TRISKELION
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STUDY REPORT

V20880/02

Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

DATE	16 August 2017
AUTHOR(S)	A.E. Wallinga, PhD
SPONSOR	Friesland Campina Innovation Bronland 20 6708 WH Wageningen The Netherlands
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Statement of GLP compliance / Report approval

I, the undersigned, hereby declare that this report constitutes a complete and accurate representation of the study and its results.

All study activities performed by Triskelion B.V. were carried out in compliance with the current OECD Principles of Good Laboratory Practice (GLP)[1]. The OECD principles of Good Laboratory Practice are accepted by Regulatory Authorities throughout the European Community, USA and Japan. Chemical analysis for the verification of the test substance identity and properties was not performed in this study.

Study director

(b) (6)

A.E. Wallinga, PhD

16 august 2017

Date

[1] The most recent endorsement of compliance of the test facility with these principles is attached to the report as Annex 1.

Quality Assurance Statement

I, the undersigned, hereby declare that this report provides an accurate record of the procedures employed and the results obtained in this study; all audits were reported to the respective study director and management on the dates indicated.

Phase	*	Start date of audit	Date of audit report
Authorised study plan	Yes	19 October 2016	19 October 2016
Authorised study plan amendment 1	Yes	8 December 2016	8 December 2016
Authorised study plan amendment 2	Yes	28 February 2017	28 February 2017
Authorised study plan amendment 3	Yes	10 August 2017	10 August 2017
Animal receipt	No	7 December 2016	8 December 2016
Animal allocation	No	29 November 2016	29 November 2016
Test diet preparation	Yes	1 December 2016	1 December 2016
Test diet preparation	Yes	3 February 2017	3 February 2017
Test substance analysis	Yes	19 October 2016	19 October 2016
Test substance analysis	Yes	1 December 2016	1 December 2016
Test substance analysis	Yes	2 February 2017	2 February 2017
Housing and logbook	Yes	5 December 2016	5 December 2016
Housing and logbook	Yes	6 February 2017	6 February 2017
Ophthalmoscopy	No	26 January 2017	26 January 2017
Body weight	Yes	5 December 2016	5 December 2016
Body weight	Yes	6 February 2017	6 February 2017
Clinical signs	Yes	5 December 2016	5 December 2016
Clinical signs	Yes	6 February 2017	6 February 2017
Test diet provision	Yes	5 December 2016	5 December 2016
Test diet provision	Yes	6 February 2017	6 February 2017
Food consumption	Yes	6 February 2017	6 February 2017
Water consumption	Yes	5 December 2016	5 December 2016
Urine collection	No	12 April 2017	12 April 2017
Detailed clinical examination	No	1 March 2017	1 March 2017
Functional observational battery	No	23 January 2017	23 January 2017
Motor Activity	No	23 January 2017	23 January 2017
Necropsy	No	21 February 2017	21 February 2017
Terminal blood collection	No	21 February 2017	21 February 2017
Haematology	No	10 February 2017	10 February 2017
Clinical chemistry	No	26 April 2017	26 April 2017

Urinalysis	No	7 February 2017	7 February 2017
Histology	No	9 March 2017	9 March 2017
Pathology	No	9 March 2017	9 March 2017
Draft report (excl. annex 12) and study file	Yes	25 July 2017	2 August 2017
Draft report (annex 12) and study file	Yes	28 July 2017	2 August 2017
Final report	Yes	16 August 2017	16 August 2017

* Study plan, report and test substance related experimental phases are audited in a study-based manner. Other experimental phases are audited in a process-based manner. This column indicates whether or not the audit was of this particular study.

(b) (6)

M.C.J. Meeuwsen, MSc.
Quality Assurance auditor

Date : 16 August 2017

Contents

Abbreviations

A/G ratio	= ratio albumin to globulin
ALAT	= alanine aminotransferase activity
ALP	= alkaline phosphatase activity
ASAT	= aspartate aminotransferase activity
AWB	= Animal Welfare Body
Baso	= basophils
Ca	= calcium
Cl	= chloride
Eosino	= eosinophils
F (or f)	= female
GALT	= gut associated lymphoid tissue (Peyer's patches)
GD	= gestation day
GGT	= gamma glutamyl transferase activity
GLP	= Good Laboratory Practice
Hb	= hemoglobin
K	= potassium
LLOQ	= Lower Limit Of Quantification
Lympho	= Lymphocytes
M (or m)	= male
MCV	= mean corpuscular volume
MCH	= mean corpuscular hemoglobin
MCHC	= mean corpuscular hemoglobin concentration
Mono	= monocytes
Na	= sodium
Neutro	= neutrophils
OECD	= Organisation for Economic Co-operation and Development
PCV	= packed cell volume
PL	= phospholipids
PND	= Postnatal Day
PO_4	= inorganic phosphate
PTT	= prothrombin time
RBC	= red blood cell count
WBC	= total white blood cell count
QA	= Quality Assurance
QAU	= Quality Assurance Unit
SPF	= specific pathogen free

Summary

The safety of the test substance 2'-Fucosyllactose was examined in a sub-chronic (13 week) oral toxicity study, starting with juvenile rats (25-days old), obtained soon after weaning from time-mated females.
The study comprised four groups of 10 Wistar rats/sex. One control group was kept on cereal based (VRF1 (FG)) diet. Three test groups received the test substance added to this diet at levels of 3%, 6% and 10%). These dietary levels provided an overall mean intake of the test substance in the low-, mid- and high-dose group of 2.17, 4.27 and 7.25 g 2'-Fucosyllactose /kg body weight/day for males, and 2.45, 5.22 and 7.76 g 2'-Fucosyllactose/kg body weight/day for females, respectively.

Analyses for homogeneity, content and stability of test substance in the test diets confirmed that the rats consumed the intended amounts of 2'-Fucosyllactose.

There was no mortality related to the treatment and there were no treatment-related clinical signs. Neurobehavioral observations and motor activity assessment did not indicate any neurotoxic potential of the test substance. Ophthalmoscopy did not reveal any treatment-related ocular changes.

In female rats of the high-dose group food consumption was slightly decreased. There were no changes in body weight and water consumption.

Hematology and clinical chemistry was conducted on all rats at necropsy. There were no relevant changes in red blood cell variables or in total and differential white blood cell counts. No significance was attached to a slight increase in thrombocytes in high-dose females, because the increase was slight and in one sex only. There were no treatment related changes in clinical chemistry variables. An increase in urea concentration in mid-dose and high-dose males was considered a chance finding in the absence of this finding in females and any corroborative findings in males,

The relative weight of the liver was slightly, but statistically significantly increased in males in the high-dose group. This elevated relative liver weight was not accompanied by changes in clinical chemistry or microscopy of the liver and was therefore not considered to be adverse.
The absolute and relative weights of the filled and empty caecum were statistically significantly increased in the mid- and high-dose group in male and female rats. Also the absolute weights of the filled caecum was statistically significantly increased in the low-dose group in male rats. This finding was ascribed to the high fiber content in the diet.

Macroscopic examination at necropsy and microscopic examination of organs and tissues did not reveal treatment-related findings.

It was concluded that 2'-Fucosyllactose did not induce any relevant changes in any test group, and therefore the no-observed-adverse-effect level (NOAEL) was placed at the highest level tested, namely 10 % in the diet (≥7.25 g/kg body weight/day).

1 General

1.1 Study Sponsor

Sponsor:	Friesland Campina Innovation Bronland 20 6708 WH Wageningen The Netherlands
Monitor:	D. Delsing, PhD Email: dianne.delsing@frieslandcampina.com Phone: +31(0)6 5359 8111

1.2 Test facility

Triskelion B.V.	www.triskelion.nl
Postal address:	P.O. Box 844 3700 AV Zeist The Netherlands
Location:	Utrechtseweg 48 3704 HE Zeist The Netherlands
Phone:	+31 88 866 2800

1.3 Responsible Personnel

Study director:	A.E. Wallinga, PhD alinde.wallinga@triskelion.nl Phone: +31 88 866 6767
Scientific contributor(s):	A.J. Kleinnijenhuis (Test substance analyses in diet) M. Otto (Neurobehavioral testing) Pathology: -M.V.W. Wijnands, PhD, DVM (Study Pathologist) -A.L. Menke, PhD -J.P. Bruijntjes

1.4 Time schedule

Arrival of the time-mated females :	2 November 2016
Allocation offspring to experimental groups:	1 December 2016
Start of the treatment (day 0):	5 December 2016
Termination of the in-life phase:	6 March (males) and 7 March (females) 2017

2 Introduction

2.1 Objective

The objective of this study was to provide data on the safety of 2'-Fucosyllactose. For this purpose the test substance was examined in a sub-chronic oral toxicity study in rats of both sexes. Because the test substance is intended for use in infant formula, the study was started with juvenile rats of 25 days old. For this purpose time-mated females were obtained and their offspring was exposed to the test substance soon after weaning. The test substance was incorporated at constant concentrations in the diet and fed to the rats during 13 weeks. Criteria for disclosing possible harmful effects included clinical observations, neurobehavioral testing, ophthalmoscopy, growth, food and water intake, hematology, clinical chemistry, urinalysis, organ weights and pathological examination of organs and tissues.

2.2 Applicable guidelines

The study plan was drafted in accordance with the following guidelines:

- OECD Guideline for the Testing of Chemicals 408. Repeated dose 90-day oral toxicity study in rodents, adopted 21st September 1998.
- B.26. Sub chronic oral toxicity test. Repeated dose 90-day oral toxicity study in rodents. Annex 5D to Commission Directive 2001/59/EC, Official Journal of the European Communities, L225, 21.8.2001.

2.3 Animal welfare

The welfare of the animals was maintained in accordance with the general principles governing the use of animals in experiments of the European Communities (Directive 2010/63/EU) and Dutch legislation (The revised Experiments on Animals Act, 2014). This included licensing of the project by the Central Committee on Animal Experimentation (project license 2016602) and approval of the study by the Triskelion Animal Welfare Body (AWB number TRIS-185).

3 Study plan and deviations

3.1 Study plan

The study was conducted according to study plan P20880/02 entitled: "Sub-chronic (13-week) oral toxicity study with 2'-fucosyllactose in rats", and 3 amendments (see Annex 14). The study plan was approved by the study director on 18 October 2016.

3.2 Deviations

The following deviations from the study plan occurred:

- On 01 December 2016, 17 January 2017 and 15 February 2017 the relative humidity in the animal room was slightly lower than 45.0% for a short period of time. On 23 January 2017 and on 02 and 04 February 2017 the relative humidity was slightly higher than 65.0% for a short period of time (see also 4.7.1 Animal room).
- On 20 February 2017 the subcutaneous transponder of rat 71 and rat 77 was broken. These rats were thereafter permanently identified by using a tail mark (see also 4.6 Identification).
- A.L. Menke, PhD, and J.P Bruijntjes were involved in the histopathological examination and therefore added to section 1.3 of the report.
- For the test substance analysis in diet, after the calibration curve was optimized a second validation was performed using matrix matched calibration solution (see also Table 1 and 2 in Annex 12).

These deviations are considered not to have affected the validity of the study.

4 Materials and methods

4.1 Test substance

Name[1,2]	: 2'-Fucosyllactose
Chemical name[1]	: 2'-FL
Chemical formula[1]	: $C_{18}H_{32}O_{15}$
CAS Reg No. [1]	: 41263-94-9
Batch number[1]	: MRS02
Appearance[1]	: White powder
Purity[1]	: 94%
Storage conditions[1]	: 2 – 10 °C, protected from light
Quantity	: 20 kg
Date of receipt	: 19 July 2016
Expiry date[1]	: 15 July 2018
Supplier	: Sponsor
Triskelion Dispense number	: 160161

[1] Information provided by the sponsor
[2] Remaining test substance was returned to the sponsor.

