds	50CFU/g	N.D					N.D					N.D				
Bacillus cereus	Neg/g	N.D					N.D					N.D				

ND = not detected

Table 11. Nature's GOS-P Shelf-Stability Data

Parameter	Date / Spec.	OGCP20161103					OGCP20161208					OGCP20170126				
		2016. 11.03	2017. 05.02				2016. 12.08	2017. 06.07				2017. 01.26				
Appearance	White to yellow powder	Passed	Passed				Passed	Passed				Passed				
Moisture (%)	≦5.0%	3.45	3.45				3.42	3.43				3.36				
GOS (%)	≧33%	33.5	33.1				34.1	34.0				34.3				
Total Mesophilic bacteria	500CFU/g	10	30				20	20				10				
Total Enterobacteriaceae	Neg/10g	N.D	N.D				N.D	N.D				N.D				
Yeast and Molds	50CFU/g	N.D	N.D				N.D	N.D				N.D				
Bacillus cereus	Neg/g	N.D	N.D				N.D	N.D				N.D				

ND = not detected

Table 12. Mother's OLIGO-L Shelf-Stability Data

Parameter	Date / Spec.	NCMO20150524					NCMO20150528					NCMO20150618				
		2015. 05.25	2015. 11.25	2016. 05.23	2016. 11.23	2017. 05.25	2015. 05.26	2015. 11.28	2016. 05.29	2016. 11.27	2017. 05.28	2015. 06.18	2015. 12.17	2016. 06.17	2016. 12.18	2017. 06.17
Appearance	Clear to yellow syrup	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed
Dry matter (%)	≥75%	76.8	76.8	76.8	76.7	76.5	76.2	76.1	76.1	76.2	75.9	75.8	75.8	75.7	75.6	75.7
GOS (%)	≥70%	73.5	73.4	73.3	73.5	73.4	72.9	72.8	72.8	72.6	72.5	73.6	73.5	73.5	73.4	73.4
Total Mesophilic bacteria	500CFU/g	N.D	N.D	N.D	10	10	N.D	20	20	20	40	N.D	N.D	30	40	40
Total Enterobacteriaceae	Neg/10g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
Yeast and Molds	50CFU/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	5	N.D	N.D	N.D	N.D	N.D
Bacillus cereus	Neg/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D

ND = not detected

Table 13. Mother's OLIGO-CL Shelf-Stability Data

Parameter	Date / Spec.	MOCL20141017					MOCL20150308					MOCL20150508				
		2014. 10.17	2015. 04.18	2015. 10.17	2016. 04.17	2016. 10.18	2015. 03.08	2015. 09.07	2016. 03.08	2016. 09.08	2017. 03.06	2015.05 06	2015. 11.05	2016. 05.07	2016. 11.08	2017. 05.09
Appearance	Clear to yellow syrup	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed
Dry matter (%)	74~76%	74.8	75.2	75.4	75.5	75.5	74.8	75.2	75.6	75.5	75.5	74.8	74.9	75.2	75.5	75.5
GOS (%)	≧75%	77.18	77.20	76.91	76.84	76.88	78.12	78.20	78.09	77.98	77.82	77.85	77.65	77.22	76.87	76.42
Total Mesophilic bactoria	500CFU/g	30	40	40	40	40	20	30	30	40	50	20	30	30	40	70
Total Enterobacteriaceae	Neg/10g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
Yeast and Molds	50CFU/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	5	N.D	N.D	N.D	N.D	N.D
Bacillus cereus	Neg/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D

ND = not detected

Table 14. Mother's OLIGO-P Shelf-Stability Data

Parameter	Date / Spec.	NCMP20140519					NCMP20140827					NCMP20141209				
		2014. 05.19	2014. 11.21	2015. 05.18	2015. 11.19	2016. 05.17	2014. 08.27	2015. 02.27	2015. 08.27	2016. 02.28	2016. 08.28	2014. 12.09	2015. 06.10	2015. 12.09	2016. 06.11	2016. 12.09
Appearance	White to yellow powder	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passec
Moisture (%)	≤5%	3.11	3.32	3.31	3.58	4.11	3.40	3.44	3.56	3.58	3.82	3.70	3.78	3.86	4.1	4.09
GOS (%)	≥70%	72.4	72.1	71.9	72.2	70.9	72.8	72.2	71.6	70.8	70.8	71.75	71.4	71.2	70.9	70.5
Total Mesophilic bacteria	500CFU/g	10	20	20	20	40	N.D	N.D	10	20	40	N.D	N.D	30	40	60
Total Enterobacteriaceae	Neg/10g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
Yeast and Molds	50CFU/g	N.D	N.D	N.D	N.D	20	N.D	N.D	N.D	N.D	10	N.D	N.D	N.D	N.D	N.D
Bacillus cereus	Neg/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D

ND = not detected

Table 15. Mother's OLIGO-CP Shelf-Stability Data

Parameter	Date / Spec.	MOCP20141025					MOCP20141130					MOCP20150208				
		2014.10.25	2015.04.24	2015.10.25	2016.04.24	2016.10.25	2014.11.30	2015.05.29	2015.11.30	2016.05.29	2016.11.30	2015.02.08	2015.08.07	2016.02.08	2016.08.07	2017.02.07
Appearance	White to yellow powder	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed
Moisture (%)	≥5.0%	3.3	3.37	3.38	3.43	3.45	3.10	3.21	3.38	3.42	3.48	3.20	3.31	3.38	3.45	3.46
GOS (%)	≥75%	77.12	77.30	76.9	76.88	76.21	77.85	77.62	76.98	76.7	76.1	77.53	76.9	77.12	76.98	76.81
Total Mesophilic bacteria	500CFU/g	10	20	20	20	30	10	20	20	20	40	20	30	30	40	40
Total Enterobacteriaceae	Neg/10g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
Yeast and Molds	50CFU/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
Bacillus cereus	Neg/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D

ND = not detected

Table 16. Goat OLIGO-CL Shelf-Stability Data

Parameter	Date / Spec.	NCGO20150415					NCGO20150504					NCGO20150602				
		2015. 04.15	2015. 10.14	2016. 04.15	2016. 10.14	2017. 02.15	2015. 05.04	2015. 11.03	2016. 05.03	2016. 11.04	2017. 05.03	2015. 06.02	2015. 12.02	2016. 06.01	2016. 12.02	2017. 06.01
Appearance	Clear to yellow syrup	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed	Passed
Dry matter (%)	74~76%	74.8	74.8	75.2	75.6	75.7	74.8	74.9	75.2	75.2	75.7	74.9	75.3	75.6	75.6	75.8
GOS (%)	≥57%	59.4	59.2	58.9	58.8	58.1	57.2	57.1	57.1	57.1	57.1	58.2	58.0	57.7	57.7	57.6
Total Mesophilic bacteria	500CFU/g	N.D	N.D	N.D	10	10	N.D	10	10	20	40	N.D	N.D	10	10	30
Total Enterobacteriaceae	Neg/10g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D
Yeast and Molds	50CFU/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	5	N.D	N.D	N.D	N.D	N.D
Bacillus cereus	Neg/g	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D	N.D

ND = not detected

The stability data in the scientific literature for GOS, the stability testing data presented for GOS in previously submitted GRNs, and the data supplied by Neo Cremar in Table 9 through Table 16, support the position that Neo Cremar's GOS preparations are well-suited for the intended food uses.

PART 3. DIETARY EXPOSURE

Neo Cremar intends to use its GOS preparations as substitutes for other GOS preparations that are currently used in selected conventional foods, coffees and teas at levels ranging from 0.3 to 11 g GOS per serving. There are no new food uses proposed for GOS by Neo Cremar. The same uses of GOS and the resulting exposures from it have been estimated in previous GRAS notices to FDA (GRN 285, 334, 484 and 518). The food categories and the intended use levels of GOS are summarized in Table 17.

As mentioned earlier, Neo Cremar also intends to market GOS as an ingredient for addition to term infant formula and follow-on formula at a use level providing up to 7.8 g of GOS per L of the reconstituted or ready to consume product as an alternative to oligosaccharides found in human milk of lactating women. Previously other GOS products in infant formula have been determined to be GRAS (GRN 620; GRN 569; GRN 495; GRN 334; GRN 286; GRN 236). Neo Cremar intends to use its GOS in the same food products and at levels proportional to those mentioned in GRN 620, which proposed to increase the use levels in infant formulas from 7.2 to 7.8 g per day and received a "no questions" letter from FDA.

Table 17. Intended Uses of Galactooligosaccharides

Food Category	Approximate serving size (g)	Maximum g GOS per serving[a]
Beverage concentrated (powder)	250	5
Bread	50	0.5
Brownies	40	0.4
Cakes, heavy weight	125	1.25
Cakes, light weight	55	0.55
Cakes, medium weight	80	0.8
Cheese soups	245	1.5
Coconut beverages	250	4
Coffee and tea	240	1.5
Coffee cakes, crumb cakes, doughnuts, Danish-style pastries, sweet rolls, sweet quick type breads, muffins, toaster pastries	55	0.55

Food Category	Approximate serving size (g)	Maximum g GOS per serving[a]
Coffee creamers and whiteners (liquid)	15	0.8
Coffee creamers and whiteners (powder)	2	0.8
Cookies	30	0.3
Crackers that are usually used as snacks	30	0.3
Egg soups; soups with legumes. as major ingredient; soups with grain products as major ingredient; potato soups; deep-yellow vegetable soups; tomato soups; other vegetable soups	245	1.5
French toast, pancakes	110	1.1
Frozen dairy desserts	125	3
Fruit drinks such as fruit juice drinks, fruit flavored drinks, sports drinks, etc.	250	5
Fruit juices (including citrus fruit juices) and nectars	250	4
Fruit juices, vegetable juices and juice mixtures baby food	125	2
Grain-based bars with or without filling or coating, e.g., breakfast bars, granola bars, rice cereal bars	40	0.4
Jellies, jams, preserves	20	5
Infant formula and follow-on formula	7.8 g/L	NA
Ice cream	125	1.28
Milk based meal replacement	250	5
Milk desserts, frozen like ice creams	75	1.5
Milk drink	250	9.5
Milk, milk substitute such as soy milk	250	5
Non-fruit beverages, including energy drinks	250	11
Novelty snacks	30	1.28
Pasta	55	1.28
Pies, cobblers, fruit crisps, turnovers, other pastries	125	1.25
Pudding and custards including baby foods	108	1.5
Ready-to-eat cereals	35	0.7
Ready-to-eat cereals (dry) for baby food	15	0.6
Ready-to-serve cereals for baby food	110	0.6
Soy beverages	240	3
Syrup flavorings	30	3
Vegetable juices	250	4
Waffles	85	0.85

Food Category	Approximate serving size (g)	Maximum g GOS per serving[a]
White sauces, milk gravies and cheese sauces	80	1
Yogurt	225	7.5

[a] Use levels are consistent with those stipulated in GRN 334, GRN 484, GRN 518 and GRN 620.

A. Estimate of Dietary Exposure to the Substance

The intended use of GOS in the same foods and at proportional use levels as those in GRN 285, GRN 334, GRN 484, and GRN 518 is not expected to noticeably affect the intake of GOS in the overall diet of the public from introduction into the market by another supplier who will have to compete in essentially the same markets and foods. Based on a statistical analysis of potential dietary intake, in the GRN 334 notice it was estimated that the mean consumption of GOS for the total population would be 12.2 g per person per day (0.28 g per kg bw per day) and the 90th percentile consumption would be 25.3 g per person per day (0.70 g per kg bw per day). For the intended uses of Neo Cremar's GOS in coffees and teas, the daily exposure to GOS from the intended uses in coffee and tea is 5.0 grams per person per day for adult males and 4.4 grams per person per day for the total population (users only), which was determined in GRN 484.

The exposures from use of GOS in infant formula have been estimated in previous GRAS notices to FDA (GRN 620; GRN 569; GRN 495; GRN 334; GRN 286; GRN 236). In the estimates reported by GTC Nutrition in GRN 286, survey data from the National Center for Health Statistics (NCHS) 2003-2004 National Health and Nutrition Examination Survey (NHANES) were used. This analysis suggests that 80% of the U.S. infant population is expected to consume GOS from these intended food uses. The intended use of GOS in infant formula at the maximum intended use level of 7.8 g per L was estimated to result in the mean and 90th percentile dietary intakes of 6.4 and 9.2 g per infant per day, respectively, for infants aged 0 through 6 months (GRN 620). For infants aged 7 through 12 months, the mean and 90th percentile all-users intakes of GOS was estimated as 5.6 and 8.6 g per infant per day, respectively. This analysis also revealed that only 3.7% of toddlers aged 1 to 2 years were estimated to consume GOS from infant formula uses with estimated intakes of 3.0 and 7.1 g per child per day for 90th percentile consumers.

B. Estimated Dietary Exposure to Any Other Substance That is Expected to be Formed In or On Food

No other substances are expected to be formed in or on food under the intended uses of Neo Cremar's GOS preparations.

C. Dietary Exposure to Contaminants or Byproducts

There are no known concerns regarding dietary exposure to contaminants or byproducts of GOS.

PART 4. SELF-LIMITING LEVELS OF USE

There are no known self-limiting levels of use.

PART 5. EXPERIENCE BASED ON COMMON USE IN FOOD BEFORE 1958

A. Other Information on Dietary Exposure

1. History of Traditional Medicinal and Human Food Use

There are no known documented medicinal or human food uses of GOS prior to January 1, 1958.

2. Summary of Regulatory History of Galactooligosaccharides

Galactooligosaccharides are approved for use in certain applications in the US, Canada, EU, and Australia and New Zealand, as described below.

3. U.S. Regulatory History

Based on available information from FDA's GRAS Notice Inventory website (FDA, 2017) as of August 1, 2017, FDA has issued 11 "no questions" letters on GRAS notices on galactooligosaccharides preparations. A summary of these filings is presented in Table 18.

Table 18. FDA's GRAS Notice Inventory on GOS Preparations[b]

Company	FDA GRAS Identifier	Intended Food Uses
1. Mead Johnson & Company	GRN 233[a]	Milk-based term infant formula at levels not to exceed 2 g/L GOS
2. Friesland Foods Domo	GRN 236	Term infant formula at a level of 5 g/L GOS, and in various foods at 1-7.5 g/serving
3. GTC Nutrition	GRN 285	Baby, infant, and toddler foods at 0.86-1.28 g/serving; in various foods at 1.28 g/serving
4. GTC Nutrition	GRN 286	Term infant formula and follow-on formula at 7.2 g GOS/L
5. Yakult Pharmaceutical Industry Co., Ltd.	GRN 334	Term infant formula at 7.2 g/L GOS and in various foods at 0.3-9.5 g/serving
6. Clasado, Inc.	GRN 484	Ingredient in foods and beverages

Company	FDA GRAS Identifier	Intended Food Uses
7. International Dairy Ingredients, Inc.	GRN 489	Infant formula at 4 g/L, infant and toddler foods at 3.8 mg/g, and in various foods at 2.66 g/serving
8. Clasado, Inc.	GRN 495	Term infant formula and follow-on formula at 7.2g/L GOS
9. New Francisco Biotechnology Corporation	GRN 518	Ingredient in foods
10. New Francisco Biotechnology Corporation	GRN 569	Term infant formula and follow-on formula at 7.2g/L GOS
11. Nestle Nutrition	GRN 620	Term infant formula and toddler formula at 7.8g/L GOS

[a] Combination of galacto-oligosaccharides and polydextrose. [b] GRN 671, submitted by Vitalus Nutrition Inc., regarding galacto-oligosaccharides, was filed by FDA on an unknown date, and FDA has since been asked to cease their evaluation.

In addition, a number of other cow's milk- and goat's milk-derived ingredients have been reviewed by FDA and subsequently issued a "no questions" letter. These GRNs are listed in Table 19 and Table 20, respectively.

Table 19. FDA's GRAS Notice Inventory on Other Cow's Milk-Derived Preparations[a]

Company	FDA GRAS Identifier	Preparation
1. Bonlac Foods Limited	GRN 11	Calcium casein peptone-calcium phosphate
2. American Dairy Products Institute	GRN 37	Whey protein isolate and dairy product solids
3. Glanbia Ingredients, Inc.	GRN 52	Whey mineral concentrate
4. Farmland National Packaging Company, L.P.	GRN 67	Milk-derived lactoferrin
5. DMV International	GRN 77	Milk-derived lactoferrin
6. Arla Foods Ingredients amba	GRN 78	D-Tagatose (produced from lactose)
7. Rhodia Inc.	GRN 128	Skim milk or dextrose culture with *Propionibacterium freudenreichii* subsp. *Shermanii*
8. aLF Ventures, LLC	GRN 130	Bovine milk-derived lactoferrin
9. Snow Brand Milk Products Co., Ltd., And IAS Co., Ltd.	GRN 196	Bovine milk basic protein fraction
10. Calpis Co. Ltd.	GRN 199	Concentrated hydrolyzed milk protein
11. CJ Cheiljedang, Inc.	GRN 352	D-Tagatose (produced from lactose)
12. Amour Proteines	GRN 376	Milk mineral concentrate
13. Morinaga Milk Industry Co., Ltd.	GRN 464	Cow's milk-derived lactoferrin
14. Moringa Milk Industry	GRN 465	Cow's milk-derived lactoferrin

Company	FDA GRAS Identifier	Preparation
Co., Ltd.		
15. American Dairy Products Institute/U.S. Dairy Export Council	GRN 504	Concentrated milk proteins
16. Leprino Foods Company	GRN 633	Whey protein
17. Synlait Milk Ltd	GRN 669	Cow's milk-derived lactoferrin

[a] Although not specified in all dossiers, there is a high likelihood that the raw material used in manufacture was derived from cow's milk.

Table 20. FDA's GRAS Notice Inventory on Goat's Milk-Derived Preparations

Company	FDA GRAS Identifier	Intended Food Uses
1. Ausnutria Hyproca	GRN 644	Non-fat dry goat milk and goat whey protein

A number of other similar oligosaccharides have also been determined to be GRAS for use in a variety of foods, as shown in Table 21.

Table 21. FDA's GRAS Notice Inventory on Other Oligosaccharide Preparations[a]

Company	FDA GRAS Identifier	Preparation
1. GTC Nutrition Company	GRN 44	Fructooligosaccharide
2. BioNeutra Inc	GRN 246	Isomalto-oligosaccharide mixture
3. Fugeia NV	GRN 343	Wheat bran extract composed primarily of xylo- and arabinoxylo-oligosaccharides
4. Shandong Longlive Bio-technology Co., Ltd.	GRN 458	Xylooligosaccharides
5. Ingredion Incorporated	GRN 537	Short-chain fructo-oligosaccharides
6. Tata Chemicals Limited	GRN 605	Fructo-oligosaccharides
7. New Francisco Biotechnology Corporation	GRN 623	Fructooligosaccharides

[a] GRN 674, submitted by BioNeutra North America Inc. regarding isomalto-oligosaccharides, was filed by FDA on October 14, 2016, and is presently under review.

4. Canadian Regulatory History

Health Canada's Food Directorate has reviewed and accepted galactooligosaccharides ("mixture of galactose oligomers enzymatically produced from lactose derived from whey") as an approved dietary fiber (Health Canada, 2013).

5. European Regulatory History

GOS produced from milk lactose has been on the EU market for many years and its use in infant and follow-on formula is regulated by Commission Directive 2006/141/EC. A combination of GOS and fructo-oligosaccharides (FOS) may be added to infant formulas and follow-on formulas such that their total content does not exceed 8 grams per L.

Vivinal GOS, produced by Friesland Foods/Campina Domo, is outside the scope of the novel food Regulation as it was on the EU market before May 15, 1997. The following Substantial Equivalence applications have been reviewed and found satisfactory by The Food Authority of Ireland in the recent years: Oligomate GOS for use in foods including infant and follow-on formulae (FSAI, 2013) and Nestle's GOS for addition to infant and follow-on formula at levels of 7.8 grams per L (FSAI, 2016).

6. Other Regulatory History

Food Standards Australia New Zealand (FSANZ) also reviewed the safety of the addition of GOS and inulin-derived substances to traditional foods, including infant formula and follow-on formula. Following its assessment, the agency concluded that the addition of GOS to infant formula up to a concentration of 8 grams per L is safe (FSANZ, 2008). The agency concluded that infant and follow-on formula containing up to 8 grams per L of inulin-derived substances and/or GOS, singularly or combined, in any ratio, are unlikely to pose a risk to infants. This conclusion was based on data from clinical trials in which infants were provided formulas supplemented with up to 10 grams per L of inulin-derived substances and GOS and no adverse effects were noted.

PART 6. NARRATIVE

GOS has been extensively reviewed by national and international agencies including FDA, SCF, and FSANZ, and have been demonstrated to be safe for use as an ingredient in a variety of foods, including infant formula. In several published experimental studies and review articles, the toxicity potential of GOS has been summarized. These studies include metabolic *(in vitro* and *in vivo)* experiments, short- and long-term toxicity in experimental animals, as well as clinical studies in adults and infants. A literature search of recent publications from scientific databases was conducted on GOS to identify any additional or new publications. Pertinent information related to the safety, primarily from recent publications, is summarized in the following sections.

A. GRAS Criteria

FDA defines "safe" or "safety" as it applies to food ingredients as:

> "…reasonable certainty in the minds of competent scientists that the substance is not harmful under the conditions of its intended use."[2]

Amplification is provided in that the conclusion of safety is to include probable consumption of the substance in question, the cumulative effect of the substance and appropriate safety factors. It is FDA's operational definition of safety that serves as the framework against which this evaluation is provided.

Furthermore, in discussing GRAS criteria, FDA notes that:

> "…General recognition of safety requires common knowledge, throughout the expert scientific community knowledgeable about the safety of substances directly or indirectly added to food, that there is reasonable certainty that the substance is not harmful under the conditions of its intended use."
>
> "'Common knowledge' can be based on either 'scientific procedures' or on experience based on common use in food prior to January 1, 1958."[3]

FDA discusses in more detail what is meant by the requirement of general knowledge and acceptance of pertinent information within the scientific community, i.e., the so-called "common knowledge element," in terms of the two following component elements:[4]

- Data and information relied upon to establish safety must be generally available, and this is most commonly established by utilizing published, peer-reviewed scientific journals; and
- There must be a basis to conclude that there is consensus (but not necessarily unanimity) among qualified scientists about the safety of the substance for its intended use, and this is established by relying upon secondary scientific literature such as published review articles, textbooks, or

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[2] See 21 CFR 170.3 (e)(i) and 81 FR 54959 Available at: https://www.federalregister.gov/documents/2016/08/17/2016-19164/substances-generally-recognized-as-safe (Accessed on 4/15/17).

[3] See 81 FR 54959 Available at: https://www.federalregister.gov/documents/2016/08/17/2016-19164/substances-generally-recognized-as-safe (Accessed on 4/15/17).

[4] See Footnote 1.

compendia, or by obtaining opinions of expert panels or opinions from authoritative bodies, such as JECFA and the National Academy of Sciences.

General recognition of safety based upon scientific procedures shall require the same quantity and quality of scientific evidence as is required to obtain approval of a food additive. General recognition of safety through scientific procedures shall be based upon the application of generally available and accepted scientific data, information, or methods, which ordinarily are published, as well as the application of scientific principles, and may be corroborated by the application of unpublished scientific data, information, or methods.

The apparent imprecision of the terms "appreciable," "at the time," and "reasonable certainty" demonstrates that the FDA recognizes the impossibility of providing absolute safety in this or any other area (Lu, 1988; Renwick, 1990; Rulis and Levitt, 2009).

As noted below, this safety assessment to ascertain GRAS status for GOS for the specified food uses meets FDA criteria for reasonable certainty of no harm by considering both the technical and common knowledge elements.

B. Neo Cremar's Findings on the Safety of Galactooligosaccharides

1. Absorption, Distribution, Metabolism & Excretion (ADME) Studies

The metabolism of GOS has been previously described, in detail and the related physiological effects of GOS consumption on gastrointestinal physiology have been well characterized (Friesland Foods Domo, 2007; GTC Nutrition, 2009a; Yakult, 2010).

It is generally recognized that GOS is not hydrolyzed by human salivary or pancreatic enzymes and passes undigested and unabsorbed to the colon. There galacto-oligosaccharides become available for bacterial fermentation by the indigenous microflora of the gut resulting in the production of innocuous metabolites (*e.g.*, short-chain fatty acids, CO_2, H_2) that are common fermentation products of the normal diet (Smiricky-Tjardes et al., 2003; Suarez et al., 1999). The unfermented dietary GOS are excreted in the feces. Although *in vitro* studies have reported slight differences in the efficiency by which particular bacterial species metabolize GOS (German et al., 2008; Ishikawa et al., 1995), fermentation by the intestinal microflora is indiscriminate to the oligosaccharide linkage and molecular weight, and bacterial metabolism of dietary galacto-oligosaccharides transported to the colon is expected to be largely complete (Matsumoto et al., 2004; Ohtsuka et al., 1991).

The consumption of galacto-oligosaccharides by humans, rats, and pigs has been demonstrated to reduce the intestinal and fecal pH, improve fecal consistency,

increase production of short-chain fatty acids and gas (i.e., CO_2 and H_2), and promote the growth of colonic *Bifidobacteria* and *Lactobacilli* spp. within the colon. These effects are generally recognized as desirable nutritional effects (Roberfroid et al., 2010). In addition, systemic effects produced by GOS in some studies of animals and in human trials include positive changes in mineral balance (i.e., calcium, magnesium, and phosphorus), beneficial effects on plasma levels of cholesterol, increased production of soluble immunoglobulin A (IgA), modulation of systemic cytokine levels and immune cell responses toward a less inflammatory state, increased numbers of immune cells that could phagocytose invading pathogens, and decreased incidence of atopic disease in at-risk subjects.

2. Toxicological Studies

GOS preparations, produced from lactose by enzymatic synthesis, have consistently been reported to be without evidence of toxicity in rodent studies (Table 22).Anthony et al. (2006) reported a no-observed-adverse-effect level (NOAEL) of 5,000 mg per kg body weight, the highest dose tested, for repeated-dose gavage administration of GOS (Vivinal GOS) to male and female Sprague-Dawley rats for 90-days. A NOAEL of 2,000 mg per kg body weight, the highest dose tested, was determined by Kobayashi et al. (2009) for Sprague-Dawley rats administered GOS (Oligomate GOS) via gavage for 90-days. In GRN 236, Friesland Foods Domo has cited findings from an unpublished subchronic feeding study supporting a NOAEL of 6,900 mg per kg body weight following dietary administration of GOS (Vivinal GOS) to Wistar rats for 90 days (Friesland Foods Domo, 2007).

The published toxicity studies include a neonatal rodent toxicity study conducted in rats (Kobayash et al., 2013). Juvenile Sprague-Dawley rats were administered GOS by gavage for 42 days starting on post-natal day 4. This study was conducted under current Good Laboratory Practice (cGLP). GOS consumption was reported to have no effect on the development of the animals and did not affect general condition, hematology, blood chemistry, or the outcome of any functional examinations. No abnormalities in any of the groups were observed during the macroscopic examination, assessment of organ weights, or histopathology of the reproductive organs. The NOAEL for Oligomate GOS in juvenile Sprague-Dawley rats was 2,000 mg per kg per day.

Moreover, Kobayashi et al. (2014) investigated the developmental and reproductive effects of Oligomate GOS in male and female parental rats, pregnant females, and their offspring. Male and female Sprague-Dawley rats (24 per sex per group) were administered GOS by gavage at doses of 0, 500, 1,000, or 2,000 mg per kg per day. Males were dosed 10 weeks prior to mating and 3 weeks thereafter; females were dosed 2 weeks before mating and GOS administration continued through pregnancy to day 20 of lactation. No toxicological effects on male or female parental animals

were noted. Consumption of GOS did not cause any adverse effects on reproduction/development from premating, copulation, implantation, or maintenance of pregnancy. The offspring were unaffected by the maternal consumption of GOS. No effects were observed on the number of live births, sex ratio, and external observation at the time of birth, body weight, pup survival, or external differentiation during lactation.

Desbuards et al. (2012) also evaluated the effects of perinatal galacto-oligosaccharides in pregnant mice and their offspring. In this study, pregnant BALB/cJ mice were fed a control diet (n=13) or a diet supplemented with a prebiotic mixture consisting of a GOS and inulin (9:1) (n=12) throughout gestation and lactation. Based on reported maternal feed intake, body weight values, and the GOS content of the test article, the resulting dose was equivalent to 1,620 mg GOS per kg bw per day and 400 mg inulin per kg bw per day. At weaning, male offspring were separated from their mothers, and weaned to the same test diet as their dams. The offspring were monitored and then killed on Day 48 after weaning. No significant differences in maternal body weight gain or feed intake during pregnancy were noted between the groups. Additionally, no significant differences in the number of offspring per dam were reported. Male pups administered GOS: inulin exhibited significantly higher body weights at weaning, and at Days 2, 40, and 48 after weaning compared to the control group. In male pups administered GOS: insulin, body length, colon length, and relative thigh muscle weights were significantly higher compared to the control group. No other developmental or reproductive toxicological endpoints were examined.

In GRN 620, a study on the subacute toxicity of Nestle GOS (Penard, 2015) was discussed (Nestle Nutrition, 2016). In brief, male and female Wistar rats (10 per sex per group) were administered Nestlé GOS by gavage for 30 consecutive days at doses of 0, 500, 1,000, or 2,000 mg per kg per day. Half of the control and 7 high-dose groups were followed for a 2-week recovery period to evaluate the regression of any toxic signs. There were no deaths, no relevant clinical signs, and no test item-related ophthalmological findings reported during the study. There was no variation in body weight or food consumption between groups. At study termination, there were no relevant changes reported in hematology, coagulation, serum clinical chemistry or urine parameters between groups. GOS consumption did not cause any significant organ weight, macroscopic, or histopathological changes. Under the defined experimental conditions, the oral administration of Nestlé GOS for 30 days in the Wistar rat at doses of 500, 1,000, and 2,000 mg per kg per day was well-tolerated clinically and histologically and did not induce any treatment-related effects. The NOAEL was 2,000 mg per kg per day, the highest dose tested.

In a recent study, described in GRN 671, the subchronic toxicity of VITAGOS GOS was assessed in Sprague-Dawley rats (10 per sex per group) for 90 consecutive

days by oral gavage at 0, 500, 1,000, or 2,000 mg GOS product per kg per day (Vitalis Nutrition, 2016). There were no deaths, relevant clinical signs, or abnormal ophthalmological findings reported at any dose levels in this study. Body weight and feed consumption were unaffected at 500 mg per kg per day dose in males and at all the doses in females. The body weight of male animals was reduced by 7 to 8% at 1,000 mg per kg per day, and 6 to 9% at 2,000 mg GOS product per kg per day dose throughout the treatment period. However, the reduction was not considered clinically adverse since the reduction was less than 10%. No adverse effects were seen on absolute or relative organ weights and no changes in gross or histopathology were seen with the exception of increased absolute and relative weights of the cecum with and without contents at 2,000 mg GOS product per kg per day in males and females. This change was considered test article-related as it was associated with mucosal hypertrophy/hyperplasia. However, there were no polyps observed in the cecum. The histological change seen in the cecum of high dose animals, although related to test article administration, is considered an adaptive rather than toxic response. Previously, Kobayashi et al. (2009) also reported relative and absolute higher caecum weight, without corresponding histopathological changes, in males at a dose of 2,000 mg per kg per day.

Hypertrophy/hyperplasia without atypical cellular features represents a compensatory and adaptive response to a large amount of GOS, consistent with the effects seen with other poorly absorbable carbohydrates (Greaves, 2012). Thus, the observed cecal hypertrophy/hyperplasia, without evidence of polyps, was considered compensatory and not pre-neoplastic and, although test article-related, was not considered to be a toxic response. In conclusion, the NOAEL for VITAGOS following oral gavage is 2,000 mg per kg body weight per day under the test conditions employed.

Table 22. Summary of GOS Toxicity Studies in Rodents

Species (Age)	Route and Dose (mg/kg/day bw)	Study Design	Duration (days)	NOAEL (mg/kg bw)	Reference
Repeat-Dose Studies					
Sprague-Dawley rat (10 male/10 female; 6 weeks)	Gavage: 2,500 or 5,000 (Vivinal GOS)	OECD 408	90	5,000	Anthony et al. (2006)
Wistar rat (10 male/10 female; 6 weeks)	Dietary: 1,600-6,900 (Vivinal GOS)	OECD 408	90	6,900	Friesland Foods Domo (2007)
Sprague-Dawley rat (10 male/10 female; 6 weeks)	Gavage: 500, 1,000 or 2,000 (Oligomate GOS)	MoHW[a]	90	2,000	Kobayashi et al. (2009)
Neonatal Sprague-Dawley rat (10 male/10 female; PND 4)	Gavage: 500, 1,000 or 2,000 (Oligomate GOS)	-	45	2000	Kobayash et al. (2013)
Wistar rat (10 male/10 female; 7 weeks)	Gavage: 500, 1,000 or 2,000 (Nestle GOS)	OECD 407	30	2,000	Penard (2015)
Sprague-Dawley rat (10 male/10 female)	Gavage: 500, 1,000 or 2,000 (VITAGOS GOS)	OECD 408	90	2,000	Vitalis Nutrition (2016)
Developmental and Reproductive Studies					
Mice (BALB/c) Pregnant females (8 weeks); Pups (weaning)	Diet: GOS, 1620 + inulin, 400 (GOS: Laiterie de Montaigu); Same diet as dams	-	Gestation to weaning; 48, post-weaning	No toxicity observed in dams or pups	Desbuards et al. (2012)
Sprague-Dawley rat (24 males; 5 weeks) (24 females; 12 weeks)	Gavage: 500, 1,000, or 2,000 (Oligomate GOS)	OECD 415	~ 90	2000	Kobayashi et al. (2014)

bw = body weight; GOS = galacto-oligosaccharides; NOAEL=No Observed Adverse Effect Level; PND = postnatal day

[a] Ministry of Health and Welfare, Japan, Ordinance No. 21; 26 March 1997; and in accordance with 'the Guidelines for Designation of Food Additives and for Revision of Standards for Use of Food Additives' (Environmental Health Bureau, Ministry of Health and Welfare, Japan, Notification No. 29; 22 March 1996.

3. Genotoxicity/Mutagenicity Studies

The genotoxicity of GOS-containing products have been extensively reviewed in GRNs 334 and 620 (Nestle Nutrition, 2016; Yakult, 2010). As described in GRN 334, Kobayashi et al. (2009) reported that GOS are not mutagenic, genotoxic, or clastogenic using a bacterial reverse mutation assay, a chromosomal aberration assay, and an *in vivo* micronucleus study. In GRN 620, three recent studies corroborating the lack of genotoxicity were summarized. Narumi et al. (2014) showed that GOS are not genotoxic using an *in vivo* comet assay. In addition, a publicly unavailable bacterial reverse mutation assay (Verspeek-Rip, 2015) and an *in vitro* micronucleus assay (Verbaan, 2015) were discussed. Table 23 summarizes the genotoxicity studies.

Table 23. Summary of GOS Genotoxicity Studies[a]

Test	Concentration	Metabolic Activation	Result	Reference
***in vitro* Assays**				
Bacterial reverse mutation (S. typhimurium & E. coli)	312.5 – 5,000 µg/plate (Oligomate GOS)	± S9	Negative	Kobayashi et al. (2009)
Mammalian chromosomal aberration (CHL/IU)	1,250, 2,500, or 5,000 µg/mL (Oligomate GOS)	± S9	Negative	
Bacterial reverse mutation (S. typhimurium & E. coli)	492 - 5,000 µg/plate (Nestlé GOS)	± S9	Negative	Verspeek-Rip (2015)
Micronucleus assay (peripheral human lymphocytes)	512, 1,600, or 5,000 µg/mL (Nestlé GOS)	± S9	Negative	Verbaan (2015)
***in vivo* Assays**				
Micronucleus, mouse (CD-1)	Gavage; 500, 1,000, or 2,000 mg/kg bw (Oligomate GOS)	N/A	Negative	Kobayashi et al. (2009)
Comet assay, rat (SD)	Gavage; 500, 1,000 or 2,000 mg/kg/day bw (Oligomate GOS)	N/A	Negative	Narumi et al. (2014)

[a]Adapted from GRN 620 (Nestle Nutrition, 2016).
bw = body weight; GOS = galacto-oligosaccharides; N/A = not applicable

4. Animal Studies on Galactooligosaccharides

a. Animal Studies on Neo Cremar's Galactooligosaccharides

Hong et al. (2016) evaluated the prebiotic effects of Neo Cremar's high-purity galactooligosaccharides (HP-GOS) *in vitro* and *in vivo.* Male Sprague Dawley rats were randomly divided into four groups (*N*=8): the control group (oral administration of saline), the HP-GOS group (oral administration of HP-GOS), the HP-GOS+BB group (oral administration of HP-GOS and *Bifidobacteria*), and the BB group (oral administration of *Bifidobacteria*). 1.5 mL of the solution of 1 gram of HP-GOS and/or 109 colony forming units (CFU) of *Bifidobacteria* were administered daily for 5 weeks. Fresh fecal samples were collected weekly for microbiological analysis. The results indicated a positive effect in the symbiotic group (HP-GOS+BB) during all periods, while the group receiving HP-GOS had significantly ($p<0.05$) higher numbers of *Bifidobacteria* in feces than groups receiving a single dose of *Bifidobacteria* during the second (days 13–15) and fourth (days 28–30) periods of the study. In addition, it was determined that HP-GOS affected the expression of genes encoding glucagon-like peptide-1 (GLP-1) and peptide YY (PYY). There was significant upregulation of GLP-1 and PYY mRNAs with HP-GOS and *Bifidobacteria* intake. No significant differences were observed in body mass, or in the masses of the liver, spleen and kidney in relation to the body mass in any of the treatment groups compared to the control group.

Furthermore, utilization of GOS by intestinal bacteria was studied *in vitro*. Neo Cremar's HP-GOS, containing 75.18 % of galactooligosaccharides (by mass), were compared to other commercial GOS: Y-GOS (52.52 % GOS, by mass), C-GOS (56.25 % GOS, by mass), and Q-GOS (41.77 % GOS, by mass). All strains (*L. acidophilus, L. casei, B. longum,* and *B. bifidum*) in a medium containing HP-GOS had a higher cell growth rate than the strains grown in the media containing commercial GOS after 12h of culture. HP-GOS mass fractions above 1% were found to be acceptable for the growth of probiotic bacteria. *B. bifidum* and *B. longum* utilized HP-GOS more rapidly than *L. acidophilus* and *L. casei*. It is considered that the utilization of non-digestible oligosaccharides by *Bifidobacteria* is mediated by the hydrolyzing enzymes produced by these strains.

In conclusion, Neo Cremar's HP GOS were found to serve as a good substrate and carbon source for supporting the growth of enteric bacteria compared with other commercial GOS. The beneficial effect of regular intake of HP-GOS is attributed to the intestinal survival of probiotic *Lactobacillus* and *Bifidobacterium* strains. The health benefits associated with the consumption of HP-GOS in humans include improvement of intestinal tract health and increase in the expression of genes encoding GLP-1 and PYY. On the basis of the findings, the authors propose that the prebiotic properties of HP-GOS are valuable in the production of potential health-

enhancing foods and supplements and that HP-GOS may be used as a functional food ingredient for human consumption.

In another study, Hong et al. (2015) investigated photoprotective effects of Neo Cremar's galacto-oligosaccharide and/or *Bifidobacterium longum* supplementation against skin damage induced by ultraviolet irradiation in hairless mice. Male SKH-1 hairless mice were randomly divided into four groups (6 mice/group): (1) UV control (control) group, (2) GOS-treated (100 mg) group (HC-GOS), (3) *Bifidobacterium longum*-treated (109 CFU) group (Bifido), (4) GOS (100 mg) and *B. longum* (109 CFU) combination-treated group (HC-GOS+Bifido). The hairless mice were exposed to UVB irradiation for four consecutive days with a total daily dose of UVB set at 84 mJ per cm^2. Changes to skin properties and gene expression were measured 24 h later. GOS and/or *Bifidobacterium* were orally administered for 12 weeks. There were no significant differences in body weight gain, organ weight, water and food intake across any of the treatment groups. In addition, no significant differences in organ weights were observed.

The results indicate that GOS and/or *Bifidobacterium* treatments inhibit UVB-induced wrinkle formation, skin thickening and water-loss. To evaluate the effect of GOS and/or *Bifidobacterium* on wrinkle formation in the skin following UVB irradiation, the status of the dorsal skin was monitored. The UVB-irradiated control group displayed thick, fixed wrinkles in the dorsal skin, whereas less wrinkle formation was observed in the GOS and *Bifido*-treated groups. The skin water-holding capacity in hairless mice was significantly increased in mice in the HC-GOS+Bifido group (56.3%) compared with the control group (44.3%, $p<0.01$). A significant increase in water-holding capacity was also observed in the HC-GOS group ($p<0.05$). Oral administration of GOS (HC-GOS), *Bifidobacterium* (Bifido), or the combination (HC-GOS+Bifido) reduced UVB-induced TEWL by 37.8%, 34.9% or 33.7% compared with the UV-irradiation control group, which indicates the strengthening of the skin barrier. Moreover, GOS and/or *Bifidobacterium*-treated groups significantly inhibited the formation of UV-induced erythema in mouse skin ($p<0.05$). The strongest effect was observed in the HC-GOS treatment group, which showed a 16.8% reduction in erythema formation. However, the differences between the treated groups (HC-GOS, Bifido and HC-GOS+Bifido group) were not significant.

Neo Cremar's GOS administration also resulted in a significantly increased CD44 gene expression, which is associated with the maintenance of hyaluronic acid homeostasis, compared to the control group. MMP2 and MMP9 are collagenases that play important roles in the degradation of collagen in tissues. Oral administration of GOS or a combination of GOS and *Bifidobacterium* significantly reduced MMP2 mRNA expression compared with the control by 40.7% or 41.9%, respectively. The single dose of GOS appeared to down-regulate MMP9 expression. However, there were no significant differences in MMP9 expression the treated groups (HC-GOS,

Bifido and HCGOS+ Bifido group) and control. Oral administration of GOS significantly up-regulated TIMP-1 mRNA expression compared with the control group ($p<0.05$). This indicates that orally administered GOS activated the gene expression of TIMP1, an inhibitor of MMP responsible for collagen degradation in skin. Oral administration of GOS significantly increased Col 1 mRNA expression compared to the control group.

Together, the findings of the study support that prebiotics, especially GOS, are beneficial not only to the intestine, but also to the skin and present the possibility of new nutritional strategies for the prevention of UV-induced skin damage.

b. Animal Studies on Other Galactooligosaccharide Preparations

Two additional studies were identified during the updated literature search investigating the effects of GOS consumption on the intestinal microbiota. Although specific safety endpoints were not assessed in these studies, the results contribute to the abundance of literature supporting the safe consumption of GOS.

The first study evaluated galacto-oligosaccharides as a dietary component in infant diets and their effects on intestinal functions in piglets (Alizadeh et al., 2016). The maturation of the intestines in piglets closely resembles that of human neonates and infants. Hence, a neonatal piglet model was used to study the multi-faceted effects of dietary GOS in early life. Naturally farrowed piglets were separated from the mother sow 24-48 h postpartum and received a milk replacer with or without the GOS for 3 or 26 d, after which several indicators of intestinal colonization and maturation were measured. Dietary GOS was readily fermented in the colon, leading to a decreased pH, an increase in butyric acid in cecum digesta and an increase in *Lactobacilli* and *Bifidobacteria* numbers at day 26. Histomorphological changes were observed in the intestines of piglets fed a GOS diet for 3 or 26 d. In turn, differences in the intestinal disaccharidase activity were observed between control and GOS-fed piglets. The mRNA expression of various tight junction proteins was up-regulated in the intestines of piglet fed a GOS diet and was not accompanied by an increase in protein expression. GOS also increased porcine β-defensin-2 in the colon and secretory IgA levels in saliva. In conclusion, by utilizing a neonatal piglet model, it was demonstrated that a GOS-supplemented milk replacer promotes the balance of the developing intestinal microbiota, improves the intestinal architecture and seems to stimulate the intestinal defense mechanism.

In another recent study, Monteagudo-Mera et al. (2016) evaluated the influence of a β(1-4) high purity galacto-oligosaccharide formulation (GOS90) on the composition and activity of the mouse gut microbiota. Germ-free mice were colonized with microbiota from four pathogen-free wt 129 mice donors (SPF), and stools were collected during a feeding trial in which GOS90 was delivered orally for 14 days.