A Certificate of analysis is provided in Annex 2.

4.2 Administration of the test substance

The test substance was administered to allocated male and female offspring at constant concentrations in the diet for 13 consecutive weeks, 7 days per week (the animals were kept on their test diet until overnight fasting prior to necropsy). Different dose groups were fed diets containing different concentrations of the test substance in the diet (see § 4.3). The oral route was used because this is an anticipated route of human exposure.
Details on the preparation, storage and refreshing of the experimental diets are given under "Food and drinking water" in § 4.7.3.

4.3 Experimental design, groups and dose levels

The 13-wk study comprised four groups of 10 males and 10 females each, viz. one control group kept on control diet and three test groups receiving different levels of 2'-Fucosyllactose added to this diet. The test substance was added to the diet as indicated in the table:

Group	Color code	2'-Fucosyllactose (%)	Number of males/ females
1 Control	White	0%	10 / 10
2 Low-dose	Blue	3%[1]	10 / 10
3 Mid-dose	Green	6%[1]	10 / 10
4 High-dose	Red	10%[1]	10 / 10

[1] These dose levels were selected in consultation with the sponsor, based on the results of a 14 day dose range finding study (Triskelion report V20880/01, 24 November 2016).

4.4 Test system

Time-mated females

The study was conducted with albino rats. The rat was used because this species is considered suitable for this type of study, and is usually required by regulatory agencies. Time-mated female Wistar Han IGS rats (Crl:WI(Han)) were obtained from a colony maintained under SPF-conditions at Charles River Deutschland, Sulzfeld, Germany. This rat strain was used because it is routinely used at the test facility for this type of studies.
The animals, 16 time-mated females, arrived on 2 November 2016, when they were at GD15 of pregnancy. A health certificate is presented in Annex 4. Upon arrival, they were taken in their shipping boxes into animal room number 05.1.08, checked for overt signs of ill health and anomalies, and kept in quarantine. During the quarantine period, their microbiological status was checked by the conduct of serology in samples taken from rats of the same shipment. On 7 November 2016, after the results of serology turned out to be satisfactory, the quarantine room was cleared for use as experimental room and the rats were further acclimatized to the conditions in this room. At 10 November 2016 all time-mated females delivered pups (PND 0). All pups were weaned at PND 21 (1 December 2016).

Allocated offspring

After allocation (§ 4.5), treatment was initiated on 5 December 2016. The male and female offspring were 25 days old at the start of the treatment period. The body weights at initiation of treatment were within ± 20% of the mean weight for each sex, and ranged from 52.2 – 75.8 g (mean 64.38 g) for males and from 48.2 - 71.7 g (mean 60.94 g) for females.

4.5 Animal allocation

On 24 November 2016 (PND 14) litter size and sex of all pups were determined and body weights were measured, in order to get a rough indication of the variability within and between litters (see Annex 7). Individual pup weight and sex were determined in all pups on PND 21 (1 December 2016) and all rats were checked for overt signs of ill health and anomalies. Out of 82 males and 87 females, 40 males and 40 females were allocated to experimental groups 1 – 4 (see § 4.3) by manual randomization, taking into account lineage, individual body weight and sex (see Annex 7 for data on all pups). The cross reference list is given in Annex 3 of the report. On day 0 of the study (5 December 2016), the rats were weighed again and checked for normal growth and abnormalities and treatment was started.

4.6 Identification

The study was identified as study 20880/02. Time-mated females were identified were identified by a transient tail mark. On the day of allocation, prior to randomization, all juvenile rats were identified by a transient mark on their tail. After the randomization procedure, on the day of allocation (1 December 2016), each allocated rat was identified by a subcutaneous transponder with a unique identification number. During the study, each group of animals was coded by a number and a color (see § 4.3 for color codes). Each cage was provided with a card showing the color code, the animal identification numbers, the cage number, the group code and the study code. From 20 February 2017 onwards, rat 71 and 77 were permanently identified with a transient tail mark because their subcutaneous transponder was broken.

4.7 Animal husbandry

4.7.1 Animal room

From their arrival, the time-mated females were housed under conventional, controlled conditions in animal room 05.1.08. After weaning, only the allocated rats remained in this animal room for the course of the study. No other test system was housed in the same room during the study. Lighting was artificial with a sequence of 12 hours light and 12 hours dark. The room was ventilated with about 10 air changes per hour and was maintained at a temperature of 20-24°C. The relative humidity was between 45-65% (except during brief periods generally associated with room cleaning when the relative humidity reached maxima up to 67.1%). On several days (see § 3.2 deviations), the relative humidity was lower than 45% for short periods of time, reaching minima up to 33.7%.

4.7.2 Caging

The time-mated females were housed individually in macrolon cages with wood shavings (Lignocel) as bedding material and strips of paper (Enviro-dri).
After weaning and allocation at PND 21 the allocated rats were kept in macrolon cages with wood shavings (Lignocel) as bedding material, and strips of paper (Enviro-dri) and a wooden block as environmental enrichment. They were housed in groups of five, separated by sex.
On the day of FOB testing and motor activity assessment (see § 4.8.4), the animals were temporarily kept singly in macrolon cages. During urine collection, animals were kept singly in stainless-steel metabolism cages (see § 4.8.11).

4.7.3 Food and drinking water

Food and drinking water were provided *ad libitum* from the arrival of the time-mated female rats until the end of the study unless precluded by the collection of concentrated urine, or the collection of blood from overnight fasted rats prior to scheduled necropsy.
Until initiation of treatment, the dams and the offspring rats received a powdered, cereal-based rodent diet (VRF1(FG)) from a commercial supplier (SDS Special Diets Services, Witham, England; batch 2619 (see Annex 5).
From the start of treatment, control rats were kept on this batch of VRF1 (FG) rodent diet (batch 2619). The animals of the test groups were kept on experimental diets prepared by mixing this batch of VRF1(FG) diet with the appropriate amounts of 2'-Fucosyllactose in a mechanical blender.

Fresh batches of the experimental diets were prepared three times during the study (on 01 December 2016, 03 January 2017 and 02 February 2017). The experimental diets were stored in closed plastic bags in a freezer (< -18°C) in portions sufficient for 3 or 4 days. The diets were provided to the rats as a powder in stainless steel cans, covered by a perforated stainless steel plate to prevent spillage. During the study, the food in the cans was replaced by fresh portions from the freezer twice a week and filled up as needed.
Each cage was supplied with domestic mains tap-water suitable for human consumption (quality guidelines according to Dutch legislation based on EC Council Directive 98/83/EC). The water was given in polypropylene bottles, which were cleaned weekly and filled as needed. Results of the routine physical, chemical and microbiological examination of drinking water as conducted by the supplier are made available to the test facility. In addition, the supplier periodically (twice per year) analyses water samples taken at the premises for a limited number of physical, chemical and microbiological variables. The results of the samples taken during the conduct of this study are given in Annex 6.

4.8 Observations analyses and measurements

4.8.1 Analysis of the experimental diets

From all three batches of diets prepared in the study (on 01 December 2016, 03 January 2017 and 02 February 2017), samples were taken and analyzed.
2'-Fucosyllactose was assayed by using using Ultra-Performance Liquid Chromatography – tandem Mass Spectrometry (UPLC-MS/MS) on a Acquity UPLC Glycan BEH amide column, held at 40 °C and 5mM ammonium formate in water (mobile phase A) and 10 mM ammonium formate in acetonitrile and water (mobile phase B) as the mobile phase. A detailed description of the analyses and the validation of the analytical methods is given in Annex 12.
The following analyses were conducted during the study:

- Homogeneity and content of the test substance at each dose level (5 samples per dose level, covering top, middle, left, right and bottom; one control sample) in the batch prepared on 01 December 2016.
- Content of the test substance at each dose level in the batches prepared on 01 December 2016 (average of 5 samples per dose level and one control sample), 03 January 2017 and 02 February 2017 (one sample per dose level and one control sample).
- Stability of the test substance under experimental conditions (one sample per dose level and one control sample of the batch prepared on 01 December 2016, after storage for 4 days in the animal room and after storage for at least 5 weeks in the freezer (≤-18°C).

All samples were measured in duplicate.

4.8.2 Intake of the test substance

For each week, the mean intake of the test substance per kg body weight per day was calculated from the nominal dietary concentration, the mean feed consumption per week and the mean of the body weight at the beginning and end of the pertaining week.

4.8.3 General clinical observations

Each animal was observed daily in the morning hours by cage-side observations and, if necessary, handled to detect signs of toxicity. All cages were checked again in the afternoon for dead or moribund animals to minimize loss of animals from the study. All abnormalities, signs

of ill health or reactions to treatment were recorded. The observations included, but were not restricted to, the signs listed in Annex 8.

4.8.4 Neurobehavioral testing (detailed clinical examinations, FOB and motor activity)

In addition to the above daily general clinical observations, detailed clinical examinations (in an arena outside the home cage) were performed on all rats prior to the first exposure and then once weekly throughout the study. Behavioral endpoints (Functional Observation Battery and motor activity assessment) were investigated in all rats at the end of the study in week 12. A detailed description of the observations and methods is given in Annex 13. Motor activity tests data recorded on DVD were removed from the study dossier after submission of the final report.

4.8.5 Ophthalmoscopic examination

Ophthalmoscopic observations were made shortly after the start of treatment (on day 1 and 2 for males and females respectively) in all rats, and in the last week of the treatment period (on day 86 and 87 for males and females, respectively) in rats of the control group (1) and the high-dose group (4). Because no treatment-related ocular changes were observed in the high-dose group, eye examination was not extended to the animals of the intermediate-dose groups at the end of the study. Eye examination was carried out using an ophthalmoscope after induction of mydriasis by a solution of atropine sulfate.

4.8.6 Body weight

The body weight of all pups were measured at PND 21 to enable allocation to the groups, see § 4.5. The body weight of each allocated rat was recorded at initiation of treatment (day 0), and once weekly thereafter. All animals were weighed on their scheduled necropsy date in order to calculate the correct organ to body weight ratios.

4.8.7 Food consumption

Food consumption was measured per (home) cage by weighing the feeders. The consumption was measured per cage over successive periods of 3 or 4 days. Food consumption was measured until day 90 (because rats were fasted overnight prior to necropsy). The results were expressed in g per animal per day.

4.8.8 Water consumption

Water consumption was measured per cage, by weighing the drinking bottles daily, during 5-day periods in weeks 1, 6 and 12. The results were expressed in g per animal per day.

4.8.9 Hematology

Hematology was conducted in samples collected from all animals at necropsy. The rats were fasted overnight before necropsy (water was freely available). Blood samples were taken from the abdominal aorta of all rats whilst under CO_2/O_2 anesthesia. EDTA or citrate (for prothrombin time) were used as anticoagulant. Blood samples were discarded after analysis. In each sample the following determinations were carried out according to the methods listed in Annex 9.

- hemoglobin (Hb)
- packed cell volume (PCV)
- red blood cell count (RBC)
- reticulocytes
- total white blood cell counts (WBC)

differential white blood cell counts[1]
prothrombin time
thrombocytes
mean corpuscular volume (MCV; calculated)
mean corpuscular hemoglobin (MCH; calculated)
mean corpuscular hemoglobin concentration (MCHC; calculated)

[1] Lymphocytes (Lympho), neutrophils (Neutro), eosinophils (Eosino), basophils (Baso) and monocytes (Mono).

4.8.10 Clinical chemistry

Clinical chemistry was conducted in samples collected from all animals at necropsy. The rats were fasted overnight before necropsy (water was freely available). Blood samples were taken from the abdominal aorta of all rats whilst under CO_2/O_2 anesthesia. The blood was collected in heparinized plastic tubes and plasma was prepared by centrifugation. Plasma samples were discarded after analysis. The measurements listed below were made in the plasma according to the methods given in Annex 10.

alkaline phosphatase activity (ALP)
aspartate aminotransferase activity (ASAT)
alanine aminotransferase activity (ALAT)
gamma glutamyl transferase activity (GGT)
total protein
albumin
ratio albumin to globulin (calculated)
urea
creatinine
glucose (fasting)
bilirubin (total)
cholesterol (total)
triglycerides
phospholipids
calcium (Ca)
sodium (Na)
potassium (K)
chloride (Cl)
inorganic phosphate (PO_4)

4.8.11 Renal concentration test and urinalysis

On day 85-86 urine was collected from all males and on day 87-88 urine was collected for females. All rats were deprived of water for 24 hours and of food during the last 16 hours of this period. During the last 16 hours of deprivation, the rats were kept individually in metabolism cages and urine was collected in glass tubes. Urine samples were discarded after analysis. The following determinations were carried out in individual samples according to the methods listed in Annex 11:

volume [1]
density (specific gravity)[1]
appearance
pH
glucose
microscopy of the urinary sediment[2]
occult blood
ketones
protein
bilirubin
urobilinogen

[1] To investigate the concentrating ability of the kidneys

[2] Red blood cells, white blood cells, epithelial cells, amorphous material, crystals, casts, bacteria, worm eggs, sperm cells.

4.8.12 Pathology

Gross necropsy

On day 91 (males) or 92 (females), the animals were killed in in such a sequence that the average time of killing was approximately the same for each group. The animals were killed after overnight fasting (water was freely available) by exsanguination from the abdominal aorta under CO_2/O_2 anesthesia and then subjected to a complete macroscopic examination.

Organ weights

At necropsy, the following organs of all rats were weighed (paired organs together) as soon as possible after dissection to avoid drying, and the relative organ weights (g/kg body weight) were calculated on the basis of the terminal body weight of the animals.

- adrenals
- brain
- cecum (full and empty)
- epididymides
- heart
- kidneys
- liver
- ovaries
- prostate
- seminal vesicles (with coagulating glands)
- spleen
- testes
- thymus
- uterus

Tissue preservation

Samples of the following tissues and organs of all animals were preserved in a neutral aqueous phosphate-buffered 4% solution of formaldehyde.

- adrenals
- aorta
- axillary lymph nodes
- brain[1]
- cecum
- colon
- duodenum
- epididymides
- esophagus
- exorbital lachrymal glands*
- eyes
- femur with joint*
- GALT (gut associated lymphoid tissue, including Peyer's patches)
- heart
- ileum
- jejunum
- kidneys
- liver
- lungs
- mammary gland (females)
- mandibular (cervical) lymph nodes*
- mesenteric lymph nodes
- nerve-peripheral (sciatic)
- ovaries
- oviducts (=fallopian tubes)
- pancreas
- parathyroid
- parotid salivary glands
- pituitary
- prostate
- rectum
- seminal vesicles + coagulating glands
- skeletal muscle (thigh)
- skin (flank)
- spinal cord[2]
- spleen
- sternum with bone marrow
- stomach[3]
- sublingual salivary glands
- submaxillary salivary glands
- testes
- thymus
- thyroid
- trachea/bronchi
- urinary bladder
- uterus (with cervix)
- vagina
- all gross lesions

* The tissues marked with * were preserved but not processed for histopathological examination, unless histopathological examination was considered necessary on the basis of the results of gross observations.
1 Three levels were examined microscopically (brain stem, cerebrum, cerebellum).
2 Retained in vertebral column, at least three levels were examined microscopically (cervical, mid-thoracic and lumbar).
3 Non glandular ('forestomach') and glandular (fundus, pyorus) parts were examined microscopically.

The carcass containing any remaining tissues was retained in formalin and discarded after completion of the histopathological examination.

Histopathological examination

The tissues to be examined microscopically were embedded in paraffin wax, sectioned and stained with hematoxylin and eosin.

Histopathological examination (by light microscopy) was performed on all tissues and organs listed above - except those marked with an asterisk - of all animals of the control group (1) and the high-dose group (4). A full microscopic examination of rat 33 (female, mid-dose) that died on day 24 (week 3) of the study was performed. Because no treatment-related changes were observed in the high-dose group, histopathology was not extended to the intermediate-dose groups. Gross lesions were examined in rats of all dose groups.

4.9 Statistical analysis of the results

The statistical procedures for analysis of data are described below.

- Body weight data collected after initiation of treatment: "AnCova & Dunnett's Test" with automatic data transformation. Day 0 body weight data are used as covariate unless removed during data preprocessing. The "AnCova & Dunnett's Test" is an automatic decision tree consisting of:
  (1) Data preprocessing tests. These tests start with transformation "None". First, suitability of the covariate is checked (criteria: sufficient cases, at least 2; variability of covariate non-zero; covariate effects sufficiently parallel over the groups, significance level parallelism test 0.01). Next, normality of data distribution (Shapiro-Wilks test; significance level 0.05) and homogeneity of variances (Levene test; significance level 0.05) are checked. If any of these three checks fail they are repeated using Log transformation.
  If checks on log-transformed, covariate-adjusted data fail, the covariate is removed and the normality and homogeneity checks are repeated. If these checks pass on transformations "None" or "Log", data are analyzed without covariate. If they fail, data are rank-transformed and the covariate is reinstated.
  (2) A group test assessing whether or not group means are all equal (one-way analysis of covariance [Ancova], or one-way analysis of variance [Anova] if the covariate is removed). If the group test shows no significant non-homogeneity of group means ($p \geq 0.05$), group summary tables do not show whether or not a covariate is used in the analysis.
  (3) Post-hoc analysis. If the group test shows significant ($p < 0.05$) non-homogeneity of group means, pairwise comparisons with the control group are conducted by Dunnett's multiple comparison test (significance levels 0.01 and 0.05).

- Pretreatment body weight data, clinical pathology (hematology, clinical chemistry, urinary volume and specific gravity) and organ weight data: "Generalized Anova Test" with automatic data transformation. This test is an automatic decision tree consisting of:
  (1) Data preprocessing tests. First, normality of data distribution (Shapiro-Wilks test) and homogeneity of variances (Levene test) are checked (initial transformation "None"). If any of these checks fail ($p<0.05$) they are repeated using Log transformation. If checks on log-transformed data fail, data are rank-transformed.
  (2) A group test assessing whether or not group means are all equal (parametric for untransformed or log-transformed data: one-way analysis of variance [Anova]; non-parametric for rank transformed data: Kruskal-Wallis test).
  (3) Post-hoc analysis. If the group test shows significant ($p<0.05$) non-homogeneity of group means, pairwise comparisons with the control group are conducted by Dunnett's multiple comparison test (parametric after Anova, non-parametric after Kruskal-Wallis; significance levels 0.01 and 0.05).
- Food/ water consumption: Dunnett's multiple comparison test.
- Semi quantitative urinalysis results: "Kruskal-Wallis & Dunnett Test" with "Rank" as data transformation method. In this test data are first rank-transformed and then analyzed by the Kruskal-Wallis test. If Kruskal-Wallis shows significant ($p<0.05$) non-homogeneity of group means, pairwise comparisons with the control group are conducted by Dunnett's multiple comparison test on the ranks of the data (significance levels 0.01 and 0.05).
- Functional observational battery: one-way analysis of variance followed by Dunnett's multiple comparison tests (continuous data), Kruskal-Wallis non-parametric analysis of variance followed by multiple comparison tests (rank order data) or Pearson chi-square analysis (categorical data).
- Motor activity data: total distance moved: one-way analysis of variance followed by Dunnett's multiple comparison tests; habituation of activity: repeated measures analysis of variance on time blocks (each session consists of 5 time blocks of 6 minutes each).
- Incidences of histopathological changes: Fisher's exact probability test.

Arithmetic means and standard deviation (SD) or standard error of the mean (SEM) are given in the tables of continuous and semi-continuous data.
Tests are performed as two-sided tests with results taken as significant where the probability of the results is <0.05 or <0.01.
Because numerous variables are subjected to statistical analysis, the overall false positive rate (Type I errors) is greater than suggested by a probability level of 0.05. Therefore, the final interpretation of results is based not only on statistical analysis but also on other considerations such as dose-response relationships and whether the results are significant in the light of other biological and pathological findings.

5 Results

Mean data are presented in tables; individual data in appendices.

5.1 Analysis of the experimental diets (Annex 12)

Details on the test substance analysis in the diet are presented in Annex 12. The analytical report concludes that:

- The method used for the quantitative analysis of 2'-fucosyllactose in diet met the pre-set validation criteria.
- The test substance was homogeneously distributed in the test diets at all dose levels.
- The content of the test substance in diet was close to the intended concentration for all diets at all dose levels.
- The test substance was stable under experimental conditions. There was no loss of test substance from any dietary level during storage for four days in the animal room, or during storage for five weeks in the freezer.

5.2 Intake of the test substance (Table 1)

Due to the decreased food intake per kg body weight with increasing age of the rats, the intake of the test substance per kg body weight gradually decreased in all groups (Table 1).
The overall mean intake of the test substance in the low-, mid- and high-dose group was respectively 2.17, 4.27 and 7.25 mg/kg body weight/day for males, and 2.45, 5.22 and 7.76 mg/kg body weight/day for females.

5.3 Clinical observations (Table 2; Appendix 1)

One female rat (number 33) in the mid-dose group died at 29 December 2017, 24 days after the start of the treatment. Because no dose-response relationship was observed and none of the male rats died during the course of the study, this death was considered an incidental finding and therefore not treatment-related. There were no other treatment-related clinical signs (Table 2). The few signs noted were considered unrelated to treatment. Abnormalities of the skin, fur or tail (sparsely haired areas, encrustations, skin wounds, tail kink) are common findings and were not ascribed to treatment. Tilted head was observed in one male in the high-dose group in various weeks of the study. Based on the incidence and on the distribution among the dose groups, this finding was considered not to be related to treatment.

5.4 Neurobehavioral testing (Annex 13)

A detailed description of the neurobehavioral testing is given in Annex 13. The results of the detailed clinical observations, functional observational battery and motor activity assessment did not indicate any neurotoxic potential of 2'-Fucosyllactose in rats.

5.5 Ophthalmoscopic examination (Table 3; Appendix 2)

Ophthalmoscopy did not reveal any treatment-related changes.

5.6 Body weights (Table 4; Appendix 3)

There were no statistically significant differences in body weights between the control group and the test groups. Body weights were not affected by the treatment (Table 4).

5.7 Food consumption (Table 5; Appendix 4)

There were no statistically significant differences in food consumption in male rats among the groups. In female rats of the high-dose group food consumption was significantly decreased compared to controls at day 35-39, 42-46, 56-60, 70-74, 74-77 and 88-90, which resulted in a slight, though statistically significant decrease in the average overall food consumption (Table 5).

5.8 Water consumption (Table 6; Appendix 5)

There were no noticeable differences in water consumption among the groups (Table 6). An incidental increase was statistically significant in males of the high-dose group on day 35-36 and in females of the high-dose group on day 38-39.

5.9 Hematology (Tables 7 & 8; Appendices 6 & 7)

There were no statistically significant differences in red blood cell variables between the test groups and the controls. Thrombocytes were slightly, though statistically significantly, increased in high-dose females (Table 7). No significance was attached to this finding because the difference with the controls was only slight and occurred in one sex only. There were no statistically significant changes in total or differential white blood cell counts (Table 8).