Pyrosequencing of 16S rDNA amplicons showed that *Bifidobacterium* and specific *Lactobacillus*, *Bacteroides* and *Clostridiales* were more prevalent in GOS90-fed mice after 14 days, although the prebiotic impact on *Bifidobacterium* varied among individual mice. Prebiotic feeding also resulted in decreased abundance of *Bacteroidales*, *Helicobacter,* and *Clostridium*. High-throughput quantitative PCR showed an increased abundance of *Bifidobacterium adolescentis*, *Bifidobacterium pseudocatenulatum*, *Bifidobacterium lactis,* and *Bifidobacterium gallicum* in the prebiotic-fed mice. GOS90 did not modify inflammatory biomarkers [interleukin (IL)-6, IL-12, IL-1β, interferon gamma and tumor necrosis factor alpha]. Decreased butyrate, acetate, and lactate concentrations in stools of prebiotic fed mice suggested an increase in colonic absorption and reduced excretion. Overall, the results demonstrate that GOS90 is capable of modulating the intestinal microbiome resulting in expansion of the probiome (autochthonous beneficial bacteria).

5. Clinical Studies with Galactooligosaccharides

A large body of clinical data characterizing effects of various galactooligosaccharide preparations on tolerance, gastro-intestinal physiology, microflora balance and mineral absorption in healthy and unhealthy adult subjects and children have been extensively reviewed previously in the FDA GRAS notices GRN 236, GRN 285, GRN 286, and GRN 334 (Friesland Foods Domo, 2007; GTC Nutrition, 2009a; b; Yakult, 2010). The recent clinical studies conducted in adults, supporting the safety of GOS for the intended use and at the intended use level, have been summarized by New Francisco Biotechnology Corporation in GRN 518 and GRN 569 (New Francisco, 2014; 2015). The subsequent GRN 620 also provided updates of published studies and received a "no questions" letter from FDA (Nestle Nutrition, 2016). No relevant clinical studies involving adults have been published since the filing of GRN 620.

In general, GOS are well tolerated, and have been reported to increase the abundance of *Bifidobacteria* and *Lactobacilli* in the gastrointestinal tract, increase fecal short-chain fatty acid concentrations and alleviate the symptoms of irritable bowel syndrome (Bouhnik et al., 2004; Davis et al., 2010; Depeint et al., 2008; Gopal et al., 2003; Ito et al., 1990; Kanamori et al., 2004; Ladirat et al., 2014; Silk et al., 2009; Vulevic et al., 2013; Walton et al., 2012).

a. Human Adult Studies with Neo Cremar's Galactooligosaccharides

Following the preliminary test in hairless mice, a randomized double blind, placebo-controlled clinical trial was conducted in healthy adults to investigate the effects of Neo Cremar's GOS on the skin (Hong et al., 2013). Eighty-four healthy Korean volunteers, aged 30–69 years, with fine wrinkles at the outer corner of the eyes, called lateral canthal lines, were chosen for this study. The subjects were divided into two (control and GOS) groups by stratified block randomization. The GOS group

received 1 g of GOS in a capsule twice a day, whereas the control group received only vehicle (100% dextrin). The total daily GOS dose (2 g) was selected based on preliminary studies. The subjects were asked not to change their diet or life style during the study. The results showed that the increase in corneometer (instrument used to measure the hydration level of the skin surface) value from baseline to week 12 was significantly greater in the GOS group than in the control group (6.91 vs. 2.88 arbitrary 37 units, $p < 0.05$). The transepidermal water loss in the GOS group was reduced significantly after 12 weeks of GOS treatment (20.1 g/h/m^2 at baseline vs. 17.5 g/h/m^2 at week 12, $p < 0.05$). The differences in total and percentage of wrinkle areas between the two groups were statistically significant after 12 weeks of GOS treatment ($p < 0.05$). The GOS group showed a reduction in total wrinkle area and percentage of wrinkle area after 12 weeks of GOS treatment (total wrinkle area: −3.25 mm^2; percentage of wrinkle area: −12.2%), whereas the control group showed a slight increase in these parameters (total wrinkle area: 1.07 mm^2, percentage of wrinkle area: 4.02%). Furthermore, the wrinkle depth and number of wrinkles in the GOS group were also lower than those in the control group, although these differences were not statistically significant. In conclusion, oral treatment with Neo Cremar's GOS is beneficial to the skin and present the possibility of new nutritional strategies for skin care.

b. Human Infant Studies with Galactooligosaccharides

The addition of GOS to infant formula is intended to provide a dietary source of oligosaccharides that are representative of oligosaccharides found in human milk from lactating mothers (Oozeer et al., 2013; Vandenplas et al., 2014; Veereman-Wauters, 2005). The totality of the published literature investigating the safety of GOS administration in infants has been the subject of multiple comprehensive reviews during previous GRAS conclusions. Clinical studies evaluating the safety of GOS consumption in infants have assessed a number of biological endpoints, including the effects of GOS on gastrointestinal physiology, fecal microflora, the immune system, and tolerance.

The use level of GOS in infant formulas has remained at 7.2 grams per L in GRN 334, GRN 489, GRN 495 and GRN 569. In GRN 620, Nestle Nutrition concluded that the addition of GOS to infant formula at a use-level of 7.8 grams per L would also be GRAS. This conclusion was not questioned by FDA and is consistent with the maximum use-level of 8 grams GOS per L currently permitted for addition to infant formula in Australia and New Zealand and China (FSANZ, 2008; Ministry of Health of the PRC, 2011).

In addition, the use-level of 7.8 grams per L is well within background exposures to resistant oligosaccharides in infants consuming human milk, where levels of human milk oligosaccharides of 25 and 12 grams per L have been reported in human

colostrum and mature milk samples, respectively, obtained from lactating women (Kunz et al., 1999; Kunz et al., 2000). Moreover, the conclusion is further corroborated by numerous studies of GOS in preterm and term infants, and children administered infant and follow-on formulas containing up to 20 grams GOS per L, in which GOS was generally well tolerated (Armanian et al., 2014; Bharani et al., 2015; Chatchatee et al., 2014; da Costa Ribeiro et al., 2015; Giovannini et al., 2014; Meli et al., 2014; Underwood et al., 2014; Williams et al., 2014). In GRN 671, several more recent studies were described which are consistent with the results reported in the clinical trials summarized in previous GRAS Notifications (Vitalis Nutrition, 2016). A summary of the recent studies is provided in Table 24.

Infant studies identified during the updated literature search include a study on the safety and tolerance of the combination of partly fermented infant milk formulae and a specific mixture of 90% short-chain galacto-oligosaccharides and 10% long-chain fructo-oligosaccharides (scGOS/lcFOS; 9:1) in healthy term infants (Huet et al., 2016). Four hundred thirty-two infants were enrolled before 28 days of age, assigned to 1 of the 4 groups: (i) formula with scGOS/lcFOS, (ii) scGOS/lcFOS+15% fermented formula (FERM), (iii) scGOS/lcFOS+50% FERM, or (iv) 50% FERM, and followed up to 17 weeks of age. Primary outcome was daily weight gain during intervention (equivalence criterion: difference in daily weight gain ≤3 g/day). Infants' anthropometrics, formula intake, number, and type of (serious) adverse events (AEs) were monitored monthly. Equivalence of weight gain per day was demonstrated in both the intention-to-treat and per-protocol populations, with a mean weight gain (SD) of 29.7 (6.1), 28.2 (4.8), 28.5 (5.0), and 28.7 (5.9) g/day for the groups i to iv, respectively. No differences were observed in other growth parameters, formula intake, or in the number or severity of AEs. In all scGOS/lcFOS-containing formulae, a beneficial effect of scGOS/lcFOS was observed, indicated by the lower pH, lower *Clostridium difficile* levels, and higher secretory immunoglobulin A levels. The partly fermented infant milk formulae containing the specific mixture scGOS/lcFOS were well-tolerated and resulted in normal growth in healthy infants.

Table 24. Recent Studies of GOS Consumption in Infants[a]

Reference and Study Design	Subjects	Dose	Duration	Results	
Civardi et al. (2015) Randomized, double- blind, placebo-controlled	117 infants (full-term, <12 months of age, healthy)	**Test Formula:** Formula enriched with 7 g GOS/L, p-palmitate and acidified milk; n=51 **Control:** Formula; n=59	135 days	Adverse event reporting	Only gastrointestinal adverse events were evaluated; those that were reported were mild and there were no differences between the two groups. No severe adverse events were reported.
				GI tolerance	Mean number of stools/day was similar between the two groups. Frequency of intestinal gas and bowel cramps were similar in both groups.
				Growth	Weight change and length change were similar in the two groups. Head circumference was similar in the two groups.
				Fecal microflora	*Clostridia* counts (determined by quantitative PCR) were similar in the two groups. *Bifidobacteria* counts (determined by quantitative PCR) were significantly increased ($p< 0.05$) in test formula group.
Matsuki et al. (2016) Randomized, double- blind, placebo-controlled	35 infants (full-term, <12 months of age, healthy)	**Test Formula:** Formula with 3g GOS/L; n=16 **Control:** Formula with dextrins; n=14 **Note:** Supplementation with up to 20% breast milk was permitted	14 days	Adverse event reporting	Adverse side effects were monitored and none were reported.
				GI tolerance	There were no significant differences between the groups in fecal short-chain fatty acid levels, pH, or stool frequency.
				Fecal microflora	Abundance of *Bifidobacteria* significantly increased ($p<0.05$) in the GOS-treated group compared to the control group. At the species level, there were no significant chances in the *Bifidobacteria*.

[a] Adapted from GRN 620 and GRN 671 (Nestle Nutrition, 2016; Vitalis Nutrition, 2016)

DOL = day of life; F = female; FOS = fructo-oligosaccharides; GI = gastrointestinal; GOS = galactooligosaccharides; GUM = growing up milk; LCPUFA = long-chain-poly-unsaturated fatty acids; M = male; NEC = necrotizing enterocolitis; RTI = respiratory tract infection

c. Allergenicity Studies

In 2012, case reports of GOS allergenicity were reported by clinicians in Vietnam and Singapore in association with the consumption of GOS containing milk formulas (Chiang et al., 2012; Vo et al., 2012). To date, the causative antigen(s) responsible for these cases has not been identified; however, in further testing of 5 individuals with GOS anaphylaxis, positive reactions to skin prick and basophil activation tests were reported against GOS fractions with 3 sugar units or greater (Chiang et al., 2012). The primary sensitizer has been speculated to be a parasitic agent specific only to the Southeast Asian region. For example, similar cases reports of sensitization leading to red meat allergy have been observed throughout the central and southern U.S. in individuals exposed to *alpha*-gal (galactose-α-1,3-galactose) glycoprotein antigens introduced to the circulation from Lone Star tick bites (Soh et al., 2015b).

Recently case-reports of GOS allergenicity from consumption of a GOS containing lactic acid beverage were reported in 12 individuals in Japan by Kaneko et al. (2014). All reactions occurred in individuals with allergic predispositions to asthmatic or urticarial episodes. The authors attempted to characterize the oligosaccharides responsible for the anaphylactic responses using the histamine release test (HRT) with heparinized peripheral venous blood from 3 of the patients. Strong HRT responses were reported for tetrasaccharide isolates of GOS, and therefore the putative antigen was identified as a GOS tetramer, which is consistent with previous observations by Chiang et al. (2012). Strong HRT responses to GOS containing a 1-4 oligomer bias (produced by *Bacillus circulans*) were reported (40 to 70%), whereas negative (<10%) to pseudo-negative (10 to 15%) responses were found to GOS containing a 1-6 oligomer bias (produced by a combination of *A. oryzae* and *Streptococcus thermophilus*). Further isolation of select GOS molecules identified Galβ1-4Galβ1-4Galβ1-3Glc as the putative allergen based on its presence in HRT positive GOS preparations and its absence from "non-immunogenic" GOS preparations from *S. singularis* and *K. lactis*. However, the authors were unable to identify anti-GOS IgE antibodies in the sera of the patients by the enzyme immunoassay method. In view of this, the clinical significance of the author's findings is unclear.

In response to the cases of GOS anaphylaxis reported in Singapore by Chiang et al. (2012), a clinical study was conducted in 487 individuals with eczema, asthma, allergic rhinitis, and food allergies to determine the prevalence of allergy in this population (Soh et al., 2015a). The 30 subjects (6.2%) that were found to be sensitized to GOS (Vivinal) by skin prick test had blood drawn for basophil activation tests, and 13 of these subjects further consented to oral challenge tests with either Vivinal GOS or Oligomate 55N GOS. Six of the 13 subjects challenged orally with Vivinal GOS tested positive, whereas none of the subjects reacted to oral exposure to Oligomate 55N. It was estimated that the prevalence of allergy to Vivinal GOS in this atopic population in Singapore might be up to 3.5%; however, the authors acknowledged that "…this estimate may not be entirely accurate as subjects were drawn from patients attending a specialized clinic in a tertiary hospital. Furthermore, the small number of subjects from which the ROC (Receiver Operating Characteristic) curves were derived limits the accuracy of the BAT (Basophil Activation Test) and,

consequently, the precision of this estimate" (Soh et al., 2015a). The difference in allergic response to Vivinal versus Oligomate 55N GOS was speculated to be related to structural differences, due to the use of different β-galactosidase enzymes during their respective manufacturing processes; however, whether this really is the case is unknown.

Despite the recent case reports of GOS allergenicity, the putative antigen(s) and the etiology of GOS anaphylaxis remain unknown. Furthermore, the strong geographical restriction of all cases of GOS allergenicity that have been reported to date implies that the primary sensitizer is confined to select regions of Southeast Asia, and is linked to very specific prior occupational/environmental exposure. GOS preparations that have been associated with GOS anaphylaxis in these specific regions of Southeast Asia have been widely consumed in other global regions for over a decade by adults, children, and infants without reported incidences of anaphylaxis, suggesting that the risk of GOS allergenicity from the introduction of GOS containing foods generally is low. Similar conclusions have been determined in previous GRAS evaluations that received "no questions" letters from FDA (amendments to GRN 236, GRN 495, and GRN 620).

Neo Cremar recognizes that no definitive cause of the rare occurrence of GOS allergenicity has been identified, and agrees that the risk of allergenicity from GOS containing foods is low, as was determined in previous GRAS assessments (GRN 236, GRN 495, and GRN 620).

C. Discussion on Safety Data of β-Galactosidase Enzyme

The subject of the present GRAS conclusion, Neo Cremar's GOS, is produced from food grade lactose via a transgalactosylation reaction catalyzed by a β -galactosidase enzyme obtained from the natural, non-GMO, non-pathogenic, bacterium *Bacillus circulans*. The *Bacillus* genus is a group of gram positive, rod-shaped bacteria that contain a large number of bacterial strains that have been used industrially in the preparation of a number of enzymes that are utilized in food production (Schallmey et al., 2004).

The β-galactosidase enzyme preparation used by Neo Cremar in the preparation of its GOS products is derived from *Bacillus circulans*, is well characterized, reproducibly meets compositional and activity standards, and complies with limits on contaminants appropriate for food grade ingredients. Unpublished safety studies have shown that the β-galactosidase is obtained from a nonpathogenic and non-toxigenic microorganism. Additional steps employed in enzyme preparations and use of the enzyme further supports the safety. The enzyme is isolated using standard procedures for the enzymatic reaction with lactose. The constituents from the enzyme preparation are unlikely to become part of the product. The manufacture of GOS involves extensive purification steps that are likely to remove potential metabolic impurities and/or toxin(s) produced during fermentation.

The use of GOS produced from lactose with β-galactosidase derived from *B. circulans* in various foods and in infant formula has been determined to be GRAS by the following companies:

Friesland Foods Domo (GRN 236), GTC Nutrition (GRN 285 and GRN 286), New Francisco Biotechnology Corporation (GRN 518 and GRN 569), for which all notifications received a "no questions" letter from FDA. Additionally, several enzymes derived from *Bacillus* species, such as a-amylase derived from *Bacillus lichenifonnis,* pullulanase from *Bacillus subtilis* and *Bacillus licheniformis;* and pectate lyase from *Bacillus subtillis* are considered GRAS. Furthermore, carbohydrase and protease enzymes derived from *Bacillus subtilis* are affirmed as GRAS for use as direct food ingredients, and ct-acetolactate decarboxylase from recombinant *Bacillus subtilis* is currently regulated by the FDA as a secondary direct food additive permitted for use in food for human consumption. In the European Union, as per Commission Directive 2003/95/EC, cycloglycosyltransferase enzyme derived from *B. circulans* is approved in the production of β-cyclodextrin.

D. Discussion on Safety Data of Baker's Yeast

For the preparation of high purity Mother's OLIGO series, GOS content is increased through fermentation by yeast. The yeast is derived from a non-toxigenic non-pathogenic microorganism, *Saccharomyces cerevisiae hansen CBS5926*, commonly used in food processing. In order to remove the yeast from the preparation, filtration is performed, followed by microfiltration, ion-exchange, and evaporation.

S. cerevisiae, also known as baker's yeast, is commonly used in commercial bread and leavened baked goods production. *S. cerevisiae* is an organism that has an extensive history of safe use. It has been used for millennia in fermentation processes, such as bread leavening and wine or beer production. Moreover, yeast is found naturally on the skins of grapes, where it is responsible for spontaneous fermentation of grape juice (Lodder and Kreger-van-Rij, 1967).

S. cerevisiae is considered GRAS through its use in the brewing, baking, and winemaking industries. Its genome has been sequenced, and it has been determined that the yeast is free of known pathogenicity traits. Selected dried yeasts, including *S. cerevisiae*, are approved food additives as noted in 21 CFR 172.325. Other food additive regulations including 21 CFR 172.590 and 172.898 authorize additives that are derived from baker's yeast. Additionally, the enzyme invertase, derived from *S. cerevisiae,* is considered GRAS based on an FDA opinion letter issued in the early 1960s (FDA, 2015).

Moreover, the European Food Safety Agency (EFSA) also came to the conclusion that baker's yeast is non-toxigenic and non-pathogenic and that it is also not a major food allergen. EFSA therefore gave baker's yeast a Qualified Presumption of Safety (QPS) status (Barlow et al., 2007). This means that in Europe, baker's yeast can be safely used in food and feed production, and is freed from the need for further safety assessment.

E. Discussion on Safety of Cow's Milk vs. Goat's Milk

Both cow's and goat's milk have been a staple of the human diet for thousands of years. Archeological evidence of milk proteins in ceramic vessels suggest dairying occurred in present-day Romania and Hungary between 7,900 and 7,450 years ago. The Romans used goat and sheep milk to produce cheese, while the Germanic and Celtic people raised cattle for dairying (University College London, 2009).

While cow's milk is the most commercially-available milk in the US, approximately one million goats are active in milk production for use in various foods such as cheese, liquid milk, yogurt, and ice cream. USDA reported that from 1987-1997, production of goat's milk doubled to 9 million gallons per year, with the fastest growing market for goat's milk being the production of cheese (USDA, 2004). Today, dairy goats are found in every US state, with a total of 360,000 milk goats as of January 1, 2013 (Geisler, 2015).

The composition of goat's milk is such that it has a natural whey protein to casein ratio of approximately 20:80, similar to that of cow's milk (Selvaggi et al., 2014). There is subsequently a high presumption of safety for goat's milk and its constituents, due to the long history of use in milk and cheese as a human food. Worldwide, approximately 4.8 million tons of goat's milk are consumed either in the form of "milk" or cheese, and this comprises approximately 2% of the world's dairy milk supply (FAO, 2007). According to FAO, the top goat's milk producers in 2008 were India (4 million metric tons), Bangladesh (2.16 million metric tons), and the Sudan (1.47 million metric tons).

Approximately 6% of the US infant population has an allergic-type response to cow's milk, with about 14% of those affected reacting to the cow's milk protein (CMP) (Heinlein and Caccse, 2003). Many of the other cow's milk constituents that elicit an allergic-type response are also found in goat's milk; however, goat's milk, as well as camel, mare, and soy milks, have been reported to be effective, non-allergenic alternatives to cow's milk (El-Agamy, 2007; Hill et al., 1999).

On a molecular level, it appears that casein fractions and beta-lactoglobulins are the components of cow's milk which are the most common causes of cow's milk allergy (El-Agamy, 2007; Koletzko et al., 2012).

Along with anecdotal reports, there is evidence that goat's milk has a lower allergenic potential than cow's milk (Ballabio et al., 2011; Ceballos et al., 2009; Lara-Villoslada et al., 2006; Restani, 2004). The evaluation of cow's and goat's milk has indicated that goat's milk lacking α-s1-casein is less allergenic than goat's milk and cow's milk with α-s1-casein (El-Agamy, 2007). A study on the cross-reactivity between individuals with cow's milk allergy and goat's milk allergy noted that that percentage of individuals with cow's milk allergy who tolerated goat's milk ranged from 7.7% to 92.7% (Restani, 2004). A more detailed review of goat's milk is presented in GRN 644 (Ausnutria Hyproca, 2016).

Although cow's and goat's milk are the sources for the lactose used to prepare the GOS, it is unlikely that an allergic-type response would be observed with the finished product, as the main allergens in the bulk milk are unlikely to be present after lactose extraction and the subsequent GOS production steps.

F. Expert Panel[5] Findings on Safety of Neo Cremar's Galactooligosaccharide Preparations

The Expert Panel, having reviewed individual studies, available comprehensive critical reviews, previous GRAS submissions, international regulatory summaries, and other evaluations on GOS, concludes that Neo Cremar's GOS preparations are generally recognized as safe in foods at the usage levels described herein.

The Expert Panel bases this conclusion on the following key factors:

- **ADME studies** demonstrate that GOS is not digested by human gastric juice or pancreatic enzymes, and passes undigested and unabsorbed to the colon where it is fermented by colonic microflora to short-chain fatty acids, carbon dioxide, methane and hydrogen gases. Any unfermented dietary GOS will be excreted in the feces.

- **Animal toxicity studies** have consistently reported no evidence of toxicity in rodents. NOAELs ranging from 2,000 mg per kg bw GOS to 5,000 mg per kg bw GOS were reported in 90-day repeated-dose studies on Sprague-Dawley rats (Anthony et al., 2006; Kobayashi et al., 2009). An unpublished subchronic feeding study supported a NOAEL of 6,900 mg per kg bw GOS was cited in GRN 236 (Friesland Foods Domo, 2007).

- **Subchronic and chronic animal studies** revealed no changes in hematological or clinical chemistry parameters or histopathology that were considered to be toxicologically significant or clinically relevant. Oral administration of up to 2,000 mg per kg per day GOS (the NOAEL) to Wistar rats for 30 days was well-tolerated both clinically and histologically, and did not induce any treatment-related effects (Nestle Nutrition, 2016; Penard, 2015). Increased absolute and relative weights of the caecum, with and without contents, was observed in Sprague-Dawley rats fed 2,000 mg GOS per kg per day; however, this response was considered an adaptive, instead of toxic, response (Vitalis Nutrition, 2016).