5.10 Clinical chemistry (Table 9; Appendix 8)

There were no statistically significant differences in clinical chemistry variables between the test groups and the controls, except for an increase in urea concentration in mid-dose and high-dose males. In the absence of this finding in females and any corroborative findings in males, the slight increase in this parameter was considered a chance finding.

5.11 Urinalysis (Tables 10 – 12; Appendices 9 - 11)

The renal concentration test showed a statistically significantly decreased specific gravity in females of the high dose group (Table 10). The decreased specific gravity was only very slight

and ascribed to a higher (although not statistically significant) urinary volume excreted. Because these changes were very slight they do not point to impaired concentrating ability of the kidneys and therefore no toxicological significance was attached to this finding.
Semi-quantitative (dipstick) urinary measurements (Table 11) and microscopic examination of the urinary sediment (Table 12) did not reveal any differences among the groups.

5.12 Organ weights (Tables 13 & 14; Appendices 12 & 13)

Absolute organ weights are presented in Table 13, the organ to body weight ratios in Table 14. The relative weight of the liver was slightly (less than 10%), but statistically significantly increased in males in the high-dose group (Table 14).
The absolute and relative weights of the filled and empty caecum were statistically significantly increased in the mid- and high-dose group in male and female rats (Table 13 and 14). In low-dose males only the absolute weight of the filled caecum was statistically significantly increased (Table 13).

5.13 Pathology (Table 15 & 16; Appendix 14)

Animal number 33 (female, mid-dose group) was found dead on day 24 of the study. Necropsy was performed. Microscopic evaluation of the collected tissues did not reveal a cause of death and was therefore not considered to be related to treatment.

5.13.1 Macroscopic examination

At necropsy no treatment related macroscopic changes were observed (Table 15).

5.13.2 Microscopic examination

Microscopic evaluation did not reveal treatment related histopathological changes (Table 16). The histopathological changes observed were about equally distributed amongst the different treatment groups or occurred in one or a few animals only. They are common findings in rats of this strain and age or occurred as individual chance findings. Therefore, they were not considered to be related to treatment.

6 Discussion and conclusions

In this sub-chronic oral toxicity study, the safety of 2'-Fucosyllactose was examined in Wistar rats. 2'-Fucosyllactose was administered at constant concentrations in the diet at levels of 0% (control), 3 %, 6% and 10% to groups of 10 rats/sex, during 13 weeks.

The administration of the test substance was well tolerated at all dose levels, and did not induce any relevant changes in general condition, growth, water intake, neurobehavioral observations, ophthalmoscopy, hematology, clinical chemistry, urinalysis, organ weights or in macroscopy and microscopy of organs and tissues. One female rat in the mid-dose group died at day 24 of the study, but did not show any relevant clinical sigs. Microscopic evaluation of the collected tissues did not reveal a cause of death and was therefore not considered treatment related.

Only a few changes were noted that could be attributed to the administration of 2'-Fucosyllactose.

- In female rats of the high-dose group overall food consumption was slightly decreased. Since the relative difference with controls was small (less than 10%), and no clear corroborative changes were observed in any of the other parameters investigated, this finding – although likely treatment related – was considered to be of little, if any, toxicological significance.
- The few slight, but statistically significant differences in clinical pathology parameters were considered chance findings – and therefore not treatment related – because they were observed in one sex only, the difference with controls was small, and no changes were observed in any of the associated parameters investigated.
- Cecal enlargement was noted in mid- and high-dose males and females and in low-dose males. This finding is ascribed to the high fiber content in the test substance. It is well established that cecal enlargement in rats may arise from the feeding of large amounts of a heterogeneous family of products, referred to as 'dietary fiber' or 'poorly digestible carbohydrates (Levrat et al., 1991, Campbell et al., 1997, Lu et al., 2000, Kim, 2002). These substances are incompletely absorbed, yet fermented in the gastrointestinal tract. The fermentation results in the production of short chain fatty acids (SCFA), which raises the osmotic value of the cecal content and may promote the growth of the mucosal layer (Jin et al., 1994, Frankel et al., 1994, Knapp et al., 2013). Another cause of cecal enlargement can be the feeding of large amounts of substances with water binding properties.
  The increased cecal weights in the present study were not accompanied by hypertrophy or other histopathological changes. In the absence of such histopathological correlates, cecal enlargement is interpreted as a physiological response rather than a toxic effect (WHO 1987).
- The relative weight of the liver was slightly increased in males in the high-dose group. This slight increase was not accompanied by changes in clinical chemistry and microscopic examination of the liver did not reveal any histopathological changes. Therefore, it is not considered adverse.

Conclusion

Because 2'-Fucosyllactose did not induce any adverse changes in any test group, the no-observed-adverse effect level (NOAEL) is placed at the highest level tested, namely 10% in the diet (≥7.25 g/kg body weight/day for males and ≥ 7.76 g/kg body weight/day for females).

7 References

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8 Documentation and retention of records, samples and specimens

The following study specific materials will be archived for 5 years:
- Raw data (or true copies if unstable)
- A reference sample of the test substance
- Tissue specimens and paraffin blocks

The following study specific materials will be archived for at least 15 years
- Original study plan and final report, and any amendments thereof
- Microscopic slides

General raw data will be retained for at least 25 years, after which they may be destroyed without further notice. These may include, but are not necessarily limited to:
- Facility-based documents
- Calibration and quality control data
- General registrations potentially used for more than one study

At the end of the archiving period, the reference sample, tissue specimens and paraffin blocks will be discarded. The sponsor will be asked whether the study plan, final report, amendments, raw data, including microscopic slides, and correspondence should be discarded, retained for an additional period, or transferred to the archives of the sponsor.

All materials will be retained in the archives of TNO, Utrechtseweg 48, 3704 HE Zeist, The Netherlands. The archiving period for starts on the cover date of the final report.

Tables

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 1: Test substance intake

Day(s) Relative to Start Date

Sex: Male		Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)
		0 - 7	7 - 14	14 - 21	21 - 28	28 - 35	35 - 42	42 - 49
0% diet	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3% diet	Mean	4.08	3.84	3.19	2.78	2.50	2.25	2.11
6% diet	Mean	8.14	7.74	6.35	5.58	4.98	4.49	4.15
10% diet	Mean	13.04	12.61	10.53	9.09	8.37	7.56	6.95

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 1: Test substance intake

Day(s) Relative to Start Date

Sex: Male		Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)
		49 - 56	56 - 63	63 - 70	70 - 77	77 - 84	84 - 90	0 - 90
0% diet	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3% diet	Mean	1.94	1.82	1.76	1.77	1.63	1.52	2.17
6% diet	Mean	3.77	3.53	3.38	3.40	3.16	2.97	4.27
10% diet	Mean	6.50	6.17	5.98	5.97	5.64	5.05	7.25

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 1: Test substance intake

Day(s) Relative to Start Date

Sex: Female		Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)
		0 - 7	7 - 14	14 - 21	21 - 28	28 - 35	35 - 42	42 - 49
0% diet	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3% diet	Mean	4.02	3.65	3.06	2.78	2.59	2.50	2.37
6% diet	Mean	8.24	7.45	6.08	5.49	5.28	5.03	4.78
10% diet	Mean	12.66	11.68	9.84	9.06	8.28	7.73	7.34

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 1: Test substance intake

Day(s) Relative to Start Date

Sex: Female								
		Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)	Test Substance Intake (g/kg BW/day)
		49 - 56	56 - 63	63 - 70	70 - 77	77 - 84	84 - 90	0 - 90
0% diet	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3% diet	Mean	2.29	2.18	2.16	2.11	1.90	1.81	2.45
6% diet	Mean	4.64	4.45	4.32	4.36	3.90	3.87	5.22
10% diet	Mean	7.00	6.69	6.69	6.80	6.15	5.62	7.76

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Table 2: Clinical observations

Observation Type: All Types	Male				Female			
From Day 0 (Start Date) to 92 (Start Date)	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
DEAD Killed scheduled	10	10	10	10	10	10	9	10
DEAD Found dead	0	0	0	0	0	0	1	0
SKIN Sparsely haired area(s)	0	1	0	1	2	2	0	2
SKIN Encrustation(s)	1	4	1	2	5	2	1	4
SKIN Wound(s)	0	0	0	1	0	0	0	1
HEAD Tilted	0	0	0	1	0	0	0	0
TAIL Kink	2	0	1	1	0	0	0	0

Values = Number of Animals Affected

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 3: Ophthalmoscopic observations

Observation Type: All Types	Male				Female			
From Day 1 (Start Date) to 2 (Start Date)	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Persistent pupillary membrane	1	0	2	0	1	2	0	0
Iris malformation	0	0	0	0	0	0	1	0
No abnormalities	9	10	8	10	9	8	9	10

Observation Type: All Types	Male				Female			
From Day 86 (Start Date) to 87 (Start Date)	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Persistent pupillary membrane	1	0	0	0	1	0	0	0
No abnormalities	9	0	0	10	9	0	0	10

Values = Number of Animals Affected

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 4: Body weight

Day(s) Relative to Start Date

Sex: Male		Bodywt day -x (g) [g]	Bodywt day 0 (g) [g]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]
		-4	0	7	14	21	28	35	42
0%	Mean	46.17	63.60	106.29	148.87	189.81	231.62	261.40	284.05
diet	SD	3.87	4.26	7.43	11.08	16.58	21.34	23.77	27.19
	N	10	10	10	10	10	10	10	10
3%	Mean	47.09	64.27	108.74	151.90	192.94	234.26	265.97	287.67
diet	SD	3.14	4.59	9.03	12.72	15.89	19.17	21.35	25.11
	N	10	10	10	10	10	10	10	10
6%	Mean	47.82	65.41	110.62	153.78	195.41	237.31	268.20	290.72
diet	SD	4.45	4.87	8.90	13.44	19.45	23.75	27.75	31.76
	N	10	10	10	10	10	10	10	10
10%	Mean	46.32	64.24	105.52	146.41	185.70	225.17	253.44	273.47
diet	SD	5.73	6.77	9.45	12.46	16.88	21.18	28.50	33.94
	N	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[c] - Ancova/Anova & Dunnett {Covariate: Bodywt day 0}: n - Inappropriate for statistics

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 4: Body weight

Day(s) Relative to Start Date

Sex: Male		Bodyweights						
		Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]
		49	56	63	70	77	84	90
0%	Mean	303.17	318.29	330.94	340.87	346.79	361.39	361.13
diet	SD	31.40	35.04	38.09	39.06	39.10	40.68	40.99
	N	10	10	10	10	10	10	10
3%	Mean	305.82	320.77	334.56	343.86	352.23	367.65	369.55
diet	SD	27.78	30.54	33.45	35.33	36.80	39.58	39.78
	N	10	10	10	10	10	10	10
6%	Mean	309.46	321.25	334.90	344.88	351.48	365.70	369.79
diet	SD	35.40	37.27	38.72	38.01	39.42	41.25	42.94
	N	10	10	10	10	10	10	10
10%	Mean	287.07	300.41	313.68	325.41	333.06	347.23	350.29
diet	SD	38.50	40.82	43.23	43.23	45.83	46.02	47.08
	N	10	10	10	10	10	10	10

[c] - Ancova/Anova & Dunnett {Covariate: Bodywt day 0}

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Table 4: Body weight

Day(s) Relative to Start Date

Sex: Female		Bodywt day -x (g) [g]	Bodywt day 0 (g) [g]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]
		-4	0	7	14	21	28	35	42
0%	Mean	45.62	60.56	96.68	122.45	142.61	157.62	170.39	182.52
diet	SD	3.83	5.06	6.86	7.44	8.82	10.96	11.77	12.73
	N	10	10	10	10	10	10	10	10
3%	Mean	45.62	60.26	96.91	125.05	143.59	163.03	174.04	184.43
diet	SD	5.05	5.87	9.44	11.16	14.43	15.88	15.38	15.16
	N	10	10	10	10	10	10	10	10
6%	Mean	45.61	61.17	97.48	125.67	143.89	159.91	172.56	183.24
diet	SD	2.89	3.16	3.53	5.41	7.80	7.98	9.79	8.95
	N	10	10	10	10	10	9	9	9
10%	Mean	46.46	61.76	97.29	124.49	143.24	159.73	173.91	182.30
diet	SD	4.24	4.41	5.14	9.33	11.63	12.06	12.97	14.32
	N	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[c] - Ancova/Anova & Dunnett {Covariate: Bodywt day 0}: n - Inappropriate for statistics

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Table 4: Body weight

Day(s) Relative to Start Date

Sex: Female		Bodyweights						
		Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c1]	Bodywt (g) [c]	Bodywt (g) [c]	Bodywt (g) [c]
		49	56	63	70	77	84	90
0%	Mean	195.32	200.72	206.00	210.50	213.62	216.04	219.67
diet	SD	12.02	14.81	19.57	15.80	14.68	14.12	16.03
	N	10	10	10	10	10	10	10
3%	Mean	193.55	201.11	206.88	213.01	216.65	219.39	219.31
diet	SD	17.98	17.17	17.34	17.59	16.37	16.64	16.73
	N	10	10	10	10	10	10	10
6%	Mean	192.26	197.01	204.82	207.61	210.59	212.16	212.99
diet	SD	10.06	8.67	8.28	9.73	8.39	8.95	8.29
	N	9	9	9	9	9	9	9
10%	Mean	189.82	195.79	202.81	204.92	205.55	209.59	212.44
diet	SD	14.41	12.35	13.22	14.96	14.33	12.17	13.49
	N	10	10	10	10	10	10	10

[c] - Ancova/Anova & Dunnett {Covariate: Bodywt day 0}
[c1] - Ancova/Anova & Dunnett(Log) {Covariate: Bodywt day 0}

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Table 5: Food consumption

Daily Food Cons Per Animal (Gram)

Sex: Male		Day(s) Relative to Animal Start Date								
		0 - 4	4 - 7	7 - 11	11 - 14	14 - 18	18 - 21	21 - 25	25 - 28	28 - 32
0%	Mean	10.5	12.9	15.4	17.2	17.5	18.1	18.6	19.6	20.4
diet	SD	0.6	0.7	0.9	1.0	1.0	0.7	1.3	1.1	1.1
	N	2	2	2	2	2	2	2	2	2
3%	Mean	10.6	13.2	15.9	17.5	17.9	18.6	19.1	20.3	20.7
diet	SD	0.9	0.1	0.2	0.2	0.3	0.6	0.5	0.7	0.4
	N	2	2	2	2	2	2	2	2	2
6%	Mean	10.7	13.4	16.2	17.9	18.0	18.7	19.6	20.4	20.5
diet	SD	0.0	0.5	0.1	0.5	0.2	0.1	0.5	0.2	0.2
	N	2	2	2	2	2	2	2	2	2
10%	Mean	10.0	12.3	14.8	17.1	17.2	17.5	18.2	19.0	20.0
diet	SD	0.5	0.1	0.4	0.2	0.1	0.7	0.3	0.1	0.2
	N	2	2	2	2	2	2	2	2	2

Dunnett

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 5: Food consumption

Daily Food Cons Per Animal (Gram)

Sex: Male		Day(s) Relative to Animal Start Date								
		32 - 35	35 - 39	39 - 42	42 - 46	46 - 49	49 - 53	53 - 56	56 - 60	60 - 63
0%	Mean	20.4	20.5	20.4	20.3	20.1	19.8	20.0	19.5	19.4
diet	SD	1.3	1.7	1.7	1.2	1.2	0.9	1.7	1.1	0.8
	N	2	2	2	2	2	2	2	2	2
3%	Mean	20.7	20.6	20.7	20.7	20.8	20.1	20.2	19.9	19.5
diet	SD	0.1	0.2	0.1	0.1	0.2	0.3	0.7	0.8	0.8
	N	2	2	2	2	2	2	2	2	2
6%	Mean	21.2	21.0	20.2	20.5	20.6	20.0	19.1	19.2	19.0
diet	SD	0.1	0.6	0.4	0.2	0.7	1.0	1.0	0.4	0.5
	N	2	2	2	2	2	2	2	2	2
10%	Mean	19.6	20.0	19.2	19.3	19.1	18.6	19.1	18.6	18.7
diet	SD	0.1	0.6	0.5	0.4	0.1	0.5	0.8	0.1	0.1
	N	2	2	2	2	2	2	2	2	2

Dunnett

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 5: Food consumption

Daily Food Cons Per Animal (Gram)

Sex: Male		Day(s) Relative to Animal Start Date								
		63 - 67	67 - 70	70 - 74	74 - 77	77 - 81	81 - 84	84 - 88	88 - 90	0 - 90
0%	Mean	19.3	19.2	19.2	19.9	19.3	18.7	17.1	20.1	18.5
diet	SD	0.5	0.9	0.3	0.8	0.8	0.2	0.1	0.6	0.9
	N	2	2	2	2	2	2	2	2	2
3%	Mean	19.7	19.8	20.2	20.6	19.7	19.0	18.0	19.4	18.9
diet	SD	0.7	0.4	0.4	0.4	0.3	0.3	0.7	0.8	0.4
	N	2	2	2	2	2	2	2	2	2
6%	Mean	18.9	19.0	19.4	19.8	18.8	18.5	17.6	18.8	18.7
diet	SD	0.9	0.6	0.4	0.7	0.1	0.4	0.8	0.3	0.4
	N	2	2	2	2	2	2	2	2	2
10%	Mean	18.5	19.2	19.1	19.6	18.7	19.0	16.9	18.3	17.9
diet	SD	0.0	0.7	0.4	0.3	0.3	1.9	0.2	0.1	0.0
	N	2	2	2	2	2	2	2	2	2

Dunnett
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 5: Food consumption

Daily Food Cons Per Animal (Gram)

Sex: Female		Day(s) Relative to Animal Start Date								
		0 - 4	4 - 7	7 - 11	11 - 14	14 - 18	18 - 21	21 - 25	25 - 28	28 - 32
0%	Mean	10.1	11.8	13.1	13.6	13.2	13.8	13.7	13.9	13.9
diet	SD	0.1	0.1	0.1	0.4	0.2	0.0	0.1	0.3	0.3
	N	2	2	2	2	2	2	2	2	2
3%	Mean	9.5	11.7	13.1	13.8	13.4	13.8	13.7	14.6	14.4
diet	SD	0.5	0.9	0.6	0.6	0.3	0.4	0.4	0.6	0.4
	N	2	2	2	2	2	2	2	2	2
6%	Mean	10.1	11.9	13.5	14.3	13.6	13.7	13.4	14.4	14.5
diet	SD	0.4	0.1	0.5	0.2	0.4	0.0	0.9	0.4	0.0
	N	2	2	2	2	2	2	2	2	2
10%	Mean	9.2	11.2	12.6	13.3	13.0	13.3	13.4	14.0	13.8
diet	SD	0.0	0.2	0.3	0.4	0.0	0.2	0.1	0.5	0.5
	N	2	2	2	2	2	2	2	2	2

Dunnett

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 5: Food consumption

Daily Food Cons Per Animal (Gram)

Sex: Female		Day(s) Relative to Animal Start Date								
		32 - 35	35 - 39	39 - 42	42 - 46	46 - 49	49 - 53	53 - 56	56 - 60	60 - 63
0%	Mean	14.3	14.7	14.9	15.0	14.9	14.8	15.0	14.7	14.6
diet	SD	0.2	0.1	0.5	0.2	0.8	0.9	0.9	0.4	0.6
	N	2	2	2	2	2	2	2	2	2
3%	Mean	14.5	14.7	15.0	15.1	14.5	14.8	15.1	14.7	14.8
diet	SD	0.4	0.1	0.2	0.4	0.3	0.0	0.5	0.3	0.5
	N	2	2	2	2	2	2	2	2	2
6%	Mean	14.8	14.9	14.8	15.0	14.9	15.0	15.1	14.7	15.1
diet	SD	0.4	0.1	0.3	0.2	0.4	0.5	0.3	0.1	0.4
	N	2	2	2	2	2	2	2	2	2
10%	Mean	13.6	13.6**	13.8	13.6*	13.6	13.2	13.8	13.3*	13.3
diet	SD	0.2	0.1	0.4	0.1	0.6	0.2	0.3	0.3	0.6
	N	2	2	2	2	2	2	2	2	2

Dunnett: * = p < 0.05; ** = p < 0.01
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 5: Food consumption

Daily Food Cons Per Animal (Gram)

Sex: Female		Day(s) Relative to Animal Start Date								
		63 - 67	67 - 70	70 - 74	74 - 77	77 - 81	81 - 84	84 - 88	88 - 90	0 - 90
0%	Mean	14.2	15.0	14.6	15.4	13.7	14.6	12.4	16.2	14.0
diet	SD	0.3	0.0	0.1	0.1	0.3	0.0	0.3	0.9	0.0
	N	2	2	2	2	2	2	2	2	2
3%	Mean	15.0	15.1	14.4	15.8	13.4	14.1	12.4	14.7	14.0
diet	SD	0.4	0.1	0.3	0.4	0.5	0.9	0.1	0.5	0.2
	N	2	2	2	2	2	2	2	2	2
6%	Mean	14.8	14.9	14.9	15.5	13.7	13.8	12.9	15.5	14.1
diet	SD	0.0	0.9	0.4	0.1	0.2	0.4	0.6	1.1	0.1
	N	2	2	2	2	2	2	2	2	2
10%	Mean	13.5	13.7	13.5*	14.4*	12.5	13.0	11.2	13.0*	13.1**
diet	SD	0.3	0.2	0.4	0.1	0.4	0.1	0.5	0.3	0.1
	N	2	2	2	2	2	2	2	2	2

Dunnett: * = p < 0.05; ** = p < 0.01
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 6: Water consumption

Daily Water Cons Per Animal (Millilitre)

Sex: Male		Day(s) Relative to Animal Start Date					
		0 - 1	1 - 2	2 - 3	3 - 4	4 - 5	0 - 5
0%	Mean	13.1	14.0	15.5	16.2	17.2	15.2
diet	SD	0.2	0.2	0.2	0.6	0.0	0.0
	N	2	2	2	2	2	2
3%	Mean	13.9	14.9	15.7	16.2	17.4	15.6
diet	SD	0.7	1.0	0.3	0.3	0.3	0.4
	N	2	2	2	2	2	2
6%	Mean	14.0	14.9	15.6	15.7	16.9	15.4
diet	SD	1.3	1.2	0.7	0.7	1.3	1.0
	N	2	2	2	2	2	2
10%	Mean	13.6	15.7	16.1	17.7	18.5	16.3
diet	SD	0.2	0.6	0.2	0.7	2.5	0.2
	N	2	2	2	2	2	2

Dunnett
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 6: Water consumption

Daily Water Cons Per Animal (Millilitre)