- **Reproductive and/or developmental toxicity** studies showed no effects on the development of animals in a neonatal rodent study on Sprague-Dawley rats administered GOS. The NOAEL was reported to be 2,000 mg per kg bw per day (Kobayash et al., 2013). In a subsequent study, consumption of GOS did not cause any adverse effects on reproduction/development from premating, copulation, implantation, or maintenance of pregnancy in male and female Sprague-Dawley rats. No effects were observed on the

[5] Drs. Omaye, Lewis, and Emmel have extensive technical backgrounds in the evaluation of food ingredient safety and in participating in the deliberations of GRAS Expert Panels. Dr. Emmel served as Chair of the Panel.

number of live births, sex ratio, or external observation at the time of birth, body weight, pup survival, or external differentiation during lactation (Kobayashi et al., 2014). Furthermore, no significant effects were observed in pregnant BALB/cJ mice or their offspring following a GOS-supplemented diet (Desbuards et al., 2012).

- **Genotoxicity and mutagenicity studies** have shown GOS are not mutagenic, genotoxic, or clastogenic using bacterial reverse mutation, chromosomal aberration, and *in vivo* micronucleus studies (Kobayashi et al., 2009; Narumi et al., 2014; Nestle Nutrition, 2016; Verbaan, 2015; Verspeek-Rip, 2015; Yakult, 2010).

- **Clinical studies** also show GOS is well-tolerated in humans. Consumption of GOS-containing infant formulas has been extensively investigated in infants. There is evidence that addition of prebiotics to infant formula alters the gastrointestinal microbiota resembling that of breastfed infants. These prebiotics, including GOS, are added to infant formula because of their presence in breast milk. In several published clinical studies, nutritional and physiological effects or safety of GOS containing infant formulas in premature infants, term infants, and infants with atopic disorders has been investigated. Findings from these studies demonstrate that addition of GOS to infant formula at use levels up to 7.8 g per L is well-tolerated and safe.

- FDA has issued 11 "no questions" letters in response to GRAS notifications for galactooligosaccharides preparations, as noted in Table 18.

- Neo Cremar Co., Ltd intends to market galactooligosaccharides (GOS) preparations as ingredients for use in food and infant formula. The GOS are prepared using raw materials and processing aids that are food grade and comply with applicable U.S. federal regulations. GOS is manufactured in compliance with ISO standards, and Neo Cremar has established food grade specifications for GOS. Neo Cremar is currently conducting stability studies on the GOS preparations described herein; initial results have indicated a shelf-stability within a two-year time frame.

In summary, a compelling case can be made that scientific consensus exists regarding the safety of GOS in support of a GRAS conclusion under the conditions of its intended use.

G. Common Knowledge Elements for GRAS Conclusions

The first common knowledge element for a GRAS conclusion requires that data and information relied upon to establish safety must be generally available; this is most commonly established by utilizing studies published in peer-reviewed scientific journals. The second common knowledge element for a GRAS conclusion requires that consensus exists within the broader scientific community.

1. Public Availability of Scientific Information

The majority of studies on GOS have been published in the scientific literature. The common use of GOS in food on a global basis and the associated absence of harm in based upon published information of all types. In addition, clinical studies, which support the safety assessment, have been published in the scientific literature.

2. Scientific Consensus

The second common knowledge element for a GRAS conclusion requires that there must be a basis to conclude that consensus exists among qualified scientists about the safety of the substance for its intended use.

Neo Cremar intends to use GOS in the same foods and at levels (0.3 to 11 g GOS per serving) proportional to those mentioned in the GRN 285, GRN 334, GRN 484, and GRN 518. The intended use of GOS in selected conventional foods, coffees, and teas is estimated to result at mean and 90th percentile intakes of 12.2 g per person per day (0.28 g per kg bw per day) and 25.3 g per person per day (0.70 g per kg bw per day), and in coffees and teas of 5.0 g per person per day for adult males and 4.4 g per person per day for the total population.

Furthermore, Neo Cremar Co., Ltd intends to market galactooligosaccharides (GOS) as ingredients for addition to infant formula and follow-on formula at a use level providing up to 7.8 g of GOS per L of the reconstituted or ready to consume product. Multiple GOS preparations produced from lactose using food grade microbial derived beta-galactosidases, for use of GOS in infant formula and follow on formula have been previously determined as GRAS. In addition to these critical reviews by Expert Panelists and FDA for safety-in-use of GOS preparations in infant formula and follow on formula, general recognition of the safety of GOS for use in infant formula is further established by opinions authorizing the safe use of GOS in infant formula preparations issued by the European Commission and FSANZ.

There is sufficient qualitative and quantitative scientific evidence to determine the safety in- use of GOS in infant formula and follow-on formula at a use level providing up to 7.8 g of GOS per L of the reconstituted or ready to consume product. Oligosaccharides resembling GOS occur naturally in human milk. Additionally, manufactured GOS products have been used in food for over 25 years, and in infant formulas for over 10 years, with no evidence of adverse effects related to the safety of its use. GOS has been the subject of twelve GRAS notices to FDA. FDA did not question the safety of GOS for the intended food uses, including infant formula uses. Neo Cremar intends to use its GOS is in the same food products and at levels proportional to those mentioned in GRN 620, which proposed to increase the use levels in infant formulas from 7.2 to 7.8 g per day and received "no questions" letter from FDA. The intended use of GOS in infant formula at the maximum intended use level of 7.8 g per L was estimated to result in the mean and 90th percentile dietary intakes 6.4 and 9.2 g per infant per day, respectively, for infants aged 0 through 6 months.

For infants aged 7 through 12 months, the mean and 90th percentile all-users intakes of GOS was estimated as 5.6 and 8.6 g per infant per day, respectively.

The subject of the present GRAS conclusion is substantially equivalent to GOS that has been the subject of FDA GRAS notified substances. The use of a similar manufacturing process in the preparation of GOS that is the subject of this GRAS assessment and those that have been the subject of FDA notices suggests that the differences between various GOS products would be limited to minor variations in the compositional distribution of the GOS oligomers and to differences in the residual levels of lactose. These observations also suggest that the safety information on GOS products can be interchangeably used. The FDA responses to GRAS notices on GOS indicate that the agency is satisfied with the safety-in-use of GOS in foods as well as in infant formula.

In summary, on the basis of scientific procedures, exposure from diet and current uses, the consumption of GOS derived from lactose as a food ingredient at use levels ranging from 0.3 to 11 g per serving in certain specified foods, coffees and teas; and in infant formula and follow-on formula at levels providing up to 7.8 g of GOS per L of the reconstituted or ready to consume product day is Generally Recognized As Safe (GRAS).

The Panel maintains that well-qualified scientists would conclude that GOS are generally recognized as safe for use in foods and infant formulas give the extensive historical, regulatory, and safety data available.

H. Conclusion

In consideration of the aggregate safety information available on GOS, Neo Cremar and the Expert Panel conclude that GOS is generally recognized as safe (GRAS) within the meaning of the Food, Drug, and Cosmetic Act when consumed in conventional foods and infant formulas as described within this GRAS notification.

Neo Cremar's galactooligosaccharides preparations, when produced in accordance with FDA Good Manufacturing Practices requirements and when meeting at a minimum those specifications presented by Neo Cremar in Table 1 through Table 8 are Generally Recognized As Safe when consumed within the proposed use levels ranging from 0.3-11 g per serving in certain conventional foods, and at levels providing up to 7.8 g of GOS per L of the reconstituted or ready-to-consume infant formula and follow on formula. It is important to observe good manufacturing practices principles in that the quantity of a substance added to food should not exceed the amount reasonably required to accomplish its intended technical effect.

This declaration has been made in accordance with FDA's standard for food ingredient safety, i.e., reasonable certainty of no harm under the intended conditions of use.

(b) (6)

Katrina V. Emmel, Ph.D.

Chair

(b) (6)

Stanley Omaye, Ph.D.

(b) (6)

Kara Lewis, Ph.D.

PART 7. LIST OF SUPPORTING DATA AND INFORMATION IN THE GRAS NOTICE.

A. List of Acronyms

ADI	Acceptable Daily Intake
ADME	absorption, distribution, metabolism, excretion
AE(s)	adverse event(s)
AOAC	AOAC International (Association of Analytical Communities
bw	body weight
CFU	colony forming unit
cGLP	current good laboratory practice(s)
cGMP	current good manufacturing practice(s)
cPs	centipoise(s)
CMP	cow's milk protein
DE	dextran equivalents
DM	dry matter
DS	dissolved solids
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FCC	Food Chemical Codex
FDA	Food and Drug Administration
FD&C	Federal Food, Drug, and Cosmetic Act
FOIA	Freedom of Information Act
FOS	fructo-oligosaccharides, fructooligosaccharides
FSANZ	Food Standards Australia New Zealand
FSSAI	Food Safety and Standards Authority of India

g	gram(s)
g/p/d	grams per person per day
GA	GRAS Associates
GOS	galactooligosaccharides
GRAS	Generally Recognized as Safe
GRN	GRAS Notification
HbA1c	glycated hemoglobin
HRT	histamine release test
HPLC	High-Performance Liquid Chromatography
IADSA	International Alliance of Dietary/Food Supplement Associations
ISO	International Organization for Standardization
JECFA	Joint FAO/WHO Expert Committee on Food Additives
kg	kilogram
L	Liter
LLC	Limited Liability Corporation
Ltd.	Limited
mg	milligram
min	minimum
mm	millimeter
MMP	matrix metalloproteinase
mpn/g	most probable number per gram
n	number
NA, N/A	Not applicable
NHANES	National Health and Nutrition Examination Survey
NHPs	Natural Health Products

NMT	Not more than
No.	Number
NOAEL	No Observed Adverse Effect Level
NOEL	No observed effect level
OECD	Organisation for Economic Co-operation and Development
PCR	polymerase chain reaction
PND	postnatal day
ppm	parts per million
QPS	qualified presumption of safety
RH	relative humidity
RO	reverse osmosis
SCF	Scientific Committee for Food
SD	standard deviation
TOS	transoligosaccharide (synonymous with GOS)
TGOS	trans-galacto-oligosaccharide (synonymous with GOS)
µg	microgram
US	United States
USDA	United States Department of Agriculture
WHO	World Health Organization

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C. Appendices

Appendix 1 Specifications and Certificates of Analysis for Production Processing Aids

Appendix 1.1 Cow's Milk Lactose

Brewster cheese

Certificate of Analysis

Grain Millers Dairy Products

Brewster Order # 57858

Customer P.O. # 34140-1

Lot number	2016123121
Production date	31-December-2016
Expiration date	31-December-2017
Lactose	99.83%
Ash	0.10%
Protein	0.07%
Moisture	0.03%
pH	6.68
Coliform	< 10 / g
SPC	< 100 / g
Yeast/Mold	< 10 / g / < 10 / g
Sediment	7.5 mg / Acceptable
Color/Flavor/Aroma	Accept
Salmonella	Negative / 125 g
Total bags	800

Brewster Dairy, Inc. certifies that this shipment is Edible Grade Lactose.

(b) (6)

Signed: _____

Food Safety Manager, Brewster Cheese Company

Date: January 11, 2017

World Class Specialty Foods

Brewster Cheese Company, 800 Wabash Avenue South, Brewster, Ohio 44613
Phone: 330-767-3492 Fax: 330-767-3586 www.brewstercheese.com

INGREDIENT CERTIFICATE

Date: June 13, 2017

Brewster Cheese Company Lactose meets the USPC standard for Lactose monohydrate (August 2, 2012).

Product: LACTOSE MONOHYDRATE
Product Composition: Lactose

(b) (6)

Name: Janice Lance
Title: Food Safety Manager

Brewster Cheese Company
800 Wabash Avenue South, Brewster OH 44613
Phone: 330-767-3492 Fax: 330-767-3386

Appendix 1.2 Organic Cow's Milk Lactose

Rumiano Cheese Company
PO Box 305
Crescent City, CA 95531
(707) 465-1535

ORGANIC LACTOSE-EDIBLE GRADE

Production Dates	7/17/2016-7/23/2016
Lot Number	Certificate of Anaylsis for Batch # 1629

Chemical	Results	Method Reference
Lactose % by Difference	99.53%	
Total Moisture	4.91%	Vacumm Oven (SMEDP Latest Edition, APHA)
Ash	0.16%	Mojonnier (SMEDP Latest Edition, APHA)
Protein	0.31%	Kjeldahl (SMEDP Latest Edition, APHA)
pH	5.60	5 % solution @ 20°C

Physical	Results	Method Reference
Scorched Particles	<7.5 mg/ 25 grams	American Dairy Products Institute (ADPI)
Color	White to Tan	American Dairy Products Institute (ADPI)
Texture	Granular free flowing	American Dairy Products Institute (ADPI)

Microbiological	Results	Method Reference
Coliform Count	< 10 CFU/gram	AOAC 991.14
Standard Plate Count	< 10 CFU/gram	AOAC 988.18
Yeast & Mold	< 10 CFU/gram	SMEDP Latest Ed
Salmonella spp.	Negative/25 gram	PCR (BAM Appx 1)
Staphylococcus aureus	Negative/25 gram	PCR (BAM Appx 1)

(b) (6)

7/28/2016

Juan Pablo Gonzalez (Lab Tech) Date

RUMIANO
SINCE 1921
FINE NATURAL CHEESE

Organic Edible Lactose

I hereby certify that the Rumiano Cheese Company's Organic Edible Lactose manufactured in Crescent City, California, USA is produced from whey from cheese manufactured from cow's milk that complies with all federal regulations (CFR) / food chemical codex (FCC).

All Organic Edible Lactose manufactured by the Rumiano Cheese Company complies with all FCC (FYR, and the FCC regulations for Lactose).

(b) (6)

Kirk Olesen

April 25, 2017

Rumiano Cheese Company
P.O. Box 305, Crescent City, CA 95531 and P.O. Box 863, Willows, CA 95988 www.rumianocheese.com

Appendix 1.3 Goat's Milk Lactose

nutegrity

Certificate of Analysis

PRODUCT CODE: 2107
LOT NUMBER: 2107-052515-C
DESCRIPTION: Goat Lactose

SPECIES: *Capra aegagrus hircus*

Product Characteristics

Allergen	DAIRY
Certification	KOSHER
Country of Origin	USA

	RESULTS
Physical Characteristics	
Appearance (Visual)	White
Flavor (Sensory)	Clean, Bland
Scorched Particles (ADPI), mg/25g	<7.5
Particle size (USP 786), % Thru 40 Mesh	99
Particle size (USP 786), % Thru 60 Mesh	66
Particle size (USP 786), % Thru 200 Mesh	33
Chemical Analysis	
Lactose (calculated), %	99.5
Ash (AOAC 900.02), %	0.1
Approximate Analysis	
Moisture (AOAC), Monohydrate %	0.1
Protein (AOAC 992.10),% as Dry Basis	0.1
Microbiological Analysis	
Coliform (AOAC 991.14 & 998.08), cfu/g	<10
Yeast & Mold (AOAC 995.21), cfu/g	<10
Total Plate Count (AOAC 990.12), cfu/g	<10
Enterobacteriacea (Compendium 4th ed. Ch. 8), cfu/g	<10
Salmonella (AOAC 2011.03) /375 g	Negative
C. Sakazaki (FDA rev. 8/2002)	Negative
Staph aureus (FDA Bact. Ch. 12), cfu/g	<10
B. cereus (FDA Bam), cfu/g	<10

Shelf Life	Two years*
Retest/Reevaluation Date	05/24/1
Manufacturing Date	05/25/15
Standard Packaging	25 kg bags: 3-ply poly-lined, square bottom, heat-sealed Kraft bag
Storage	Recommend that product is stored below 25° C and below 65% humidity
Issue Date	10/15/2015
Issued By	Jeannine Wirz, Quality Assurance Manager

*Based on industry standards pending shelf life studies

(b) (6)

THE INFORMATION CONTAINED IN THIS TECHNICAL AND PRODUCT BULLETIN IS BELIEVED TO BE ACCURATE AND IS OFFERED IN GOOD FAITH FOR THE BENEFIT OF THE BUYER. HOWEVER, NUTEGRITY MAKES NO WARRANTY AND TAKES NO RESPONSIBILITY AS TO LABELING OF GOODS INTENDED FOR SALE TO OR USE BY CONSUMERS, INCLUDING BUT NOT LIMITED TO COMPLIANCE WITH CALIFORNIA PROPOSITION 65

Bioriginal
Anticipate • Innovate • Grow

522 Greenway Court
Reedsburg, WI
53959 USA
T: (608) 768-9439
F: (608) 768-9441
www.bioriginal.com

Lactose Codex Compliance Statement

Bioriginal (a division of Omega Protein Corporation) certifies that the lactose produced in the Reedsburg, WI facility; and is from a Caprine source, complies with Codex Standard for Sugars, Codex STAN 212-1999.

Sincerely,

(b) (6)

Jeannine Wilz
Quality Assurance Manager
Email: jwilz@bioriginal.com
Date: 06/09/17

Appendix 1.4 β-Galactosidase

GENOFOCUS
GenoFocus,Inc. (www.genofocus.com)
65, Techno1-ro, Yuseong-gu, Daejeon, Korea (34014)
Tel : 82 42 862 4483 Fax : 82 42 862 4484

Doc. No. : GF17-0425
DATE : April 25. 2017

Certificate of Analysis

PRODUCT : Lactazyme-B
Lot No: L170329

MANUFACTURE DATE : March. 29. 2017
EXPIRY DATE : March. 28. 2018

SPECIFICATIONS

Test Item	Specification	Test Result
Color	Yellow to light brown	CONFORMS
Appearance	Powder	CONFORMS
Activity of Lactase (GF)	Min. 4,000 Unit / g	4,834 Unit / g
Heavy Metal Content (As)	Max. 4 ppm	CONFORMS
Heavy Metal Content (Pb)	Max. 5 ppm	CONFORMS
Salmonella	Negative	CONFORMS
E.coli	Negative	CONFORMS
E. coli cpecies	Max.30 CFU/g	CONFORMS

*This product is an enzyme that converts lactose to galacto-oligosaccharide.

*Quantity of delivery: 30 kg
*Delivery date: April. 11. 2017
*Packing size: 5 kg
*Storage condition: Keep cool and dry, under 4℃

(b) (6)

Eun Young Kim
(Analyzed by)

(b) (6)

Taek Ho Yang
(Director of Quality Control)

Appendix 1.5 Citric Acid

ENSIGN

WEIFANG ENSIGN INDUSTRY CO., LTD.

NO.1567,CHANGSHENG STREET,CHANGLE,WEIFANG,SHANDONG PROVINCE, CHINA

Certificate of Analysis

Product:Citric Acid Anhydrous Food Grade Mesh Size 30-100 Mesh
Molecular Formula $C_6H_8O_7$
CAS No.: 77-92-9
Production Date:MAR.03.2017
Quantity: 20,000KG

Date:MAR.06.2017
Invoice No.:FQIM170207B
Batch No.: 1AX1703006
Expiry Date: MAR.02.2020

ITEM		Unit	Quality Standards	Analysis Results
Description		----	White or almost white, crystalline powder, colourless crystals or granules. Odorless, has a strongly acid taste. Very soluble in water, freely soluble in ethanol.	Pass
Identification		----	Pass Test	Pass
Appearance of solution		----	Pass Test	Pass
Assay		%	99.5~100.5	99.9
Moisture		%	≤0.2	0.1
Readily Carbonisable Substances	A @470nm	----	≤0.52	<0.52
	T @470nm	%	≥30	>30
Sulphate		PPM	≤150	<150
Oxalate		PPM	≤100	<100
Calcium		PPM	≤75	<75
Iron		PPM	≤5	<5
Sulphated Ash		%	≤0.05	0.02
Lead		PPM	≤0.5	<0.5
Arsenic		PPM	≤1	<1
Mercury		PPM	≤1	<1
Aluminium		PPM	≤0.2	<0.2
Heavy Metals(as Pb)		PPM	≤5	<5
Bacteria Endotoxin		IU/mg	<0.5	<0.5
Volatile Organic Impurities		----	Pass Test	Pass
Conclusion: The product is in conformity with BP/USP/FCC/E330				

Signature & Stamp:

Appendix 1.6 Diatomite Filter

From:Celite Korea Ltd. To:보성양산 07/10/2016 10:23 #779 P.001/001

12-5834

IMERYS

Imerys Minerals California, Inc.
2500 Miguelito Rd.
Lompoc, CA 93436
Contact:LompocCoA@Imerys.com
http://www.imerys-filtration.com

Certificate of Analysis

Product Designation: Imerys Minerals Korea Ltd.
Customer PO: IMK160503-3
Ship Date: 07/27/2016
Order Number: 6302S129069R001
Container: NYKU4834320
Product Type: Diatomaceous Earth
Product: Kenite 700
Manufacture Date: 07/10/2016
ot #.Production Code: 4AP16190
Sample #: 3846292
Customer Code: 600285

Certificate Recipient:
Attn: Jaeko Ko
cc:
Imerys Minerals Korea Ltd
7F, 64, Saimdang-ro (Gyodai Venture Tower)
Seocho-dong, Seocho-gu
Seoul, Korea 06640
Recipient Method:
Fax:
e-mail: brian.wi@imerys.com; jaeko.ko@imerys.com
Recipient Date: 7/27/2016

	Min	Max	Method	Result	Units
Supplier Test Methods					
150 mesh Tyler sieve retain (140M US)	0.0	12.0	LO-412-210	9.3	pct
Beer soluble aluminum - EBC	10	150	LO-412-433C	26	ppm
Beer soluble arsenic - EBC	0.1	7.0	LO-412-433C	0.1	ppm
Beer soluble calcium	0	750	LO-412-497	104	ppm
Beer soluble iron - EBC	0.5	60.0	LO-412-433C	62.0	ppm
Beer soluble lead - EBC	0.1	5.0	LO-412-433C	0.3	ppm
Beer soluble antimony - EBC	0.1	3.0	LO-412-433C	0.1	ppm
Odor in acid - .1N H2SO4	1.0	2.0	LO-412-384	1.0	pass
Centrifuged wet density	16.5	21.5	LO-412-234	18.1	lbs/ft3
Permeability	0.73	1.60	LO-412-331	1.23	darcy
Supplier Test Methods (Metric)					
Centrifuged wet density	263	346	LO-412-234	290	gm/L

Regards
(b) (6)
Paul Orangetree
Quality Manager

The Quality System of this facility is ISO 9001:2008 Registered by SAI Global

Seller's standard product inspection and testing procedures in effect at the time of testing were used to provide the information herein. Tests fixed by Seller at time of shipment shall be conclusive and binding upon Buyer as to all product sold and/or shipped. Seller represents and warrants to Buyer that all product conforms, as of shipment from Seller's plant, in all material respects to Seller's product specifications in effect at the time of shipment. Seller makes no other written, oral, express or implied warranties. Seller disclaims all warranties of merchantability and fitness for a particular purpose.

For additional information including MSDS see http://www.imerys-filtration.com/techdocs.asp
E-mail With Shipment 2500 Miguelito Rd

Page 1 of 1

Celite Corporation
P.O. Box 519
Lompoc, California 93438-0519
Telephone: (805) 735-7791

TECHNICAL DATA

Kenite 700

TYPICAL PHYSICAL PROPERTIES

Color	White
Appearance	Powder
Origin	Plankton Marine Diatomite
Description	Flux Calcined Filter Aid
Density,	
Dry(lbs/ft^3)	10.0
Wet(lbs/ft^3)	19.0
150 Mesh Screen Residue, %	7.0
Median Cake Pore Size, Microns	7.0
pH	10.0
Specific Gravity, g/cm^3	2.3
Moisture, as Shipped, %	0.1
Loss on Ignition	0.2

TYPICAL CHEMICAL PROPERTIES

SiO_2	89.6
$A1_2O_3$	4.0
Fe_2O_3	1.5
P_2O_5	0.2
TiO_2	0.2
CaO	0.5
MgO	0.6
$Na_2O + K_2O$	3.3

Typical values are not to be used as specifications.

2500 Miguelito Road
Lompoc, CA 93436
Ph: 805 737 2463
FAX: 805 737 1402

January 1, 2016

Regulatory Statement

Food Chemicals Codex (FCC) & Generally Recognized As Safe (GRAS)

Products produced by Imerys Filtration Minerals[1] in North America meet the requirements of the Food Chemicals Codex (FCC) 10th Edition. The warranty is printed on each bag with the words "Food Chemicals Codex grade", which warrants that the product meets federal and internationally recognized standards of purity and manufacturing. Imerys Filtration Minerals' policy describes how we continue to improve our level of compliance to meet the Food Chemicals Codex requirements for good manufacturing practices (GMP) and purity.

The monograph properties and limits from the FCC 10th edition for diatomaceous earth (DE) and perlite are reported in the table below:

Properties	Natural DE	Calcined DE	Flux-calcined DE	Perlite
Arsenic, mg/kg	10	10	10	10
Lead, mg/kg	10	10	10	10
Loss on Drying, %	10	3	3	3
Loss on Ignition, %	7	0.5	0.5	7
Non-siliceous substances, %	25	25	25	N/A
pH	5.0-10.0	5.0-10.0	8.0-11.0	5.0-11.0

The monograph properties and limits from the FCC 10th edition for calcium silicate (diatomaceous earth feed) are reported in the table below:

Properties	Calcium Silicate
Fluoride, mg/kg	10
Lead, mg/kg	5
Loss on Drying, %	Conform
Loss on Ignition, %	Conform

The Food and Drug Administration considers the use of diatomaceous earth, perlite and calcium silicate (diatomaceous earth feed) of suitable purity to be G.R.A.S. (Generally Recognized As Safe) for certain applications. Suitable purity is warranted by adherence to the relevant FCC monograph.

[1] Product portfolios of Imerys Filtration Minerals include the following brands: Aqua-Cel®, Aqua-Perl®, Calflo®, Celite®, Celkate®, Celpure®, CelTiX™, Cynergy ®, DiaFil®, Harbortite®, Hyflo® Super-Cel®, Kenite®, Micro-Cel®, Standard Super-Cel®, Super Floss®, and Super Fine Super Floss®

Imerys Filtration Minerals standard product inspection and testing procedures are used to release product for shipment. Imerys Filtration Minerals represents and warrants that all products conform in all material respects to Imerys Filtration Minerals product specifications in effect at the time of shipment. Imerys Filtratior Minerals can not make any claim of fitness for a particular use.

Regards.

(b) (6)

Kim Rivera

Quality Process Manager
Imerys Filtration Minerals.
kim.rivera@imerys.com

Appendix 1.7 Cartridge Filter

Woongjin Filtec

Tel : +82-52-223-1884 Fax : +82-52-223-1885

CERTIFICATE OF MATERIALS

This document is being provided to our customer to allow investigation into conformance to material specification. the specification is listed below.

CUSTOMER	
PRODUCT	HMI-0.5
CUSTOMER ORDER NO.	N/A
ORDER NUMBER	
DATE	05/10/2016
SPECIFICATION	Materials Of Construction, Operation conditions

Part of construction	Part Type/ Function	Materials of construction		Maximum Differential Pressure	Maximum Temperature
Media	Filtration Layer	polypropylene		60psi(4.1bar) at 25℃	90℃ at 30psi(2.1bar)
Endcaps	Sealing / Positioning	Polyprorylene		60psi(4.1bar) at 25℃	90℃ at 30psi(2.2bar)
Adhesives	Integrity	Polyprorylene		60psi(4.1bar) at 25℃	90℃ at 30psi(2.3bar)
Gaskets	Sealing	Polyethylene		85psi(4.1bar) at 25℃	90℃ at 30psi(2.4bar)
Outer Netting	Support Layer			60psi(4.1bar) at 25℃	90℃ at 30psi(2.5bar)
Inner Netting	Support Layer			60psi(4.1bar) at 25℃	90℃ at 30psi(2.6bar)
Core	Support			60psi(4.1bar) at 25℃	90℃ at 30psi(2.7bar)
Dimension	Size(IDXOD)	30±1 x 62±1 mm			
	Effective Filtertion area	0.2m²			
Operating Codition	Maximum Differential pressure	30 psid/2.1bar at 60 ℃			
		60 psid/4.2bar at 30 ℃			
	Maximum Operating Temperature	176 ℉/80 ℃			
	Pressure Drop vs.Water Flow Rate	0.09 bar	0.21 bar		
		13 L/min	31L/min		
	Removal Rating	β=100(99.00%)	β=10(90.00%)		
		2.5μm	1.2μm		

Note1 : It is suitable in operates condition at 90℃, 2hours, from sodium hydroxide-30% concentration and acid hydrochloric acid-30% concentration.

Note2 : All materials are contained in list of the FDA. (FDA I.D Code : 2030950)

Q.A Manager JH Kim

Woongjin Filtec

Tel : +82-52-223-1884 Fax : +82-52-223-1885

CERTIFICATE OF QUALITY

CUSTOMER	
PRODUCT	HMI-0.5
CUSTOMER ORDER NO.	N/A
ORDER NUMBER	N/A
DATE	05/10/2016
CERTIFICATE DATE	15/08/2016

※Filter Performance

ASTM F 316-68, ASTM 795-88&89 : Standrad Practice for Determining the performance of a Filter Medium Employing a Single-Pass, Constant-Rate,Liquid Test

※Product Quality

This products is developed, produced and distributed according to a Quality Management System that is certified for compliance with KS A 9001:2001 / ISO 9001:2000.

Manufactured in a clena room Environment(class 10,000)

※Materials of Construction

Polypropylene and Silicon-All materials are contained in list of the FDA. (FDA I.D Code : 2030950)

※This document is to certify that the designated product was manufactured by KAIZER FILTER.

Q.A Manager JH Kim

Compliance statement

WOONGJIN FILTEC confirms that Microfilter (ADM 0.5-500) conforms to the US Code of Federal Regulations 21CFR 177.1520(Polypropylene)

AUTHORIZED SIGNATURE (b) (6)

Kim Yun Suk

COMPANY NAME	WOONGJIN FILTEC
POSITION	President
NAME	Kim Yun Suk
DATE	2017.07.12

Appendix 1.8 Membrane Filter

ERTEL ALSOP

THE FIRST NAME IN LIQUID FILTRATION™

CONFIDENTIAL

SPECIFICATION SHEET

Product Code : Zeta -Pak®

Grade Designation : 12PFY5M95416

Materials : Cellulose/Diatomaceous Earth

Wet Strength Resin : Non-Hazardous, listed as safe under 21CFR 176.170

Physical Properties :

Surface :	Mottled
Color :	White to Off-White
Flowrate :	10-20 GPH per Pak® Average
Retention :	0.25 micron nominal
Configuraion :	16 Cells
Filtration Area :	18.5 sq. ft

Components :

Gasket :	Buna-N
Support Members :	Polypropylene

* Flowrate based on 70°F water flow through a 2 inch diameter filter at 10 PSI
* Retention based on retaining 98% of a given micron particle
* All components are listed in the CFR as generally recognized as safe for contact with food.

Note Manufactured in accordance with ErtelAlsop Drug Master File located at the United States Food and Drug Administration Center for Drug Evaluation and Research.

ERTELALSOP. OUR MISSION IS CLEAR.™
P.O. BOX 3358, KINGSTON, NY 12402
TELEPHONE: 800.553.7835 845.331.4552 FAX: 845.339.1063
SALES@ERTELALSOP.COM WWW.ERTELALSOP.COM

Appendix 1.9 Maltodextrin

SHAFI GLUCO CHEM

ORGANIC RICE MALTODEXTRIN 12DE

Product Code: ORMD012

Category	Rice Maltodextrin
Form	Dehydrated
Country Of Origin	Pakistan
Ingredient Declaration	Organic Rice Maltodextrin
Non-GMO	Yes
Suitable for	Halal , Kosher & Vegetarian diets
Functionalities	Bulking Agent

Description

This product is white crystalline solids and has a clean sweet flavor with light buttery and honey flavor notes. It is made from the enzymatic treatment of rice, using GMO free natural enzymes, which is filtered , concentrated and is spray dried.

Certifications

- ✓ NOP , EU & FIPA Organic Certified
- ✓ FSSC 22000:2010
- ✓ ISO 9001:2008
- ✓ Kosher

Packaging:

Materials :Paper Bag with Polythene Liner
Size :20 Kg / Bag
Packaging is Food grade approved

Shelf Life:
18 Months (When stored under recommended condition)

Storage Condition

Maltodextrin Should be stored at temperature < 90 °F in a cool dry environment, away from sunlight

ANALYSIS

Chemical Parameters	Unit	Limits
Dextrose Equivalent	%	9 - 15
Total Carbohydrates *	g/100g	92.5
Glucose (DP 1) *	g/100g	1.5
Maltose (DP 2) *	g/100g	3.0
Other Carbohydrates *	g/100g	88
Dry Solid Substance	%	93 - 97
Moisture	%	3 - 7
pH		4.5 - 6.5
Ash Contents	%	< 0.5
Energy *	Kcal/100g	372
Starch	%	Negative
Protein	%	< 0.5
Fat	%	< 0.5

Heavy Metals	Unit	Limits
Lead	ppm	< 0.05
Arsenic	ppm	< 0.1
Cadmium	ppm	< 0.05
Mercury	ppm	< 0.01

Microbiological	Units	Limits
Total Plate Count	cfu/g	<1000
Total Coliforms	cfu/g	<10
E.Coli	cfu/g	<10
Yeast	cfu/g	<200
Mold	cfu/g	<100
Salmonella	cfu/25g	Nil

Allergen	Present (Y/N)
Cereals containing gluten	N
Crustaceans, molluscs and their derivatives	N
Fish and their derivates	N
Egg or Egg products	N
Peanuts and their derivates	N
Others	N

Uses

Ice Cream, Drinks, Yoghurts, Desserts, pharmacy, Biscuits, Break fast foods, Baby foods, Cosmetics, Snacks, confectionary, fruit-based preparations, Dehydrated soups, etc.

* These indicative analytical values reflect the actual position of our knowledge and do not constitute any guarantee

Shafi GlucoChem (Pvt.) Ltd. B-22 to 26 Hub Industrial Trading Estate, Distt. Lasbela, Balochistan, Pakistan
Tel. +92-853303719 Fax +92-853303952, sgc@glucochem.com, www.glucochem.com

Last Updated : March 2016
Spec # SSD40

SHAFI GLUCO CHEM
(Pvt) Ltd.
Plot No: B-22 to 26 & B-35 to 42, Hub Industrial Trading Estate, Distt. Lasbella, Balochistan, Pakistan
Ph: (92-853) 303719-21 Fax: (92-853) 303952 E-mail: sgc@glucochem.com Web: www.glucochem.com

May 31, 2017

TO WHOM IT MAY CONCERN

We, Shafi Gluco Chem (Pvt.) Ltd., declare and certify that our Rice Maltodextrin meets the FCC Specification for Maltodextrin.

(b) (6)

Shafi Gluco-Chem (Pvt) Ltd. HUB

Muhammad Qasim Abbasi
Manager Quality Assurance

Appendix 1.10 Yeast

CERTIFICATE OF ANALYSIS

Product Name : FRESH YEAST

(High sugar)

Quantity : kg
Production Dates : 2017. 04. 24
Expiry Date: 25days from Production Date

Test Items		Specifications	Result
Appearance		Lump of milk - yellowish brown color	Lump of milk - yellowish brown color
Smell		Yeast smell	Yeast smell
Fermentating power (2hr)	F10(㎖)	110 min	180
	F40(㎖)	60 min	124
Lead	(ppm)	1.0 max	passed
Arsenic	(ppm)	3 max	passed
E.Coli	/g	Negative	Negative
Moisture	(%)	70 max	66.74

CHOHEUNG CHEMICAL IND. CO., LTD
(Tel : 031-433-3883~7)

CHOHEUNG CORPORATION
38, Silhwa-ro, Danwon-gu, Ansan-si, Gyeonggi-do, Korea
tel:82-31-319-7001~7004 FAX:82-31-433-0081

Compliance statement

CHOHEUNG CORPORATION confirms that fresh yeast meets the Korean Food Additives Codex [B. Natural Additives_99. Yeast].

AUTHORIZED

(b) (6)

COMPANY NAME	CHOHEUNG CORPORATION
POSITION	QA. Manager
NAME	Shin Myeong Ho
DATE	26.Apr.2017

Certificate of the use of non-GMO ingredients

Product	Fresh Yeast

Manufacturer	Name	Choheung Corporation
	Address	38 Shihwa-ro, Danwon-gu, Ansan-si Gyeonggi-do, 15410, Korea
	CEO	Yikje Yoo
Customer	Name	
	Address	
	CEO	

This is to certify that Fresh Yeast supplied by Choheung Corporation is manufactured with non-GMO ingredients, and to the best of our knowledge, this information herein, as of April 25, 2017, is accurate and true.

April 25, 2017

Head of Research & Development Center: Jae-Yoo Kim

Appendix 1.11 Activated Carbon

JACOBI CARBONS
www.jacobi.net

Certificate of Analysis

Customer:	CS Corporation	**Cust Ref:**	CSC-161206C
Lot No.:	81612175	**Date Issued:**	7-Dec-2016
Quantity:	6000 kg	**Date Manufactured:**	10-Jan-2017
Grade.:	ColorSorb HP90 N PAC-S 15 kg PJ 20BP	**Date Printed:**	11-Jan-2017

Parameter	Method	Spec. min	Spec. max	Value	Unit
Molasses Number (EU)	EU T4007		90	85	
Moisture, as packed	ASTM D2867		10.0	8.2	%
Total Ash Content	ASTM D2866		6.0	4.4	%
Phosphate Content	Jacobi-GB T4043		2.0	0.6	%
Acid Soluble Iron	ASTM D0647	Report	Report	117	ppm
pH	ASTM D3838	3.5	6.5	5.8	
Particle Size	Wet Sieve				
< 100		95.0	100.0	98.0	%
< 200		85.0	100.0	89.1	%
< 325			80.0	69.5	%

This document is valid and generated automatically from our Enterprise Quality Management system.

Jacobi Carbons is certified to ISO 9001:2008

Jacobi | PICA

TECHNICAL BULLETIN

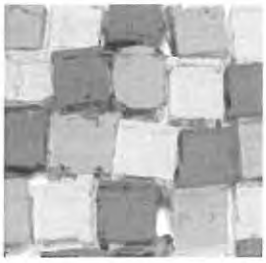
Analysis of ColorSorb® HP90N activated carbon produced by Jacobi Carbons to Food Chemical Codex standard for materials to be used in the treatment of food stuffs

Test Results **Sample No. INO102719**

Parameter	Value	Specification
Lead (Pb) content	<0.06mg/Kg	<10mg/Kg
Cyanogen compounds	Pass	Pass/Fail
Higher aromatic compounds	Pass	Pass/Fail
Water extractables	0.24%	<4.0%
Loss on drying	0.1%	Report only
Residue on ignition	2.81%	Report only
Iodine number	1154mg/g	>400mg/g
Arsenic content	<0.004mg/Kg	<3mg/Kg

Conclusion

The activated carbon ColorSorb® HP90N is manufactured by Jacobi Carbons in accordance with the current Food Chemical Codex for materials used for the treatment of food products.



For more information or to contact Jacobi visit www.jacobi.net

Appendix 1.12 Ion-Exchange Resins

2017.05.26 09:06/생산파트/SYC209047

이온교환수지제품검사서
Certificate Of Analysis Report

弊社 귀사에 의거 이온交換樹脂(ION EXCHANGE RESIN)에 대한 試驗成績書를 다음과 같이 提出합니다.

(We hereby certify that under-mentioned products were duly inspected by us and were found to conform to our specifications.)

1. 품 명 (Commodity) : TRILITE AMP24

2. 총수량 (Total Quantity) :

항목 (Items)	규격 (Specification)	단위 (Unit)	Lot No
성상(Sensory attribute)	BT	-	BT
출하가밀도(Shipping Density)	700 ↓	g / ℓ	670
수분함유율(Water Retetion)	54.0 ~ 64.0	%	59.8
외관지수(Appearance Index)	95.0 ↑	%	99.7
교환용량(Total Capacity)M	3.30 ↑	meq/g-R	3.87
교환용량(Total Capacity)V	0 ↑	meq/㎖-R	1
유효경(Effective Size)	40 ↑	mm	0.48
균일계수(Uniform Coefficient)	1.6 ↓	-	1.6
고형분(Solid)	2.5 ↑	g	7.4
물가용분(Water-Soluble Substances)	2.5 ↓	mg	0.6
비소(Arsenic)	4.0 ↓	ppm	0
납(Lead)	2.0 ↓	ppm	0
입도Size1180(㎛)↑	0 ↑	%	0
입도Size850(㎛)↑	0 ↑	%	27.17
입도Size710(㎛)↑	0 ↑	%	35.51
입도Size600(㎛)↑	0 ↑	%	17.39
입도Size425(㎛)↑	0 ↑	%	14.49
입도size300(㎛)↑	0 ↑	%	5.43
입도Size300(㎛)↓	0 ↑	%	0
	수량 (Quantity)		

비고 :

BT : Brown granular substance

우리 시험결과가 틀림이 없음을 증명함

CERTIFY THE ABOVE STATEMENT OF QUALITY TO BE TRUE AND CORRECT

Confirmer : (b) (6)

3F, Jong-ro 33-gil, Jongno-gu, Seoul 03129, Korea T.+82.740.7742 F.+82.740.7709
IER Sales Team Samyang Corporation

2017.05.26 09:06/생산파트/SYC209047

이온교환수지제품검사서
Certificate Of Analysis Report

품목 명칭의 의거 이온交換樹脂(ION EXCHANGE RESIN)에 대한 試驗成績書를 다음과 같이 發行합니다

(We hereby certify that under-mentioned products were duly inspected by us and were found to conform to our specifications.)

1. 품 명 (Commodity) TRILITE SCR-B

2. 총수량 (Total Quantity)

항목 (Items)	규격 (Specification)	단위 (Unit)	Lot No.
성상(Sensory attribute)	BT	-	BT
입도기일도(Shipping Density)	850 ↓	g / ℓ	830
수분함유율(Water Retetion)	43.0 ~ 50.0	%	46.5
외관지수(Appearance Index)	80.0 ↑	%	99.2
교환용량(Total Capacity)M	4.50 ↑	meq/g-R	4.55
교환용량(Total Capacity)V	2.0 ↑	meq/㎖-R	2.1
유효경(Effective Size)	40 ↑	㎜	0.49
균일계수(Uniform Coefficient)	1.6 ↓	-	1.6
고형분(Solid)	2.5 ↑	g	2
물가용분(Water-Soluble Substances)	2.0 ↓	mg	0.6
비소(Arsenic)	4.0 ↓	ppm	0
납(Lead)	2.0 ↓	ppm	0
입도Size1180(㎛) ↑	0 ↑	%	0
입도Size850(㎛) ↑	0 ↑	%	21.16
입도Size710(㎛) ↑	0 ↑	%	34.39
입도Size600(㎛) ↑	0 ↑	%	20.28
입도Size425(㎛) ↑	0 ↑	%	20.63
입도size300(㎛) ↑	0 ↑	%	3.53
입도Size300(㎛) ↓	0 ↑	%	0
	수량 (Quantity)		

비고

BT Brown granular substance

위와 시험결과가 틀림이 없음을 증명함

CERTIFY THE ABOVE STATEMENT OF QUALITY TO BE TRUE AND CORRECT

Confirmed (b) (6)

31, Jong-ro 33-gil, Jongno-gu, Seoul 03139, Korea T.+82.740.7742 F.+82.740.7726

R&D Sales Team Samyang Corporation

2017.05.26 09:06/생산팀트/SYC269047

이온교환수지제품검사서
Certificate Of Analysis Report

(We hereby certify that under-mentioned products were duly inspected by us and were found to conform to our specifications.)

1. 품 명 (Commodity) AWSC

2. 총수량 (Total Quantity)

항목 (Items)	규격 (Specification)	단위 (Unit)	Lot No
성상(Sensory attribute)	BT	-	BT
충보가밀도(Shipping Density)	650 ↓	g / l	646
수분함유율(Water Relation)	40.0 ~ 50.0	%	44.4
외관지수(Appearance Index)	95.0 ↑	%	99.6
교환용량(Total Capacity)M	4.80 ↑	meq/g-R	
교환용량(Total Capacity)V	1.8 ↑	meq/ml-R	1.6
유효경(Effective Size)	40 ↑	mm	0.45
균등계수(Uniform Coefficient)	1.1 ↓	-	1.1
고형분(Solid)	2.5 ↑	g	7.4
물가용분(Water-Soluble Substances)	2.5 ↓	mg	0.6
비소(Arsenic)	4.0 ↓	ppm	0
납(Lead)	2.0 ↓	ppm	0
입도Size1180(㎛)↑	0 ↑	%	0
입도Size850(㎛)↑	0 ↑	%	0
입도Size710(㎛)↑	0 ↑	%	0
입도Size600(㎛)↑	0 ↑	%	0.78
입도Size425(㎛)↑	0 ↑	%	98.47
입도Size300(㎛)↓	0 ↑	%	0.77
입도Size300(㎛)↓	0 ↑	%	0

수량 (Quantity)

비고 :

BT : Brown granular substance

위와 시험결과가 품질이 같음을 증명함

CERTIFY THE ABOVE STATEMENT OF QUALITY TO BE TRUE AND CORRECT

(b) (6)

Confirmer

31, Jong-ro 33-gil, Jongno-gu, Seoul 03179, Korea T.+82 760 7743 F.+82 760 7709

IER Sales Team Samyang Corporation

2017.06.07 11:31/생산파트/SYC209047

이온교환수지제품검사서
Certificate Of Analysis Report

[illegible] 귀사 주문에 의거 이온交換樹脂(ION EXCHANGE RESIN)에 대한 試驗成績書를 다음과 같이 發行합니다.
(We hereby certify that under-mentioned products were duly inspected by us and were found to conform to our specifications.)