Sex: Male		Day(s) Relative to Animal Start Date					
		35 - 36	36 - 37	37 - 38	38 - 39	39 - 40	35 - 40
0%	Mean	24.0	25.7	24.1	25.4	23.5	24.6
diet	SD	0.4	1.6	2.0	1.1	1.7	1.3
	N	2	2	2	2	2	2
3%	Mean	25.5	25.9	25.9	25.2	25.1	25.5
diet	SD	0.3	0.6	0.5	1.2	2.0	0.9
	N	2	2	2	2	2	2
6%	Mean	25.6	25.6	24.4	25.2	24.5	25.0
diet	SD	0.9	0.4	0.7	1.2	0.8	0.2
	N	2	2	2	2	2	2
10%	Mean	27.0*	26.7	26.4	25.8	25.9	26.4
diet	SD	0.0	0.8	0.6	0.5	1.9	0.5
	N	2	2	2	2	2	2

Dunnett: * = $p < 0.05$
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 6: Water consumption

Daily Water Cons Per Animal (Millilitre)

Sex: Male		Day(s) Relative to Animal Start Date					
		77 - 78	78 - 79	79 - 80	80 - 81	81 - 82	77 - 82
0%	Mean	22.9	24.3	24.4	26.9	21.1	23.9
diet	SD	1.7	1.7	0.2	1.9	0.0	0.4
	N	2	2	2	2	2	2
3%	Mean	24.5	26.0	26.0	27.3	22.9	25.3
diet	SD	1.7	1.2	1.0	0.4	0.4	0.2
	N	2	2	2	2	2	2
6%	Mean	23.2	24.1	25.7	24.8	21.9	24.0
diet	SD	1.0	2.0	0.3	1.9	1.4	0.2
	N	2	2	2	2	2	2
10%	Mean	25.6	25.8	26.8	28.4	24.3	26.2
diet	SD	2.8	3.2	0.7	0.5	1.0	1.7
	N	2	2	2	2	2	2

Dunnett
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 6: Water consumption

Daily Water Cons Per Animal (Millilitre)

Sex: Female		Day(s) Relative to Animal Start Date					
		0 - 1	1 - 2	2 - 3	3 - 4	4 - 5	0 - 5
0%	Mean	13.3	14.4	15.9	15.6	17.2	15.3
diet	SD	0.2	1.0	0.4	0.7	0.4	0.5
	N	2	2	2	2	2	2
3%	Mean	12.8	13.1	14.0	14.5	16.7	14.2
diet	SD	1.2	2.0	1.3	1.5	1.0	1.4
	N	2	2	2	2	2	2
6%	Mean	13.2	13.8	14.9	15.1	16.3	14.6
diet	SD	0.9	0.5	1.9	0.5	1.0	1.0
	N	2	2	2	2	2	2
10%	Mean	13.1	14.5	15.0	16.6	18.2	15.5
diet	SD	0.8	0.1	1.1	0.7	0.9	0.3
	N	2	2	2	2	2	2

Dunnett
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 6: Water consumption

Daily Water Cons Per Animal (Millilitre)

Sex: Female		Day(s) Relative to Animal Start Date					
		35 - 36	36 - 37	37 - 38	38 - 39	39 - 40	35 - 40
0%	Mean	21.7	24.0	20.5	18.8	20.1	21.0
diet	SD	0.5	0.6	0.3	1.3	0.2	0.4
	N	2	2	2	2	2	2
3%	Mean	21.8	19.8	20.0	17.7	21.2	20.1
diet	SD	0.8	2.7	1.5	0.0	1.9	0.8
	N	2	2	2	2	2	2
6%	Mean	18.0	22.5	20.9	20.6	18.2	20.0
diet	SD	0.4	1.0	3.0	0.3	0.3	0.7
	N	2	2	2	2	2	2
10%	Mean	20.6	21.9	21.6	21.7*	20.9	21.3
diet	SD	2.3	0.4	1.2	0.6	0.7	0.5
	N	2	2	2	2	2	2

Dunnett: * = p < 0.05
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 6: Water consumption

Daily Water Cons Per Animal (Millilitre)

Sex: Female		Day(s) Relative to Animal Start Date					
		77 - 78	78 - 79	79 - 80	80 - 81	81 - 82	77 - 82
0%	Mean	20.6	20.7	23.4	22.6	20.9	21.7
diet	SD	0.3	1.8	0.9	2.2	1.2	0.6
	N	2	2	2	2	2	2
3%	Mean	17.4	20.3	23.6	21.4	18.6	20.3
diet	SD	3.8	0.8	0.3	1.7	2.2	0.6
	N	2	2	2	2	2	2
6%	Mean	19.1	21.4	22.0	23.1	17.7	20.7
diet	SD	0.3	1.2	0.8	3.2	0.8	1.3
	N	2	2	2	2	2	2
10%	Mean	18.4	20.5	21.3	22.3	18.2	20.1
diet	SD	0.6	0.6	2.6	1.1	1.0	0.3
	N	2	2	2	2	2	2

Dunnett
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 7: Red blood cell and coagulation parameters

Day: 91 Relative to Start Date

Sex: Male		RBC (10E12/L) [g]	Hb (mmol/L) [g]	PCV (L/L) [g1]	MCV (fL) [g2]	MCH (fmol) [g]	MCHC (mmol/L) [g]	Reticulocytes (%) [g]	Thrombocytes (10E9/L) [g]	Prothrom Time (s) [g]
0%	Mean	8.984	9.65	0.4956	55.19	1.075	19.48	2.316	826.2	18.73
diet	SD	0.366	0.30	0.0159	1.22	0.044	0.44	0.341	79.5	0.89
	N	10	10	10	10	10	10	10	10	10
3%	Mean	9.007	9.69	0.5010	55.63	1.076	19.34	2.381	858.0	18.87
diet	SD	0.222	0.37	0.0144	1.15	0.037	0.32	0.292	147.1	0.93
	N	10	10	10	10	10	10	10	10	10
6%	Mean	8.875	9.58	0.4937	55.68	1.081	19.41	2.418	851.3	18.77
diet	SD	0.384	0.31	0.0161	1.98	0.047	0.22	0.325	168.0	0.81
	N	10	10	10	10	10	10	10	10	10
10%	Mean	8.951	9.65	0.5006	55.92	1.078	19.29	2.183	804.5	18.62
diet	SD	0.442	0.48	0.0288	1.07	0.022	0.25	0.282	96.4	0.73
	N	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)
[g2] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 7: Red blood cell and coagulation parameters

Day: 92 Relative to Start Date

Sex: Female		RBC (10E12/L) [g]	Hb (mmol/L) [g]	PCV (L/L) [g]	MCV (fL) [g]	MCH (fmol) [g]	MCHC (mmol/L) [g]	Reticulocytes (%) [g]	Thrombocytes (10E9/L) [g]	Prothrom Time (s) [g1]
0%	Mean	8.334	9.46	0.4823	57.91	1.136	19.62	2.477	742.0	18.85
diet	SD	0.382	0.30	0.0160	1.46	0.042	0.33	0.379	78.0	0.63
	N	10	10	10	10	10	10	10	10	10
3%	Mean	8.360	9.49	0.4791	57.32	1.135	19.81	2.182	802.9	18.70
diet	SD	0.193	0.34	0.0161	1.67	0.039	0.31	0.330	85.7	0.54
	N	10	10	10	10	10	10	10	10	10
6%	Mean	8.397	9.46	0.4797	57.14	1.127	19.73	2.064	809.8	19.04
diet	SD	0.448	0.38	0.0245	1.10	0.031	0.45	0.348	84.2	1.01
	N	9	9	9	9	9	9	9	9	9
10%	Mean	8.184	9.39	0.4713	57.64	1.149	19.93	2.399	855.6*	18.66
diet	SD	0.463	0.36	0.0203	1.62	0.034	0.31	0.412	97.1	1.30
	N	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett: * = p < 0.05
[g1] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 8: Total and differential white blood cell counts

Day: 91 Relative to Start Date

Sex: Male		WBC (10E9/L) [g]	Lympho Absolute (10E9/L) [g1]	Neutro Absolute (10E9/L) [g1]	Eosino Absolute (10E9/L) [g]	Baso Absolute (10E9/L) [g2]	Mono Absolute (10E9/L) [g]	Lympho cytes (%) [g2]	Neutro phils (%) [g1]	Eosino phils (%) [g]	Baso phils (%) [g2]	Mono cytes (%) [g]
0%	Mean	5.29	4.00	1.09	0.058	0.008	0.111	74.81	21.34	1.13	0.15	2.09
diet	SD	1.37	1.26	0.19	0.019	0.006	0.043	5.24	4.99	0.45	0.08	0.50
	N	10	10	10	10	10	10	10	10	10	10	10
3%	Mean	6.28	4.87	1.17	0.071	0.010	0.119	76.69	19.57	1.14	0.15	1.95
diet	SD	1.84	1.70	0.32	0.034	0.007	0.037	5.39	4.90	0.43	0.07	0.60
	N	10	10	10	10	10	10	10	10	10	10	10
6%	Mean	5.40	4.01	1.20	0.057	0.009	0.100	74.19	22.43	1.02	0.15	1.86
diet	SD	1.54	1.31	0.56	0.025	0.005	0.033	7.72	7.71	0.30	0.08	0.43
	N	10	10	10	10	10	10	10	10	10	10	10
10%	Mean	5.66	4.35	1.13	0.051	0.008	0.091	76.23	20.67	0.90	0.13	1.67
diet	SD	1.87	1.59	0.26	0.028	0.006	0.029	3.44	3.10	0.43	0.07	0.50
	N	10	10	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)
[g2] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 8: Total and differential white blood cell counts

Day: 92 Relative to Start Date

Sex: Female		WBC (10E9/L) [g]	Lympho Absolute (10E9/L) [g]	Neutro Absolute (10E9/L) [g1]	Eosino Absolute (10E9/L) [g]	Baso Absolute (10E9/L) [g2]	Mono Absolute (10E9/L) [g]	Lympho cytes (%) [g2]	Neutro phils (%) [g1]	Eosino phils (%) [g1]	Baso phils (%) [g]	Mono cytes (%) [g]
0%	Mean	3.84	2.99	0.71	0.042	0.005	0.077	78.69	17.66	1.07	0.13	1.98
diet	SD	1.15	0.81	0.41	0.021	0.003	0.031	6.09	6.01	0.37	0.07	0.48
	N	10	10	10	10	10	10	10	10	10	10	10
3%	Mean	3.99	3.10	0.71	0.061	0.008	0.086	77.40	18.14	1.56	0.19	2.15
diet	SD	1.02	0.86	0.21	0.023	0.006	0.034	4.34	4.09	0.56	0.12	0.71
	N	10	10	10	10	10	10	10	10	10	10	10
6%	Mean	3.80	2.96	0.67	0.044	0.004	0.091	77.87	17.91	1.17	0.11	2.32
diet	SD	1.43	1.14	0.31	0.022	0.004	0.051	5.87	5.72	0.37	0.06	0.67
	N	9	9	9	9	9	9	9	9	9	9	9
10%	Mean	4.04	3.16	0.72	0.054	0.006	0.082	77.87	18.17	1.31	0.15	2.02
diet	SD	0.80	0.72	0.14	0.022	0.005	0.030	4.53	4.70	0.40	0.11	0.53
	N	10	10	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)
[g2] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 9: Clinical chemistry