1. 품 명 (Commodity) : SPC180H

2. 총수량 (Total Quantity) :

항목 (Items)	규격 (Specification)	단위 (Unit)	Lot No
성상(Sensory attribute)	BT	-	BT
겉보기밀도(Shipping Density)	750 ↓	g / ℓ	741
수분함량율(Water Retetion)	53.0 ~ 60.0	%	55.6
외관지수(Appearance Index)	85.0 ↑	%	89.5
교환용량(Total Capacity)M	4.50 ↑	meq/g-R	5.09
교환용량(Total Capacity)V	1.5 ↑	meq/㎖-R	1.6
유효경(Effective Size)	40 ↑	mm	0.53
균일계수(Uniform Coefficient)	1.6 ↓	-	1.5
고형분(Solid)	2.5 ↑	g	8.00
수가용분(Water-Soluble Substances)	2.5 ↓	mg	0.60
비소(Arsenic)	4.0 ↓	ppm	0.00
납(Lead)	2.0 ↓	ppm	0.00
입도Size1180(㎛)↑	0 ↑	%	0.00
입도Size850(㎛)↑	0 ↑	%	29.35
입도Size710(㎛)↑	0 ↑	%	34.27
입도Size600(㎛)↑	0 ↑	%	19.14
입도Size425(㎛)↑	0 ↑	%	14.42
입도 size300(㎛)↑	0 ↑	%	2.87
입도 Size300(㎛)↓	0 ↑	%	0.00
	수량 (Quantity)		

비고
BT Brown granular substance

위와 시험결과가 틀림이 없음을 증명함
CERTIFY THE ABOVE STATEMENT OF QUALITY TO BE TRUE AND CORRECT

(b) (6)

Confirmer 검순

31, Jong-ro 30-gil, Jongro-gu, Seou 03170, Korea T +82 740 7742 F +82 740 7729
E-R Sales Team Semyang Corporation

Compliance statement

We, Samyang Corporation confirms that ion exchange resin,TRILITE SCRB, AW90, AMP24, CMP16 conforms to the US Code of Federal Regulations 21C.F.R. sec.173.25 for use in the purification of foods and potable water.

AUTHORIZED SIGNATURE

SAMYANG CORPORATION

(b) (6)

Executive Vice President

DATE April 26, 2017

Appendix 1.13 Sodium Hydroxide

Certificate Of Analysis

(CUSTOMER USE)

ITEM DESCRIPTION	GOOD	ISSUED NO	81169165
MF_CA_1/M NaOH 50%_BULK		ORDER NO	676252
CUSTOMER NAME		PRODUCTION DATE	
(주)엠에스씨		LOT NO	20170609_1
		AMOUNT MT	
		PICKING DATE	2017.06.09

TEST ITEM	UNIT	SPECIFICATIONS	TEST RESULT	METHOD
NaCl.	wtppm	MAX. 150.0	47.0	HCY-I-67761
환경관리등급			통과율	
확인시험(1)			강알카리성	
확인시험(2)			나트륨염 반응	
Na2SO4	wtppm	MAX. 250.0	LT 10	HCY-I-67763
Fe2O3	wtppm	MAX. 10.00	0.43	HCY-I-67762
Na2CO3	wt%	MAX. 0.20	0.04	HCY-I-67769
Na2O	wt%	38.6 ~ 39.4	39.0	HCY-I-67769
NaClO3	wtppm			HCY-I-67767
Cr	wtppm		0.036	HCY-I-67769
As	wtppm	MAX. 1.000	0.010	HCY-I-67769
Cd	wtppm		0.010	HCY-I-67769
Hg	wtppm	MAX. 0.100	0.010	HCY-I-67769
Pb	wtppm	MAX. 2.000	0.010	HCY-I-67769
성상			무색/약간 황색	HCY-I-67776
용상			무색/침전 이하	HCY-I-67777
확인시험			정상	HCY-I-67778
NaOH	wt%	49.60 ~ 50.70	50.26	HCY-I-67769

End Of Item

** ONLY MARKED USE IS ALLOWED **

I CERTIFY THE ABOVE STATEMENT OF QUALITY TO BE TRUE AND CORRECT.

Manager

(b) (6)

TEL NO 061)688-1642 FAX NO. 061)688-1640

HANWHA CHEMICAL CO. #612 WOLHA-DONG, YEOSU. JUNNAM-DO, KOREA. YEOSU PLANT

Hanwha Chemical

1/1

Compliance statement

[Hanwha Chemical Corporation] confirms that [Caustic Soda] meets Food Chemical Codex specifications.

AUTHORIZED SIGNATURE
(b) (6)

COMPANY NAME	Hanwha Chemical Corporation
POSITION	QA Part Leader
NAME	Honggi Jin
DATE	2017 06 19

Appendix 1.14 Hydrochloric Acid

Certificate Of Analysis

(CUSTOMER USE)

ITEM DESCRIPTION GOOD	ISSUED NO		81167303
MF_CA_HCL 35%(VCM/ECH)_BULK	ORDER NO		673807
CUSTOMER NAME	PRODUCTION DATE		
	LOT NO		20170519_3
	AMOUNT MT		
	PICKING DATE		2017.05.19

TEST ITEM	UNIT	SPECIFICATIONS	TEST RESULT	METHOD
HCL(농도%)	wt%	MIN. 35.0	35.8	HCU-F-03222
Fe	wtppm	MAX. 5.00	0.08	HCU-F-03223
SO4	wtppm	MAX. 200.00	117.12	HCU-F-03224
As	wtppm	MAX. 2.0	0.1	HCU-F-03225
I.R	wtppm	MAX. 60.00	2.58	HCU-F-03227
Pb	wtppm	MAX. 1.0	0.5	HCU-F-03226
Hg	wtppm	MAX. 1.00	0.10	HCU-F-03228
산화성물질(as Cl2)	wtppm	MAX. 30	20	HCU-F-03228
환원성물질(as SO2)	wtppm	MAX. 70	0	HCU-F-03228
NVM	wtppm	MAX. 6000.00	3.45	HCU-F-03228

End Of Item

** ONLY MARKED USE IS ALLOWED **

I CERTIFY THE ABOVE STATEMENT OF QUALITY TO BE TRUE AND CORRECT

Manager

(b) (6)

TEL NO (052)279-2373 FAX NO (052)279-2389
HANWHA CHEMICAL CO. #482 SANGGAE DONG, NAMGU,
ULSAN, KOREA. ULSAN PLANT #1

Hanwha Chemical

1/1

Compliance statement

[Hanwha Chemical] confirms that [Hydrochloric acid] meets or exceeds Food Chemical Codex specifications .

AUTHORIZED SIGNATURE
(b) (6)

COMPANY NAME	Hanwha Chemical
POSITION	Manager
NAME	Hong-gi, Jin
DATE	2. June. 2017

Appendix 2 Certificates of Analysis for Neo Cremar's Cow's Milk Lactose-Derived GOS Preparations

Appendix 2.1 Nature's GOS-L

Appendix 2.2 Nature's GOS-CL

Appendix 2.3 Nature's GOS-P

Appendix 2.4 Mother's OLIGO-L

Appendix 2.5 Mother's OLIGO-CL

Appendix 2.6 Mother's OLIGO-P

Appendix 2.7 Mother's OLIGO-CP

Appendix 2.1 Nature's GOS-L

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-L

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : NCOG20161025
Date of Manufacture : 25. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	More than 75.0 %	76.5	Refractometer at 20℃
GOS/DM	More than 55.0 %	63.46	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.20	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH (10% solution)	4.0 - 7.0	6.23	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,468	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0008	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.004	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	11th. Nov. 2016

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-L

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : NCOG20161026
Date of Manufacture : 26. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	More than 75.0 %	76.66	Refractometer at 20℃
GOS/DM	More than 55.0 %	62.88	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.22	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH (10% solution)	4.0 ~ 7.0	6.22	pH meter
Viscosity (25℃)	1,000 ~ 5,000 cPs	1,387	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0009	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.004	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	12th. Nov. 2016

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-L

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)

Date of Manufacture : 01. Nov. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	More than 75.0 %	76.4	Refractometer at 20℃
GOS/DM	More than 55.0 %	61.48	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.19	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH (10% solution)	4.0 ~ 7.0	5.95	pH meter
Viscosity (25℃)	1,000 ~ 5,000 cPs	1,432	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0008	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.006	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE
(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	16th. Nov. 2016

Appendix 2.2 Nature's GOS-CL

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : OGCL20170116
Date of Manufacture : 16. Jan. 2017

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.3	Refractometer at 20℃
GOS/DM	More than 57.0 %	62.1	AOAC 2001.02
Lactose/DM	Less than 23.0 %	18.08	HPLC
Glucose/DM	Less than 22.0 %	18.98	HPLC
Galactose/DM	More than 0.8 %	0.82	HPLC
Sulfated Ash	Less than 0.3 %	0.2	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.53	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,478	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0014	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.009	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	30	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA: (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	2nd. Feb. 2017

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b)(4)
Date of Manufacture : 20. Jan. 2017

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.8	Refractometer at 20℃
GOS/DM	More than 57.0 %	62.0	AOAC 2001.02
Lactose/DM	Less than 23.0 %	18.02	HPLC
Glucose/DM	Less than 22.0 %	19.12	HPLC
Galactose/DM	More than 0.8 %	0.83	HPLC
Sulfated Ash	Less than 0.3 %	0.21	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.57	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,495	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0018	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.01	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE
(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	6th. Feb. 2017

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro 11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 23. Jan. 2017

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.2	Refractometer at 20℃
GOS/DM	More than 57.0 %	61.9	AOAC 2001.02
Lactose/DM	Less than 23.0 %	18.01	HPLC
Glucose/DM	Less than 22.0 %	19.21	HPLC
Galactose/DM	More than 0.8 %	0.87	HPLC
Sulfated Ash	Less than 0.3 %	0.21	550℃ till constant
Nitrogen	Less than 0.1 %	0.001	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.72	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,423	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0014	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.009	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	8th. Feb. 2017

Appendix 2.3 Nature's GOS-P

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-P

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : OGCP20161103
Date of Manufacture : 03. Nov. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.45	Loss on drying at 110℃
GOS/DM	More than 33.0 %	27.7	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.11	550℃ till constant
Nitrogen	Less than 0.1 %	0.001	Kjeldahl method
Nitrate	Less than 50 ppm	23.2	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	3.0 - 6.0	4.2	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0007	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.004	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	10	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	18th.Nov. 2016

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Nature's GOS-P

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 08. Dec. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.42	Loss on drying at 110℃
GOS/DM	More than 27.0 %	28.9	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.12	550℃ till constant
Nitrogen	Less than 0.1 %	0.001	Kjeldahl method
Nitrate	Less than 50 ppm	24.8	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	3.0 ~ 6.0	4.71	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0006	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.002	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	20	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE
(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	23rd.Dec. 2016

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-40[illegible]-4087

Nature's GOS-P

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : (b) (4)

Date of Manufacture : 26. Jan. 2017

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powde[illegible]	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.36	Loss on drying at 110℃
GOS/DM	More than 27.0 %	29.2	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.11	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrate	Less than 50 ppm	26.3	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	3.0 - 6.0	4.32	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0008	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.001	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	10	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	11th.Feb. 2017

Appendix 2.4 Mother's OLIGO-L

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-L

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : NCMO20160928
Date of Manufacture : 28. Sep. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	More than 75.0 %	76.36	Refractometer at 20℃
GOS/DM	More than 70.0 %	71.62	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.14	550℃ till constant
Nitrogen	Less than 0.1 %	0.05	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH (10% solution)	4.0 - 7.0	6.21	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,882	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP (inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0028	ICP (inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.006	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	30	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	13th. Oct. 2016

Neo Cremar Co., Ltd.

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Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-L

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 29. Sep. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	More than 75.0 %	76.69	Refractometer at 20℃
GOS/DM	More than 70.0 %	72.43	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.15	550℃ till constant
Nitrogen	Less than 0.1 %	0.06	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH (10% solution)	4.0 - 7.0	6.30	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,869	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0028	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.007	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE
(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	14th. Oct. 2016

Neo Cremar Co., Ltd.

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Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
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Mother's OLIGO®-L

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)

Date of Manufacture : 14. Nov.2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	More than 75.0 %	76.78	Refractometer at 20℃
GOS/DM	More than 70.0 %	72.64	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.14	550℃ till constant
Nitrogen	Less than 0.1 %	0.05	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH (10% solution)	4.0 – 7.0	6.12	pH meter
Viscosity (25℃)	1,000 – 5,000 cPs	1,879	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0029	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.008	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	29th. Nov. 2016

Appendix 2.5 Mother's OLIGO-CL

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : MOCL20161018
Date of Manufacture : 18. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.4	Refractometer at 20℃
GOS/DM	More than 75.0 %	77.16	AOAC 2001.02
Lactose/DM	Less than 23.0 %	17.57	HPLC
Glucose/DM	Less than 5.0 %	1.86	HPLC
Galactose/DM	More than 0.8 %	3.41	HPLC
Sulfated Ash	Less than 0.3 %	0.21	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.21	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,427	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0038	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.006	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	30	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	3rd. Nov. 2016

Neo Cremar Co., Ltd.

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Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 22. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.8	Refractometer at 20℃
GOS/DM	More than 75.0 %	77.23	AOAC 2001.02
Lactose/DM	Less than 23.0 %	17.3	HPLC
Glucose/DM	Less than 5.0 %	1.87	HPLC
Galactose/DM	More than 0.8 %	3.60	HPLC
Sulfated Ash	Less than 0.3 %	0.20	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.48	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,486	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0038	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.007	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	30	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	7th. Nov. 2016

Neo Cremar Co., Ltd.

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Mother's OLIGO®-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 05. Nov. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 ~76.0 %	75.9	Refractometer at 20℃
GOS/DM	More than 75.0 %	77.19	AOAC 2001.02
Lactose/DM	Less than 23.0 %	17.46	HPLC
Glucose/DM	Less than 5.0 %	1.88	HPLC
Galactose/DM	More than 0.8 %	3.53	HPLC
Sulfated Ash	Less than 0.3 %	0.21	550℃ till constant
Nitrogen	Less than 0.1 %	0.001	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 ~ 3.8	3.52	pH meter
Viscosity (25℃)	1,000 ~ 5,000 cPs	1,476	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0039	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.006	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	40	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	20th. Nov. 2016

Appendix 2.6 Mother's OLIGO-P

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-P

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : NCMP20160212
Date of Manufacture : 12. Feb. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	4.20	Loss on drying at 110℃
GOS/DM	More than 70.0 %	71.4	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.16	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrate	Less than 50 ppm	19.8	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	4.0 - 7.0	6.08	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0005	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.007	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	10	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	27th.Feb. 2016

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-P

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 13. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.20	Loss on drying at 110℃
GOS/DM	More than 70.0 %	72.54	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.15	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrate	Less than 50 ppm	19.8	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	4.0 ~ 7.0	6.07	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0006	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.008	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	10	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	28th.Oct. 2016

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil. Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-P

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 23. Nov. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.30	Loss on drying at 110℃
GOS/DM	More than 70.0 %	71.14	AOAC 2001.02
Sulfated Ash	Less than 0.3 %	0.16	550℃ till constant
Nitrogen	Less than 0.1 %	0.01	Kjeldahl method
Nitrate	Less than 50 ppm	20.1	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	4.0 - 7.0	6.27	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0005	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.008	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	20	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungChoul Shin
DATE	8th Dec. 2016

Appendix 2.7 Mother's OLIGO-CP

Neo Cremar Co., Ltd.

A-714, hyundai Knowledge Center, 11,
Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-CP

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : MOCP20161025
Date of Manufacture : 25. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.3	Loss on drying at 110℃
GOS/DM	More than 75.0 %	77.12	AOAC 2001.02
Lactose/DM	Less than 23.0 %	17.71	HPLC
Glucose/DM	Less than 5.0 %	1.86	HPLC
Galactose/DM	More than 0.8 %	3.31	HPLC
Sulfated Ash	Less than 0.3 %	0.11	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrate	Less than 50 ppm	24.6	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	3.0 - 6.0	4.67	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0006	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.005	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	10	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	11th.Nov. 2016

Neo Cremar Co., Ltd.

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TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®-CP

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 30. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.1	Loss on drying at 110℃
GOS/DM	More than 75.0 %	76.75	AOAC 2001.02
Lactose/DM	Less than 23.0 %	18.01	HPLC
Glucose/DM	Less than 5.0 %	1.95	HPLC
Galactose/DM	More than 0.8 %	3.29	HPLC
Sulfated Ash	Less than 0.3 %	0.11	550℃ till constant
Nitrogen	Less than 0.1 %	0.001	Kjeldahl method
Nitrate	Less than 50 ppm	24.7	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	3.0 - 6.0	4.62	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0006	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.005	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	10	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE
(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	15th.Nov. 2016

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TEL : +82-2-401-4088 FAX : +82-2-401-4087

Mother's OLIGO®–CP

(Galacto-oligosaccharide Powder)

Certificate of Analysis

Lot NO : MOCP20161027
Date of Manufacture : 27. Oct. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	White to yellow powder	Passed	Sensory Test (Visible observation)
Moisture	Less than 5.0 %	3.2	Loss on drying at 110℃
GOS/DM	More than 75.0 %	77.53	AOAC 2001.02
Lactose/DM	Less than 23.0 %	17.34	HPLC
Glucose/DM	Less than 5.0 %	1.89	HPLC
Galactose/DM	More than 0.8 %	3.24	HPLC
Sulfated Ash	Less than 0.3 %	0.12	550℃ till constant
Nitrogen	Less than 0.1 %	N.D	Kjeldahl method
Nitrate	Less than 50 ppm	25.8	IC (Ion Chromatography)
Nitrite	Less than 0.5 ppm	N.D	Diazotization method
pH (10% solution)	3.0 ~ 6.0	4.55	pH meter
Arsenic	Less than 0.1 ppm	N.D	ICP (Inductively coupled plasma)
Lead	Less than 1.0 ppm	N.D	ICP (Inductively coupled plasma)
Cadmium	Less than 0.06 ppm	0.0007	ICP (Inductively coupled plasma)
Mercury	Less than 0.1 ppm	0.007	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 1,000 CFU/g	20	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	12th.Nov. 2016

Appendix 3 Representative Chromatograms for Cow's Milk Lactose-Derived GOS Preparations

Appendix 3.1 Nature's GOS-L

Appendix 3.2 Nature's GOS-CL

Appendix 3.3 Nature's GOS-P

Appendix 3.4 Mother's OLIGO-L

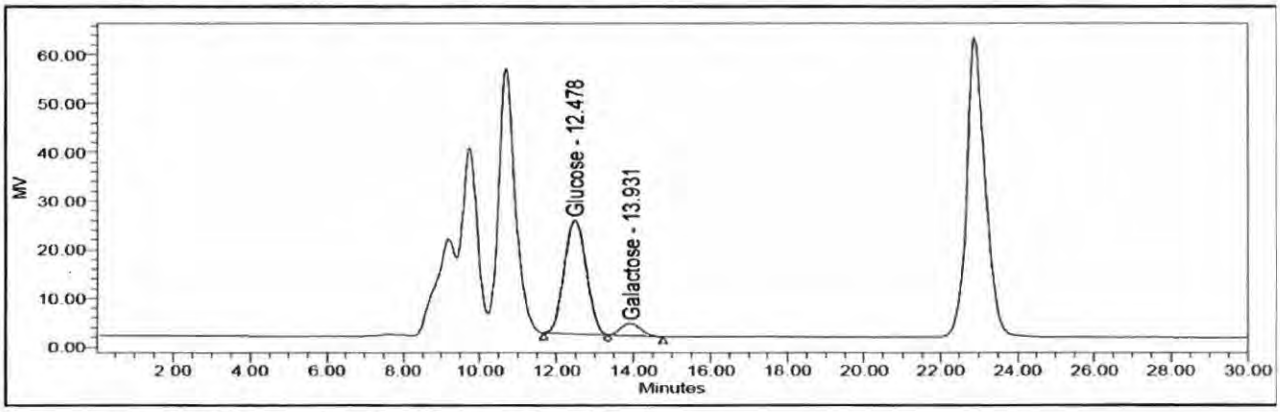
Appendix 3.5 Mother's OLIGO-CL

Appendix 3.6 Mother's OLIGO-P

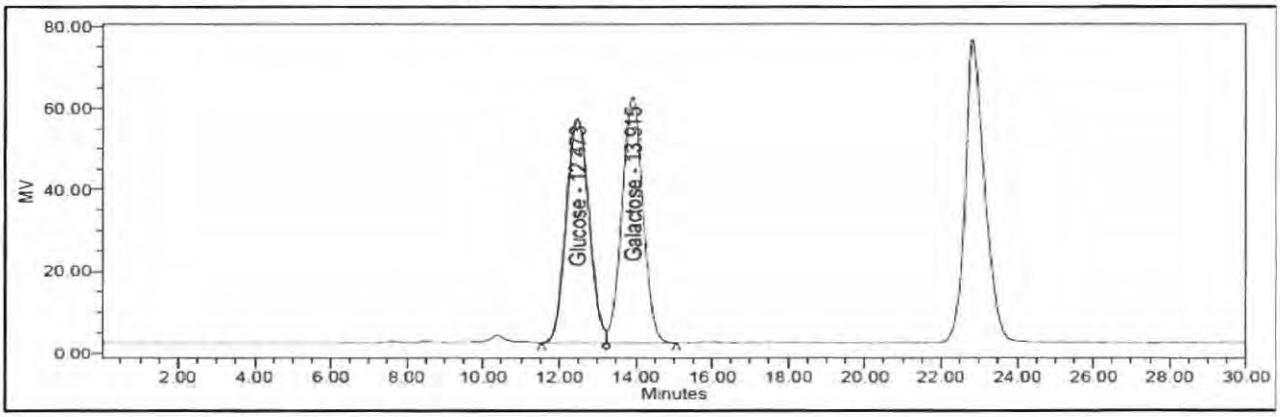
Appendix 3.7 Mother's OLIGO-CP

Appendix 3.1 Nature's GOS-L

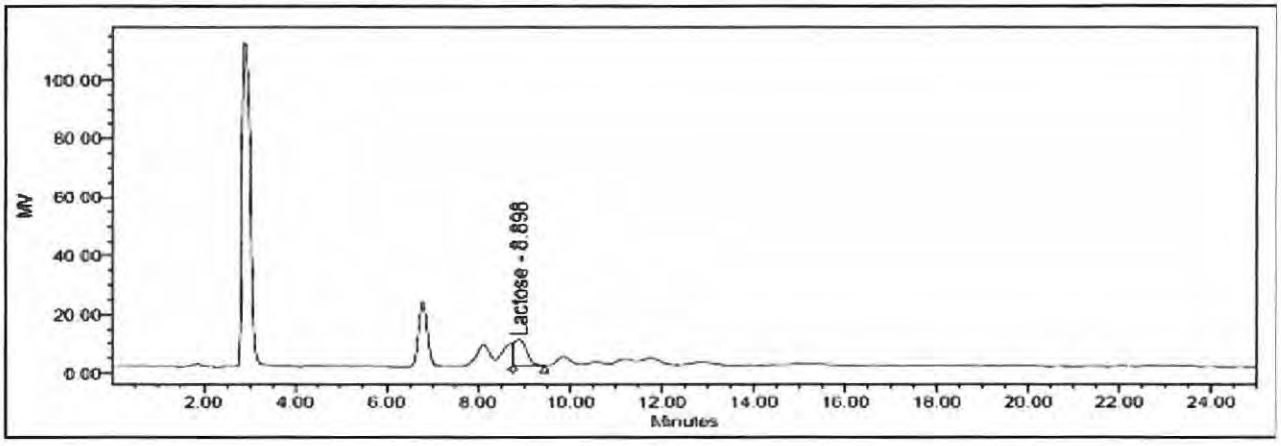
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure 2. (Assay2. After Enzyme Reaction)

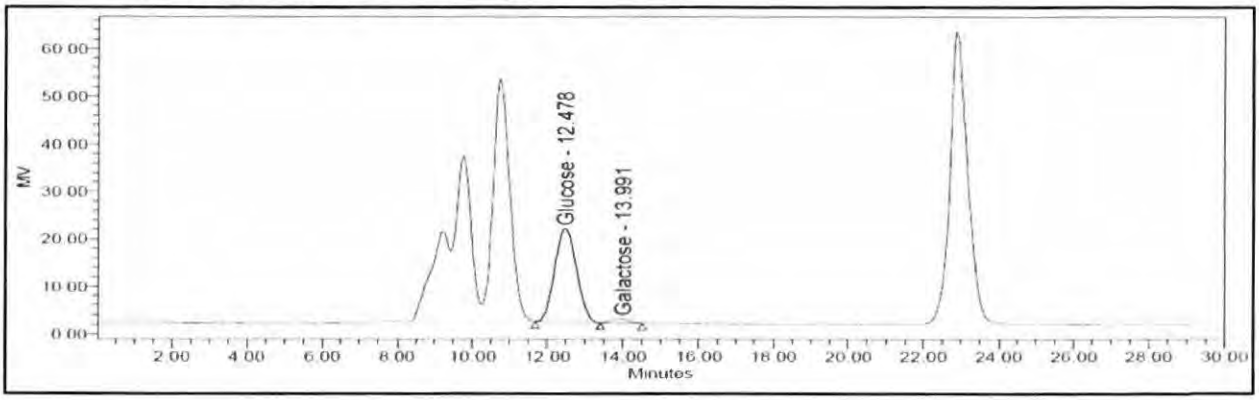


- Figure 3. (Free lactose in sample)

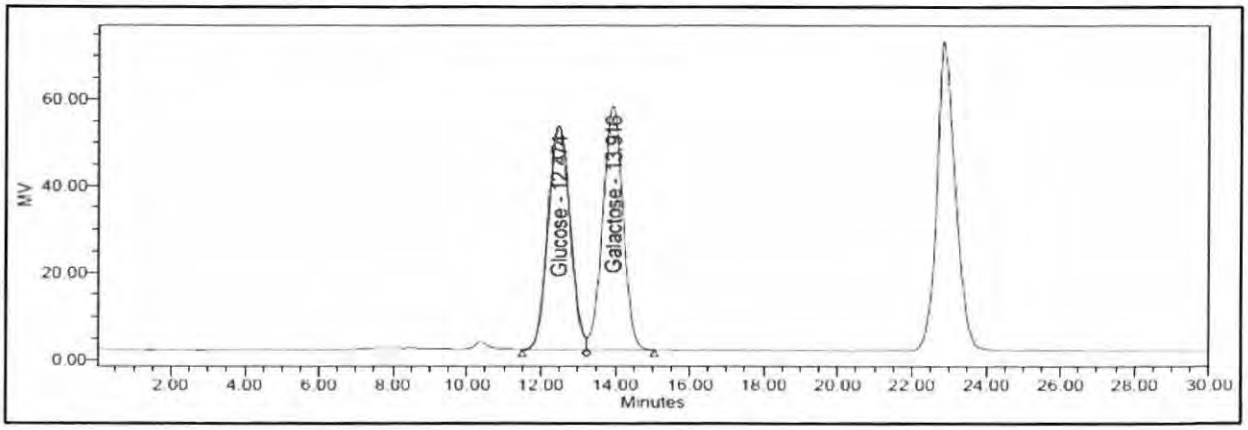


Appendix 3.2 Nature's GOS-CL

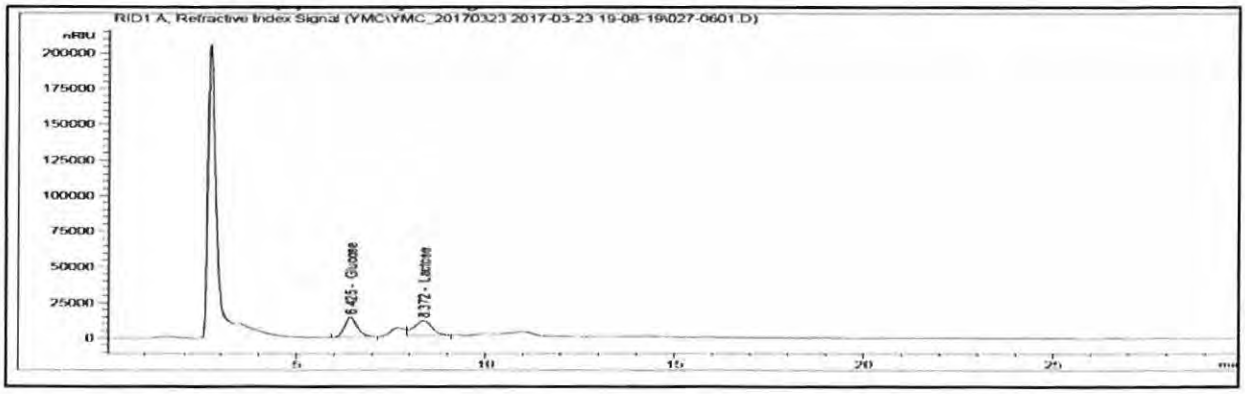
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure 2. (Assay2. After Enzyme Reaction)

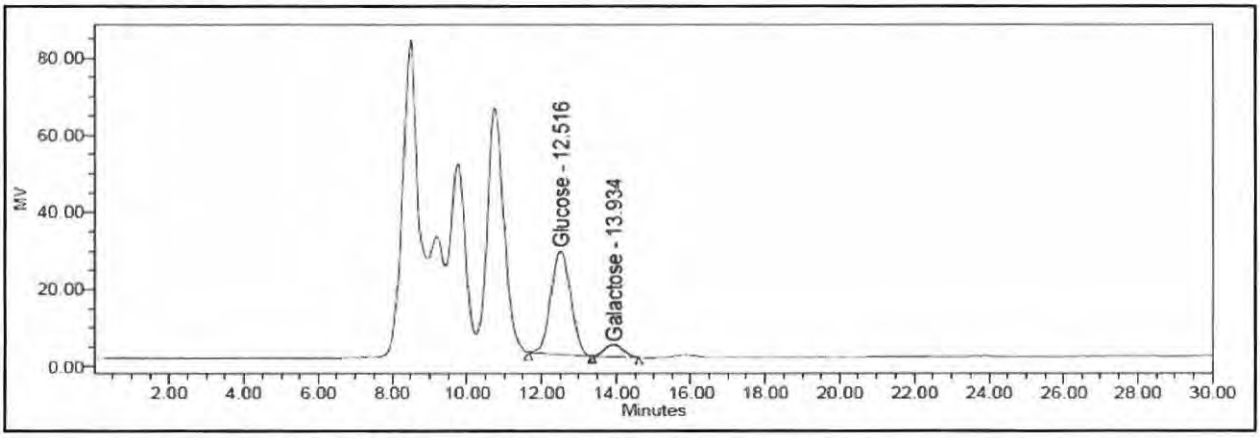


- Figure 3. (Free lactose in sample)

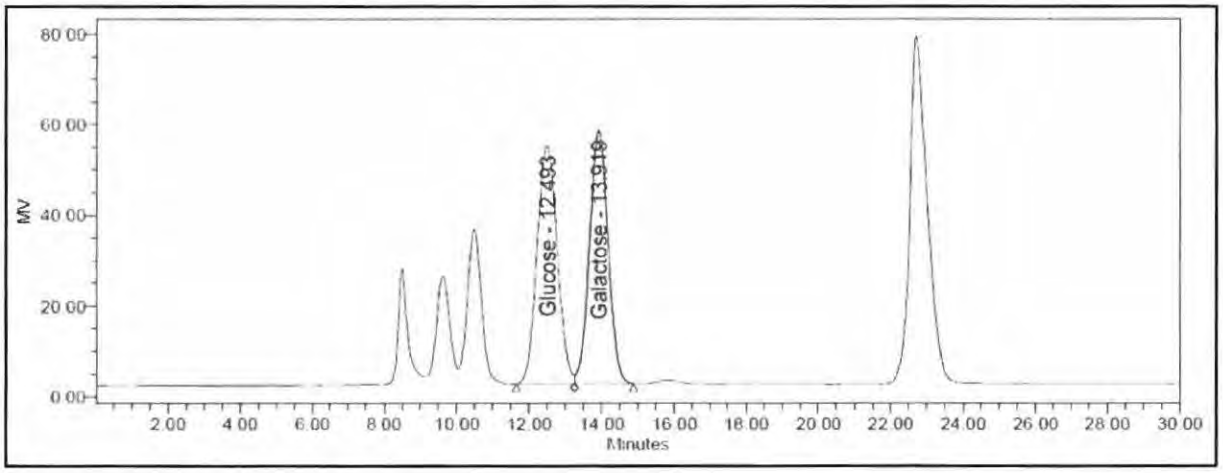


Appendix 3.3 Nature's GOS-P

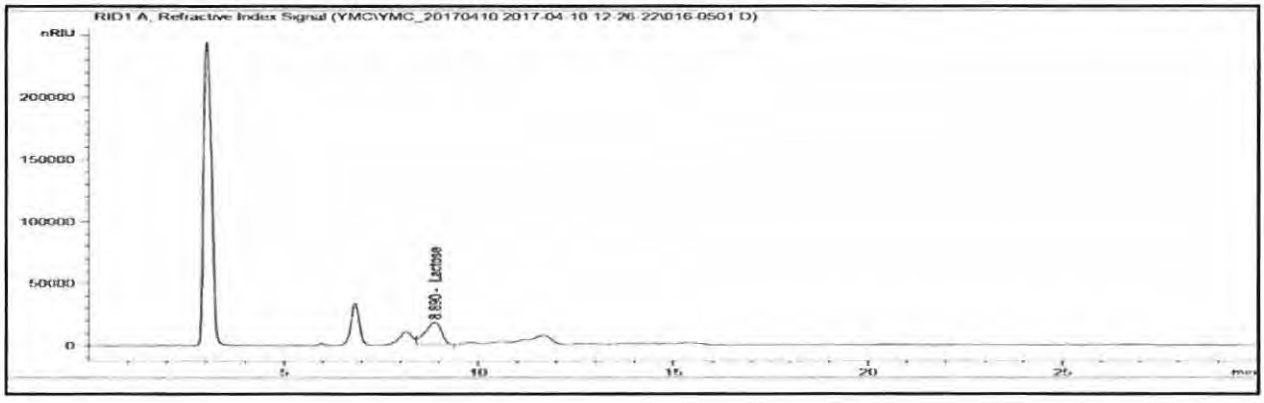
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure 2. (Assay2. After Enzyme Reaction)

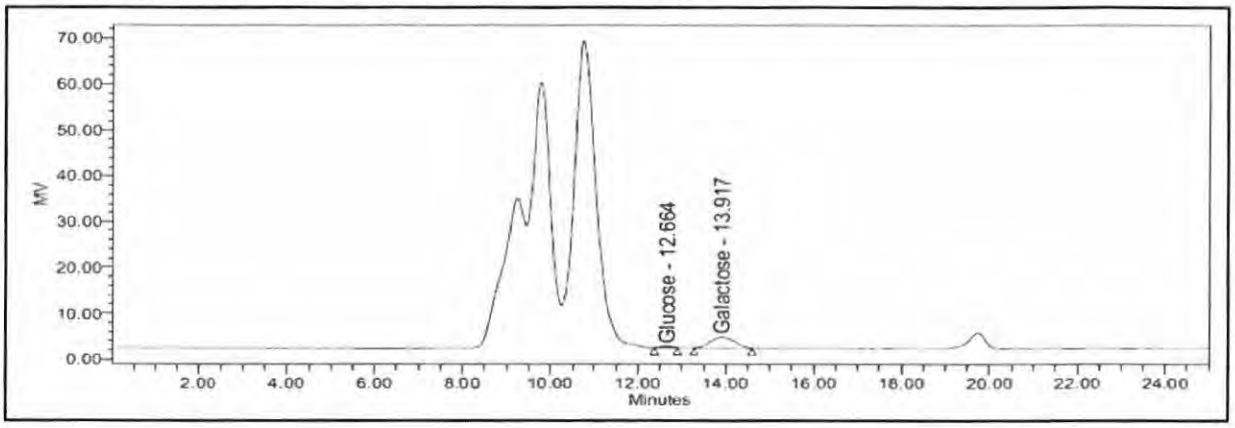


- Figure 3. (Free lactose in sample)

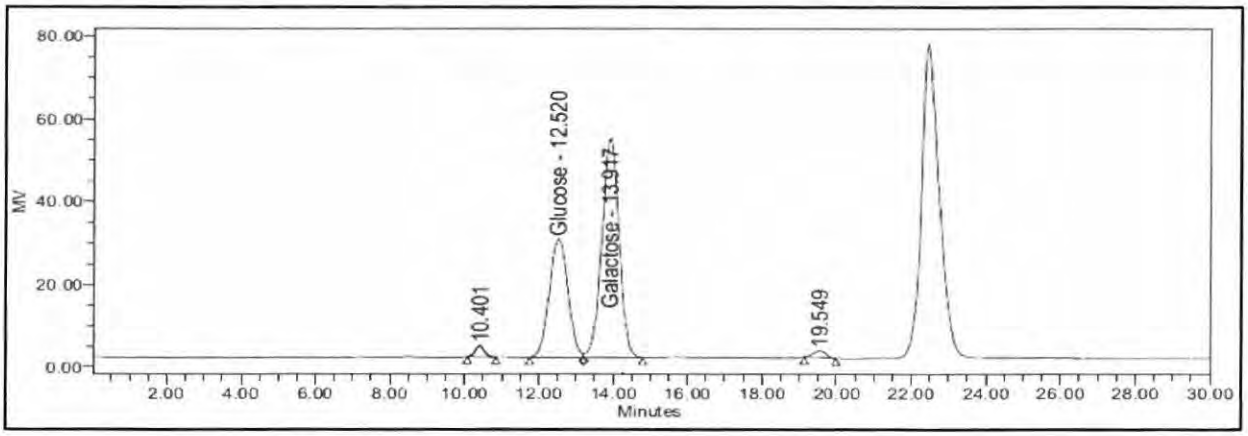


Appendix 3.4 Mother's OLIGO-L

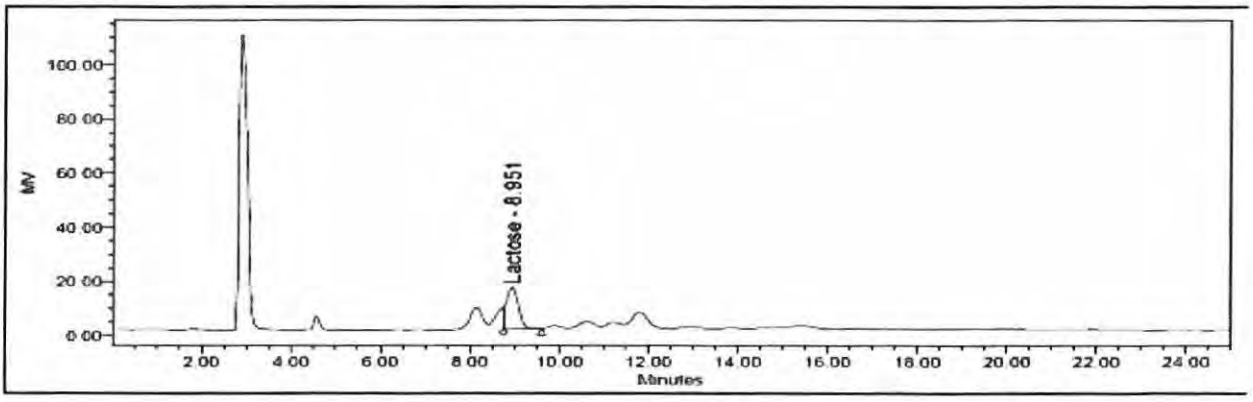
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure2. (Assay2. After Enzyme Reaction)

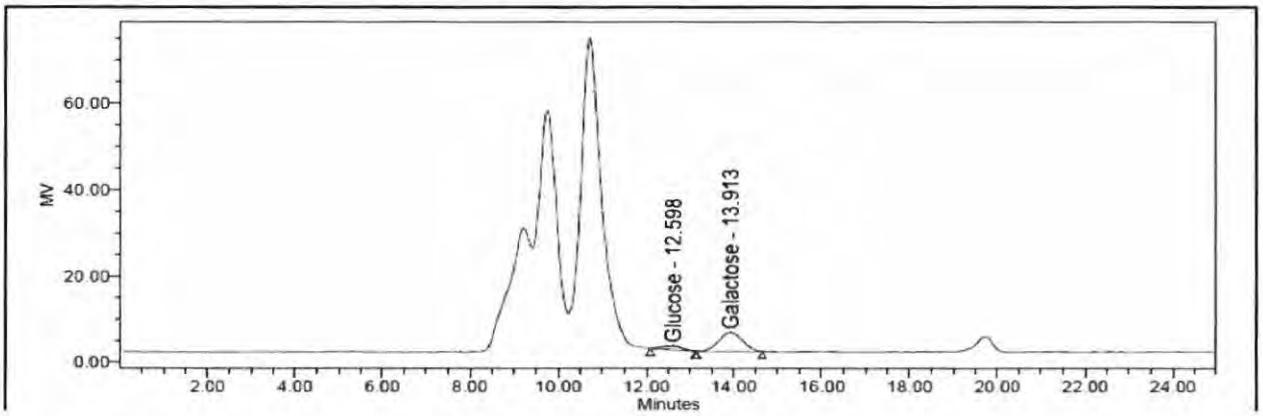


- Figure 3. (Free lactose in sample)

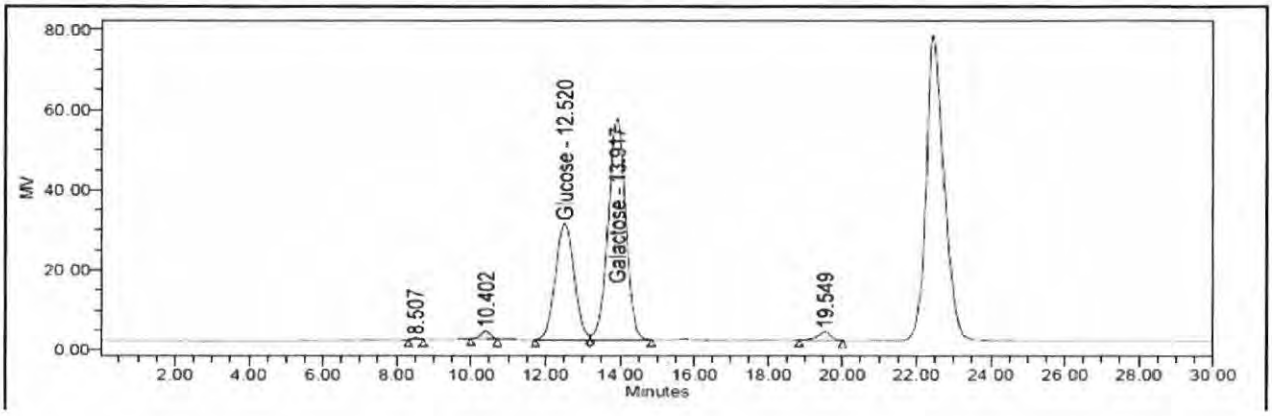


Appendix 3.5 Mother's OLIGO-CL

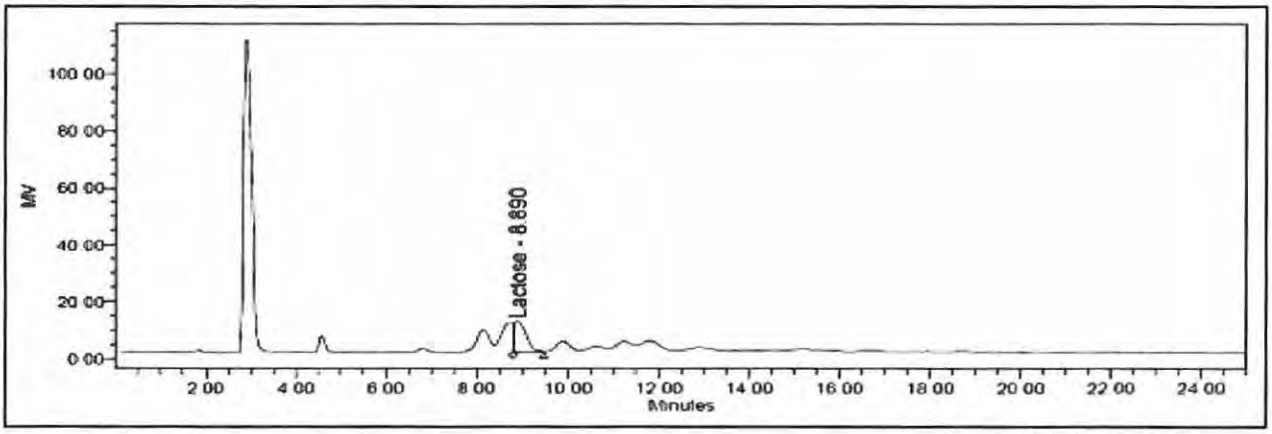
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure 2. (Assay2. After Enzyme Reaction)