Day: 91 Relative to Start Date

Sex: Male		ALP (U/L) [g]	ASAT (U/L) [g]	ALAT (U/L) [g]	GGT (U/L) [g1]	Bilirub Total (umol/L) [g]	Creatinine (umol/L) [g]	Total Protein (g/L) [g]	Albumin (g/L) [g]	Albumin/ Globulin [g]	Glucose Plasma (mmol/L) [g]
0%	Mean	123.9	69.4	46.9	0.00	1.36	34.3	63.4	34.4	1.188	7.706
diet	SD	36.3	9.2	7.3	0.00	0.31	4.1	2.4	1.2	0.059	1.222
	N	10	10	10	10	10	10	10	10	10	10
3%	Mean	135.1	67.8	43.5	0.00	1.20	33.0	63.9	34.1	1.148	8.089
diet	SD	32.1	5.8	5.1	0.00	0.28	3.5	3.1	1.2	0.064	1.872
	N	10	10	10	10	10	10	10	10	10	10
6%	Mean	139.7	67.4	43.0	0.00	1.15	34.7	63.7	34.6	1.192	7.996
diet	SD	31.9	5.4	8.4	0.00	0.33	2.9	2.5	1.2	0.062	1.361
	N	10	10	10	10	10	10	10	10	10	10
10%	Mean	129.4	66.1	41.6	0.00	1.15	34.3	62.7	33.9	1.179	7.676
diet	SD	31.9	8.1	8.7	0.00	0.21	2.5	3.4	1.5	0.046	1.896
	N	10	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[g1] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 9: Clinical chemistry

Day: 91 Relative to Start Date

Sex: Male		Cholesterol (mmol/L) [g]	Phospholipids (mmol/L) [g]	Triglycerides (mmol/L) [g]	Urea (mmol/L) [g]	PO4 (mmol/L) [g]	Ca (mmol/L) [g]	Cl (mmol/L) [g1]	K (mmol/L) [g]	Na (mmol/L) [g1]
0%	Mean	1.838	1.648	1.156	6.16	2.581	2.764	100.1	5.82	148.5
diet	SD	0.276	0.180	0.315	0.81	0.433	0.062	0.6	0.42	1.1
	N	10	10	10	10	10	10	10	10	10
3%	Mean	1.764	1.649	1.096	6.79	2.625	2.769	99.8	5.84	147.9
diet	SD	0.385	0.213	0.469	0.60	0.415	0.090	1.0	0.45	1.4
	N	10	10	10	10	10	10	10	10	10
6%	Mean	1.759	1.619	1.140	7.03*	2.624	2.769	100.6	5.87	147.2
diet	SD	0.335	0.131	0.253	0.90	0.212	0.043	2.2	0.35	2.0
	N	10	10	10	10	10	10	10	10	10
10%	Mean	1.619	1.537	0.973	7.18**	2.711	2.757	100.3	5.81	147.9
diet	SD	0.240	0.137	0.341	0.40	0.486	0.084	1.9	0.48	1.5
	N	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett: * = p < 0.05; ** = p < 0.01
[g1] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 9: Clinical chemistry

Day: 92 Relative to Start Date

Sex: Female		ALP (U/L) [g]	ASAT (U/L) [g1]	ALAT (U/L) [g2]	GGT (U/L) [g2]	Bilirub Total (umol/L) [g]	Creatinine (umol/L) [g]	Total Protein (g/L) [g]	Albumin (g/L) [g]	Albumin/ Globulin [g]	Glucose Plasma (mmol/L) [g1]
0%	Mean	61.3	78.5	38.1	0.00	1.19	40.1	68.7	38.0	1.241	5.638
diet	SD	18.8	5.8	11.2	0.00	0.85	4.0	3.0	1.4	0.062	0.822
	N	10	10	10	10	10	10	10	10	10	10
3%	Mean	59.9	74.8	35.2	0.00	0.80	37.5	68.2	38.2	1.274	5.886
diet	SD	18.9	7.3	5.7	0.00	0.61	4.1	2.2	1.7	0.061	0.603
	N	10	10	10	10	10	10	10	10	10	10
6%	Mean	66.8	75.9	37.9	0.00	0.97	37.6	67.0	37.1	1.244	5.474
diet	SD	18.5	7.3	10.3	0.00	0.57	2.6	4.0	2.3	0.074	0.559
	N	9	9	9	9	9	9	9	9	9	9
10%	Mean	60.5	75.4	36.9	0.01	0.78	37.2	66.9	37.5	1.277	6.017
diet	SD	23.1	11.9	13.8	0.03	0.75	5.4	2.7	1.8	0.070	1.482
	N	10	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)
[g2] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 9: Clinical chemistry

Day: 92 Relative to Start Date

Sex: Female		Cholesterol (mmol/L) [g]	Phospholipids (mmol/L) [g]	Triglycerides (mmol/L) [g1]	Urea (mmol/L) [g]	PO4 (mmol/L) [g]	Ca (mmol/L) [g]	Cl (mmol/L) [g2]	K (mmol/L) [g1]	Na (mmol/L) [g]
0%	Mean	1.582	1.851	0.980	6.92	2.271	2.808	97.1	5.65	140.2
diet	SD	0.430	0.445	0.647	0.53	0.494	0.067	0.7	0.34	0.6
	N	10	10	10	10	10	10	10	10	10
3%	Mean	1.385	1.668	1.023	6.61	2.130	2.828	98.0	5.52	141.2
diet	SD	0.264	0.260	0.281	0.65	0.445	0.051	1.7	0.40	1.1
	N	10	10	10	10	10	10	10	10	10
6%	Mean	1.420	1.639	0.867	6.82	2.349	2.770	98.1	5.62	140.9
diet	SD	0.381	0.363	0.279	0.94	0.402	0.056	1.3	0.41	1.6
	N	9	9	9	9	9	9	9	9	9
10%	Mean	1.420	1.770	1.444	7.08	2.311	2.820	97.3	5.53	140.3
diet	SD	0.249	0.179	0.688	0.90	0.422	0.078	2.3	0.30	1.8
	N	10	10	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)
[g2] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 10: Urinalysis: volume and density

Day: 86 Relative to Start Date

Sex: Male		ConcUrin Volume (mL) [g]	Urinary Spec.Gravity (kg/L) [g1]
0% diet	Mean	2.80	1.0680
	SD	1.14	0.0169
	N	10	10
3% diet	Mean	2.25	1.0648
	SD	0.54	0.0104
	N	10	10
6% diet	Mean	3.35	1.0511
	SD	1.93	0.0168
	N	10	10
10% diet	Mean	2.80	1.0617
	SD	1.49	0.0199
	N	10	10

[g] - Kruskal-Wallis & Dunnett on Ranks
[g1] - Anova & Dunnett

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 10: Urinalysis: volume and density

Day: 88 Relative to Start Date

Sex: Female		ConcUrin Volume (mL) [g]	Urinary Spec.Gravity (kg/L) [g]
0%	Mean	1.75	1.0684
diet	SD	0.98	0.0227
	N	10	10
3%	Mean	1.60	1.0701
diet	SD	0.77	0.0209
	N	10	10
6%	Mean	1.63	1.0609
diet	SD	0.92	0.0143
	N	8	8
10%	Mean	2.90	1.0430*
diet	SD	1.41	0.0115
	N	10	10

[g] - Anova & Dunnett: * = p < 0.05

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 11: Urinalysis: semi-quantitative observations

Day: 86 Relative to Start Date

Sex: Male		pH (strip) [k]	Protein ((0-4)) [k]	Glucose ((0-4)) [k]	Ketones ((0-4)) [k]	Urobili (umol/L) [k]	Bilirubin ((0-3)) [k]	Occ bld ((0-3)) [k]
0%	Mean	7.05	2.1	0.2	1.3	3.20	0.7	0.1
diet	SD	0.64	0.3	0.4	0.5	0.00	0.5	0.3
	N	10	10	10	10	10	10	10
3%	Mean	6.65	2.0	0.0	1.0	3.20	0.9	0.1
diet	SD	0.53	0.0	0.0	0.7	0.00	0.3	0.3
	N	10	10	10	10	10	10	10
6%	Mean	7.75	2.0	0.0	1.2	3.20	0.5	0.2
diet	SD	0.79	0.5	0.0	0.4	0.00	0.5	0.4
	N	10	10	10	10	10	10	10
10%	Mean	7.25	2.1	0.2	1.5	3.20	0.7	0.1
diet	SD	0.79	0.3	0.4	0.5	0.00	0.5	0.3
	N	10	10	10	10	10	10	10

[k] - Kruskal-Wallis & Dunnett

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 11: Urinalysis: semi-quantitative observations

Day: 88 Relative to Start Date

Sex: Female		pH (strip) [k]	Protein ((0-4)) [k]	Glucose ((0-4)) [k]	Ketones ((0-4)) [k]	Urobili (umol/L) [k]	Bilirubin ((0-3)) [k]	Occ bld ((0-3)) [k]
0%	Mean	6.30	2.0	0.0	0.4	3.20	0.7	0.0
diet	SD	0.42	0.7	0.0	0.5	0.00	0.5	0.0
	N	10	10	10	10	10	10	10
3%	Mean	5.95	1.8	0.1	0.3	3.20	0.7	0.0
diet	SD	0.37	0.8	0.3	0.5	0.00	0.7	0.0
	N	10	10	10	10	10	10	10
6%	Mean	6.31	1.6	0.0	0.5	3.20	0.6	0.0
diet	SD	0.92	0.5	0.0	0.5	0.00	0.5	0.0
	N	8	8	8	8	8	8	8
10%	Mean	6.85	1.3	0.0	0.4	3.20	0.2	0.2
diet	SD	1.03	0.5	0.0	0.5	0.00	0.4	0.4
	N	10	10	10	10	10	10	10

[k] - Kruskal-Wallis & Dunnett

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 12: Urinalysis: microscopic observations

Day: 86 Relative to Start Date

Sex: Male		Red Bld Cells ((0-5)) [k]	WhiteBld Cells ((0-5)) [k]	Epithel Cells ((0-5)) [k]	Amorph Material ((0-5)) [k]	Crystals ((0-5)) [k]	Casts ((0-5)) [k]	Bacteria ((0-5)) [k]	Worm Eggs ((0-1)) [k]	Sperms ((0-1)) [k]
0%	Mean	0.1	0.0	1.8	1.8	2.7	0.0	3.4	0.0	1.0
diet	SD	0.4	0.0	1.2	1.4	2.1	0.0	0.5	0.0	0.0
	N	8	8	8	8	10	8	8	8	8
3%	Mean	0.6	0.6	1.1	1.4	3.4	0.0	2.7	0.0	1.0
diet	SD	0.7	1.0	0.6	1.1	1.6	0.0	0.5	0.0	0.0
	N	9	9	9	9	10	9	9	9	9
6%	Mean	0.8	0.6	1.9	1.8	3.1	0.0	4.1	0.0	1.0
diet	SD	0.7	0.9	1.1	1.2	1.7	0.0	0.8	0.0	0.0
	N	9	9	9	9	10	9	9	9	9
10%	Mean	0.4	0.2	1.3	1.7	2.8	0.0	3.9	0.0	0.9
diet	SD	0.5	0.4	0.9	1.2	1.8	0.0	1.1	0.0	0.3
	N	9	9	9	9	10	9	9	9	9

[k] - Kruskal-Wallis & Dunnett

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 12: Urinalysis: microscopic observations