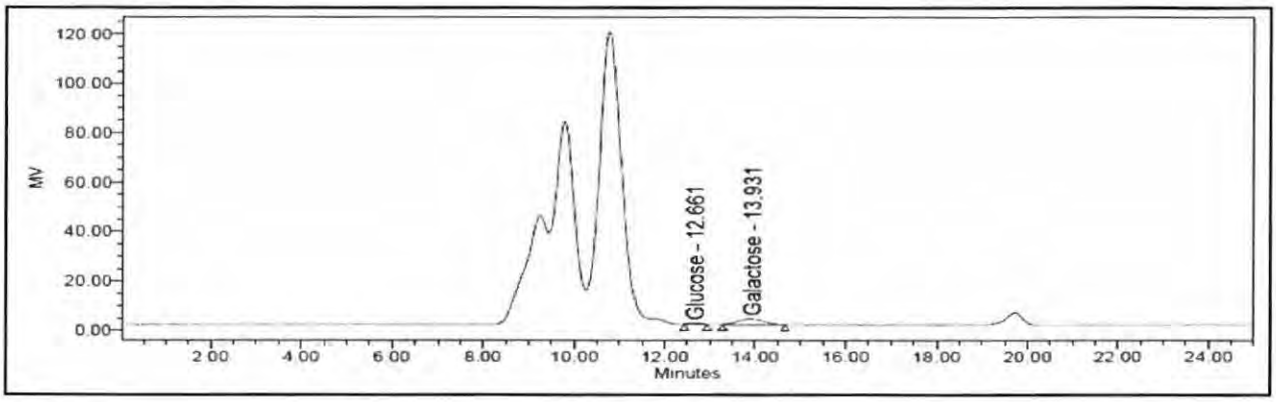


- Figure 3. (Free lactose in sample)

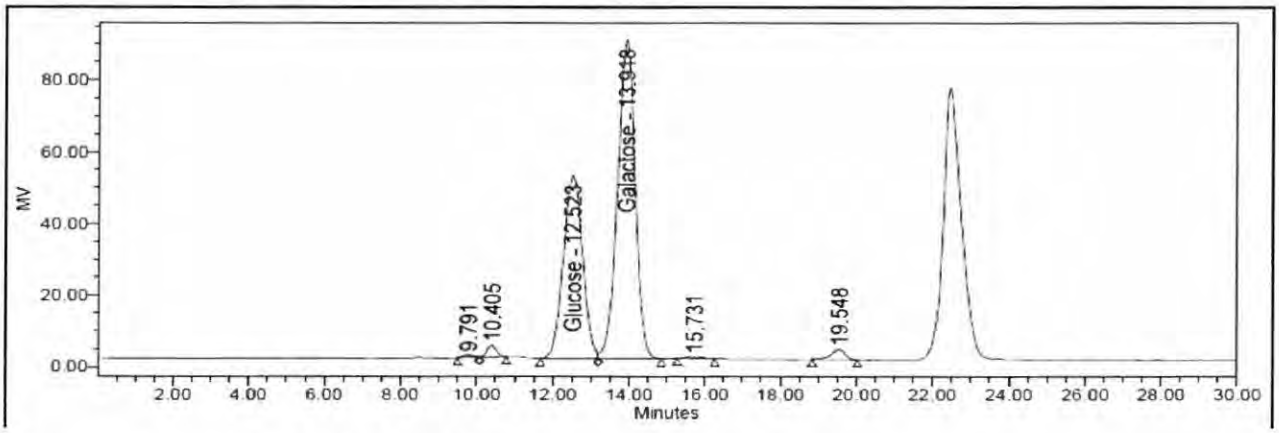


Appendix 3.6 Mother's OLIGO-P

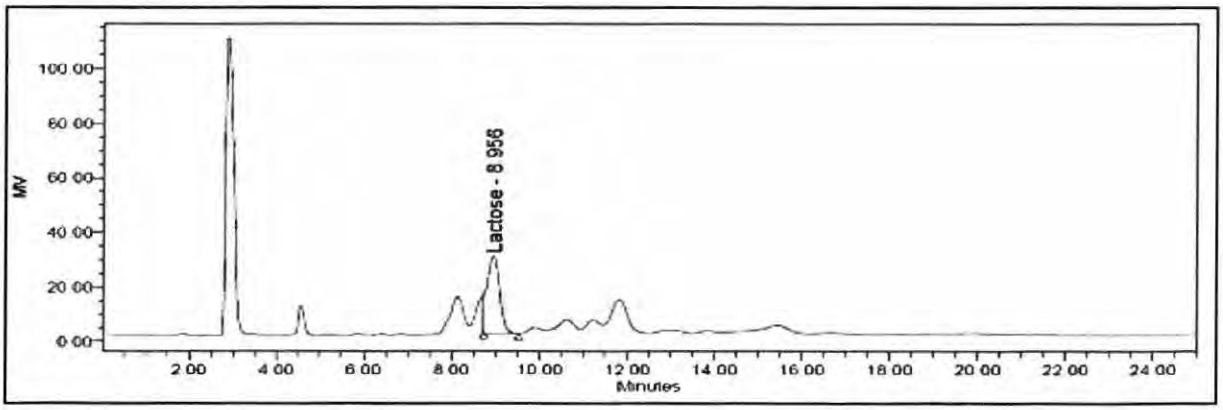
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure 2. (Assay2. After Enzyme Reaction)

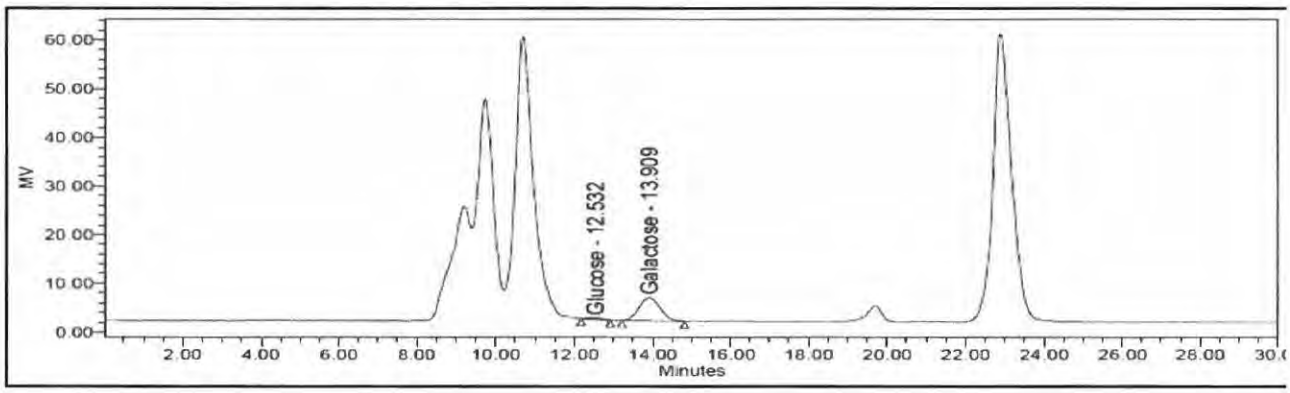


- Figure 3. (Free lactose in sample)

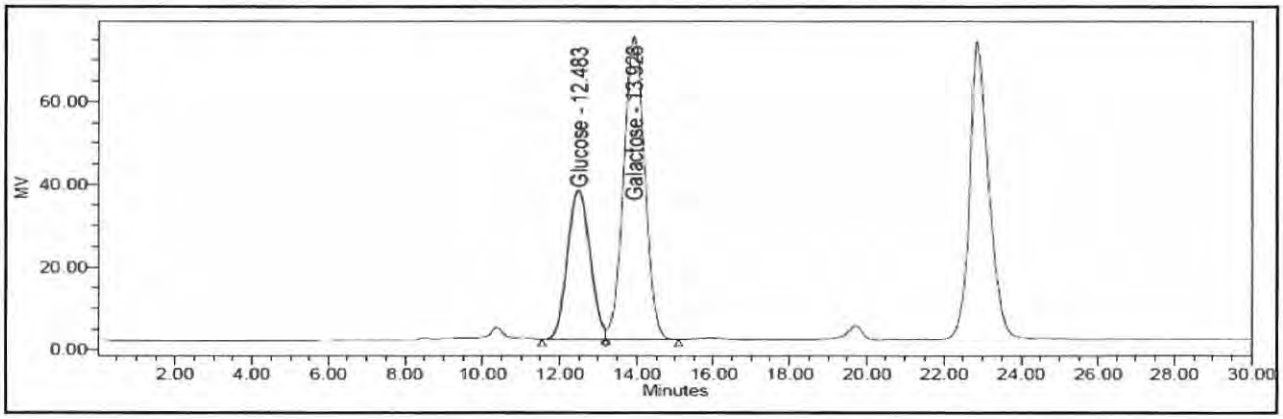


Appendix 3.7 Mother's OLIGO-CP

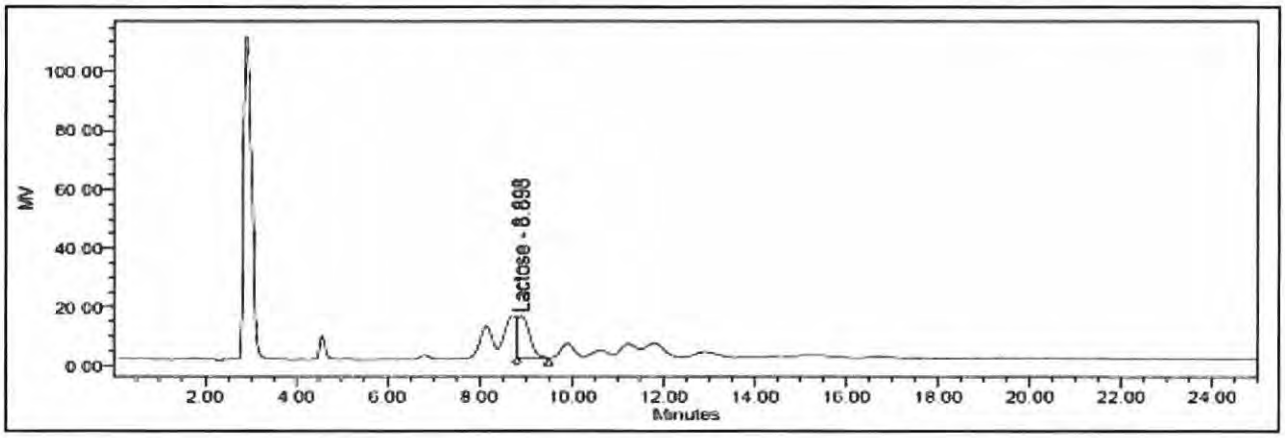
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure 2. (Assay2. After Enzyme Reaction)



- Figure 3. (Free lactose in sample)



Appendix 4 Certificates of Analysis for Goat OLIGO-CL Preparations

Neo Cremar Co., Ltd.

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TEL : +82-2-401-4088 FAX : +82-2-401-4087

GOAT OLIGO-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : NCGO20161228
Date of Manufacture : 28. Dec. 2016

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.8	Refractometer at 20℃
GOS/DM	More than 57.0 %	59.4	AOAC 2001.02
Lactose/DM	Less than 23.0 %	17.29	HPLC
Glucose/DM	Less than 22.0 %	21.53	HPLC
Galactose/DM	More than 0.8 %	1.83	HPLC
Sulfated Ash	Less than 0.3 %	0.05	550℃ till constant
Nitrogen	Less than 0.1 %	0.008	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.55	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,212	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0012	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.009	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	30	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	12th. Jan. 2017

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TEL : +82-2-401-4088 FAX : +82-2-401-4087

GOAT OLIGO-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)

Date of Manufacture : 02. Feb. 2017

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.3	Refractometer at 20℃
GOS/DM	More than 57.0 %	59.2	AOAC 2001.02
Lactose/DM	Less than 23.0 %	20.14	HPLC
Glucose/DM	Less than 22.0 %	18.72	HPLC
Galactose/DM	More than 0.8 %	1.98	HPLC
Sulfated Ash	Less than 0.3 %	0.05	550℃ till constant
Nitrogen	Less than 0.1 %	0.008	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.66	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,527	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0015	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.01	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration)

Expiration Date : Two years from the date of manufacture

AUTHORIZED SIGNATURE

(b) (6)

COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	17th. Feb. 2017

Neo Cremar Co., Ltd.

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Beobwon-ro11-gil, Songpa-gu, Seoul, Korea
TEL : +82-2-401-4088 FAX : +82-2-401-4087

GOAT OLIGO-CL

(Galacto-oligosaccharide Liquid)

Certificate of Analysis

Lot NO : (b) (4)
Date of Manufacture : 03. Feb. 2017

PARAMETER	SPECIFICATION	RESULT	REFERENCE
Appearance	Clear to yellow syrup	Passed	Sensory Test (Visible observation)
Dry matter	74.0 - 76.0 %	75.2	Refractometer at 20℃
GOS/DM	More than 57.0 %	59.3	AOAC 2001.02
Lactose/DM	Less than 23.0 %	18.8	HPLC
Glucose/DM	Less than 22.0 %	20.6	HPLC
Galactose/DM	More than 0.8 %	1.92	HPLC
Sulfated Ash	Less than 0.3 %	0.05	550℃ till constant
Nitrogen	Less than 0.1 %	0.008	Kjeldahl method
Nitrite	Less than 2.0 ppm	N.D	Diazotization method
pH	3.2 - 3.8	3.57	pH meter
Viscosity (25℃)	1,000 - 5,000 cPs	1,463	Viscometer at 25℃
Arsenic	Less than 0.1 ppm	N.D	ICP- Inductively coupled plasma
Lead	Less than 1.0 ppm	N.D	ICP- Inductively coupled plasma
Cadmium	Less than 0.06 ppm	0.0013	ICP- Inductively coupled plasma
Mercury	Less than 0.1 ppm	0.009	Mercury analyzer (Atomic absorbtiometry)
Total Plate count	Less than 3,000 CFU/g	50	KFDA
Yeast and Molds	Less than 50 CFU/g	Negative	KFDA
E. Coli	Negative(/25g)	Negative	KFDA
Coliform(MPN/g)	Negative(/25g)	Negative	KFDA
Salmonella spp.	Negative(/75g)	Negative	KFDA
Staphylococcus aureus	Negative(/75g)	Negative	KFDA
Enterobacter sakazakii	Negative(/300g)	Negative	KFDA

*KFDA : (Korea food &drug administration) Expiration Date : Two years from the date of manufacture

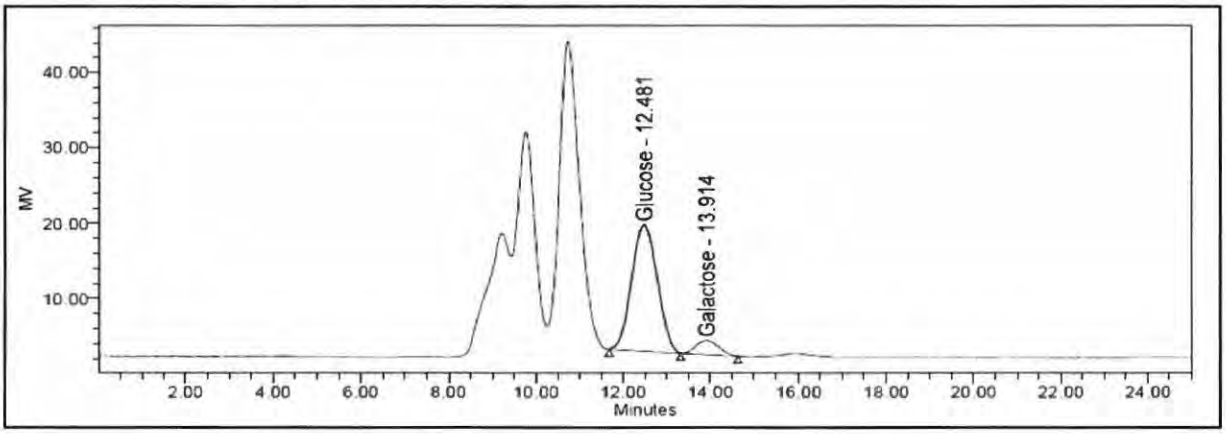
AUTHORIZED SIGNATURE

(b) (6)

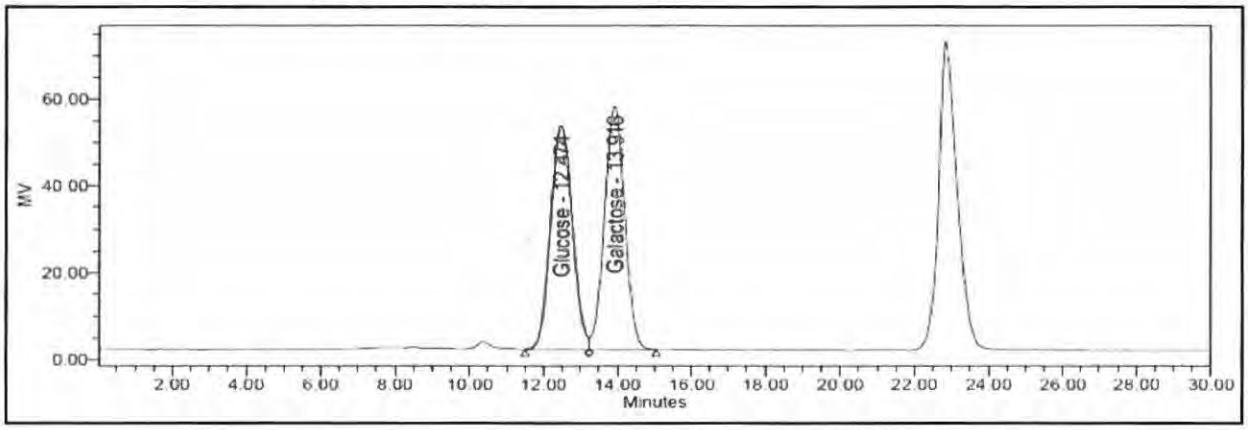
COMPANY NAME	Neo Cremar Co.,Ltd.
POSITION	Q.C. manager
NAME	JungCheul Shin
DATE	18th. Feb. 2017

Appendix 5 Representative Chromatograms for Goat OLIGO-CL Preparations

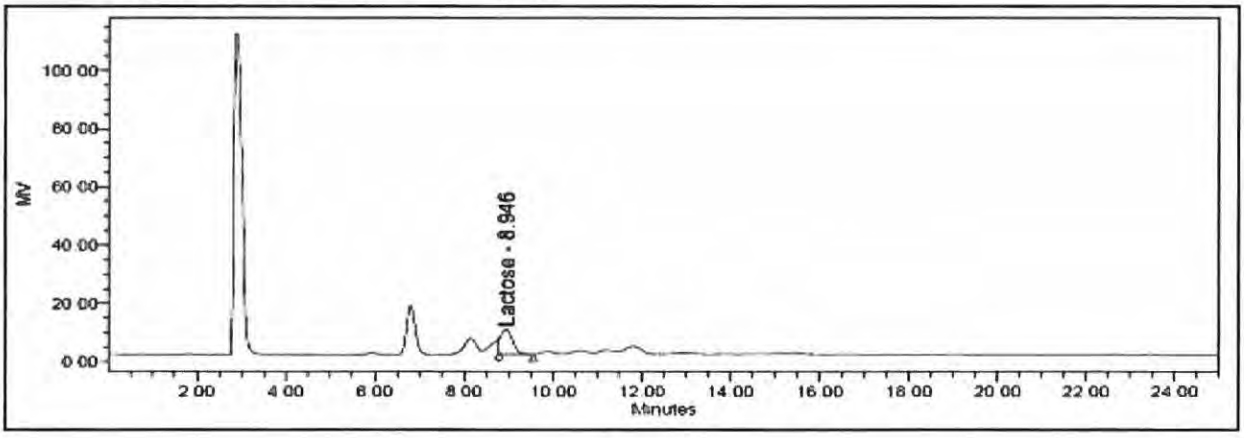
- Figure 1. (Assay 1. Before Enzyme Reaction)



- Figure 2. (Assay2. After Enzyme Reaction)



- Figure 3. (Free lactose in sample)



END

Bonnette, Richard

From: Katrina Emmel <emmel@gras-associates.com>
Sent: Friday, September 15, 2017 12:32 PM
To: Bonnette, Richard
Cc: Steven Overgaard; Robert McQuate
Subject: Re: GOS submission to FDA GRAS notification program - confidential information?

Dear Mr. Bonnette,

I apologize for the oversight on our part. There is no confidential information contained within the GOS submission.

Please let me know if there are any other concerns or questions.

Thank you,

Katrina

Katrina Emmel, Ph.D.
Senior Scientist/Project Manager/Associate
GRAS Associates, LLC.

emmel@gras-associates.com

On Sep 15, 2017, at 8:33 AM, Bonnette, Richard <Richard.Bonnette@fda.hhs.gov> wrote:

Dear Dr. Emmel,
As I was looking through your submission for GOS received here on Sept 6, as part of our pre-filing review I noticed that many pages are marked "CONFIDENTIAL" in the bottom margin beginning on page 54 of the PDF. I noticed earlier in the submission in part 1 that no claims of confidentially were made. I assume this is probably a typo/oversight? Please let me know if this is indeed the case via email and I'll add your response to the record for this submission and we'll proceed from there.
Regards,
Richard

Richard E. Bonnette, M.S.
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richard.bonnette@fda.hhs.gov

<image001.png>

<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>