Day: 88 Relative to Start Date

Sex: Female		Red Bld Cells ((0-5)) [k]	WhiteBld Cells ((0-5)) [k]	Epithel Cells ((0-5)) [k]	Amorph Material ((0-5)) [k]	Crystals ((0-5)) [k]	Casts ((0-5)) [k]	Bacteria ((0-5)) [k]	Worm Eggs ((0-1)) [k]
0%	Mean	0.5	0.0	1.9	1.2	1.2	0.1	2.5	0.0
diet	SD	0.7	0.0	0.7	0.6	1.4	0.3	0.5	0.0
	N	10	10	10	10	10	10	10	10
3%	Mean	0.7	0.1	1.6	1.1	1.1	0.0	2.9	0.0
diet	SD	0.8	0.3	1.0	0.9	1.3	0.0	0.7	0.0
	N	10	10	10	10	10	10	10	10
6%	Mean	0.5	0.0	2.1	1.5	1.3	0.1	2.8	0.0
diet	SD	0.5	0.0	0.8	0.8	1.9	0.4	0.7	0.0
	N	8	8	8	8	8	8	8	8
10%	Mean	1.1	0.0	2.0	1.1	0.8	0.0	2.6	0.0
diet	SD	0.9	0.0	1.1	0.6	0.8	0.0	1.0	0.0
	N	9	9	9	9	9	9	9	9

[k] - Kruskal-Wallis & Dunnett

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 13: Absolute organ weights

Day(s): 91 Relative to Start Date

Sex: Male		Terminal body wgt (g) [g]	Brain (g) [g]	Heart (g) [g1]	Adrenals (g) [g]	Kidneys (g) [g]	Liver (g) [g]	Spleen (g) [g]
0%	Mean	345.25	2.072	0.947	0.0552	1.933	7.965	0.5575
diet	SD	38.51	0.113	0.099	0.0098	0.197	1.112	0.0840
	N	10	10	10	10	10	10	10
3%	Mean	351.60	2.065	0.974	0.0529	2.025	8.384	0.6082
diet	SD	36.27	0.091	0.136	0.0114	0.249	0.936	0.0509
	N	10	10	10	10	10	10	10
6%	Mean	351.76	2.068	1.011	0.0549	1.952	8.360	0.6007
diet	SD	39.74	0.095	0.129	0.0088	0.211	1.249	0.0774
	N	10	10	10	10	10	10	10
10%	Mean	331.16	2.023	0.939	0.0524	1.932	8.254	0.5876
diet	SD	42.87	0.084	0.125	0.0103	0.228	1.149	0.0833
	N	10	10	10	10	10	10	10

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 13: Absolute organ weights

Day(s): 91 Relative to Start Date

Sex: Male		Caecum full (g) [g]	Caecum empty (g) [g]	Thymus (g) [g1]	Testes (g) [g1]	Epididymides (g) [g1]	Prostate (g) [g1]	Seminal vesicles (g) [g1]
0%	Mean	4.0987	1.0207	0.3322	3.478	1.123	0.911	1.012
diet	SD	0.7466	0.1800	0.0514	0.223	0.101	0.136	0.151
	N	10	10	10	10	10	10	10
3%	Mean	5.2282*	1.2139	0.3544	3.439	1.154	0.906	1.008
diet	SD	0.9177	0.1781	0.0796	0.257	0.072	0.151	0.166
	N	10	10	10	10	10	10	10
6%	Mean	6.8007**	1.4565**	0.3694	3.504	1.159	0.923	1.000
diet	SD	1.6408	0.3894	0.0906	0.306	0.083	0.111	0.111
	N	10	10	10	10	10	10	10
10%	Mean	7.8187**	1.5951**	0.3218	3.394	1.125	0.896	0.995
diet	SD	1.1468	0.2303	0.0978	0.337	0.122	0.166	0.175
	N	10	10	10	10	10	10	10

[g] - Anova & Dunnett(Log): * = $p < 0.05$; ** = $p < 0.01$
[g1] - Anova & Dunnett

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 13: Absolute organ weights

Day(s): 92 Relative to Start Date

Sex: Female		Terminal body wgt (g) [g]	Brain (g) [g1]	Heart (g) [g1]	Adrenals (g) [g]	Kidneys (g) [g1]	Liver (g) [g1]	Spleen (g) [g2]
0%	Mean	206.80	1.934	0.667	0.0710	1.315	5.254	0.3925
diet	SD	14.21	0.067	0.055	0.0134	0.110	0.488	0.0503
	N	10	10	10	10	10	10	10
3%	Mean	208.66	1.926	0.668	0.0697	1.322	5.028	0.4029
diet	SD	16.68	0.073	0.093	0.0145	0.131	0.448	0.0497
	N	10	10	10	10	10	10	10
6%	Mean	202.67	1.880	0.674	0.0683	1.298	5.336	0.4026
diet	SD	6.71	0.041	0.041	0.0070	0.067	0.536	0.0694
	N	9	9	9	9	9	9	9
10%	Mean	200.64	1.903	0.631	0.0637	1.290	5.233	0.4362
diet	SD	11.83	0.055	0.046	0.0057	0.080	0.378	0.0302
	N	10	10	10	10	10	10	10

[g] - Kruskal-Wallis & Dunnett on Ranks
[g1] - Anova & Dunnett
[g2] - Anova & Dunnett(Log)

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 13: Absolute organ weights

Day(s): 92 Relative to Start Date

Sex: Female		Caecum full (g) [g]	Caecum empty (g) [g]	Thymus (g) [g]	Ovaries (g) [g]	Uterus (g) [g1]
0%	Mean	2.7851	0.7174	0.2776	0.0939	0.8214
diet	SD	0.6912	0.1018	0.0477	0.0130	0.5800
	N	10	10	10	10	10
3%	Mean	3.2094	0.8223	0.2929	0.0885	0.6552
diet	SD	0.5869	0.1247	0.0438	0.0130	0.3163
	N	10	10	10	10	10
6%	Mean	3.7067**	0.9552**	0.3034	0.0977	0.6536
diet	SD	0.5819	0.1677	0.0764	0.0179	0.4208
	N	9	9	9	9	9
10%	Mean	5.0184**	1.2088**	0.2939	0.0912	0.7189
diet	SD	0.3805	0.1935	0.0403	0.0143	0.3751
	N	10	10	10	10	10

[g] - Anova & Dunnett: ** = p < 0.01
[g1] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 14: Relative organ weights

Day(s): 91 Relative to Start Date

Sex: Male		Terminal body wgt (g) [g]	Brain rel.wgt (g/kg body wgt) [g]	Heart rel.wgt (g/kg body wgt) [g]	Adrenals rel.wgt (g/kg body wgt) [g]	Kidneys rel.wgt (g/kg body wgt) [g]	Liver rel.wgt (g/kg body wgt) [g]	Spleen rel.wgt (g/kg body wgt) [g]
0%	Mean	345.25	6.046	2.749	0.1603	5.609	23.03	1.617
diet	SD	38.51	0.512	0.159	0.0257	0.282	1.23	0.184
	N	10	10	10	10	10	10	10
3%	Mean	351.60	5.917	2.765	0.1502	5.765	23.85	1.741
diet	SD	36.27	0.520	0.195	0.0273	0.477	1.16	0.173
	N	10	10	10	10	10	10	10
6%	Mean	351.76	5.926	2.878	0.1568	5.558	23.73	1.720
diet	SD	39.74	0.490	0.217	0.0226	0.280	1.81	0.239
	N	10	10	10	10	10	10	10
10%	Mean	331.16	6.175	2.838	0.1587	5.863	24.93*	1.778
diet	SD	42.87	0.577	0.157	0.0270	0.533	1.50	0.162
	N	10	10	10	10	10	10	10

[g] - Anova & Dunnett: * = p < 0.05

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 14: Relative organ weights

Day(s): 91 Relative to Start Date

Sex: Male		Caecum-F rel.wgt (g/kg body wgt) [g]	Caecum-E rel.wgt (g/kg body wgt) [g]	Thymus rel.wgt (g/kg body wgt) [g1]	Testes rel.wgt (g/kg body wgt) [g]	Epididy rel.wgt (g/kg body wgt) [g]	Prostate rel.wgt (g/kg body wgt) [g]	Sem ves rel.wgt (g/kg body wgt) [g]
0%	Mean	11.91	2.98	0.965	10.155	3.272	2.645	2.967
diet	SD	2.11	0.56	0.142	0.963	0.323	0.343	0.550
	N	10	10	10	10	10	10	10
3%	Mean	14.93	3.47	1.006	9.837	3.304	2.583	2.863
diet	SD	2.69	0.54	0.194	0.845	0.287	0.374	0.339
	N	10	10	10	10	10	10	10
6%	Mean	19.20**	4.13**	1.046	10.015	3.315	2.634	2.880
diet	SD	3.52	0.98	0.215	0.799	0.244	0.264	0.473
	N	10	10	10	10	10	10	10
10%	Mean	23.71**	4.85**	0.964	10.297	3.412	2.720	3.056
diet	SD	2.58	0.70	0.241	0.617	0.229	0.465	0.710
	N	10	10	10	10	10	10	10

[g] - Anova & Dunnett: ** = p < 0.01
[g1] - Kruskal-Wallis & Dunnett on Ranks

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 14: Relative organ weights

Day(s): 92 Relative to Start Date

Sex: Female		Terminal body wgt (g) [g]	Brain rel.wgt (g/kg body wgt) [g1]	Heart rel.wgt (g/kg body wgt) [g1]	Adrenals rel.wgt (g/kg body wgt) [g2]	Kidneys rel.wgt (g/kg body wgt) [g1]	Liver rel.wgt (g/kg body wgt) [g]	Spleen rel.wgt (g/kg body wgt) [g]
0%	Mean	206.80	9.376	3.230	0.3427	6.367	25.40	1.899
diet	SD	14.21	0.436	0.234	0.0539	0.463	1.54	0.218
	N	10	10	10	10	10	10	10
3%	Mean	208.66	9.264	3.196	0.3331	6.333	24.11	1.937
diet	SD	16.68	0.525	0.292	0.0580	0.306	1.22	0.255
	N	10	10	10	10	10	10	10
6%	Mean	202.67	9.283	3.330	0.3375	6.409	26.38	1.994
diet	SD	6.71	0.303	0.212	0.0359	0.370	3.22	0.388
	N	9	9	9	9	9	9	9
10%	Mean	200.64	9.515	3.147	0.3178	6.433	26.12	2.185
diet	SD	11.83	0.629	0.184	0.0260	0.251	1.76	0.246
	N	10	10	10	10	10	10	10

[g] - Kruskal-Wallis & Dunnett on Ranks
[g1] - Anova & Dunnett
[g2] - Anova & Dunnett(Log)

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 14: Relative organ weights

Day(s): 92 Relative to Start Date

Sex: Female		Caecum-F rel.wgt (g/kg body wgt) [g]	Caecum-E rel.wgt (g/kg body wgt) [g1]	Thymus rel.wgt (g/kg body wgt) [g]	Ovaries rel.wgt (g/kg body wgt) [g]	Uterus rel.wgt (g/kg body wgt) [g2]
0%	Mean	13.56	3.46	1.343	0.4558	3.948
diet	SD	3.64	0.34	0.210	0.0677	2.765
	N	10	10	10	10	10
3%	Mean	15.38	3.94	1.414	0.4265	3.142
diet	SD	2.56	0.54	0.259	0.0745	1.519
	N	10	10	10	10	10
6%	Mean	18.26**	4.71**	1.499	0.4817	3.264
diet	SD	2.66	0.81	0.378	0.0849	2.237
	N	9	9	9	9	9
10%	Mean	25.07**	6.02**	1.469	0.4547	3.587
diet	SD	2.13	0.89	0.213	0.0680	1.863
	N	10	10	10	10	10

[g] - Anova & Dunnett: ** = p < 0.01
[g1] - Anova & Dunnett(Log): ** = p < 0.01
[g2] - Kruskal-Wallis & Dunnett on Ranks

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 15: Macroscopic observations

Removal Reason(s): ALL	Male				Female			
	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Number of Animals:	10	10	10	10	10	10	10	10
all organs / tissues								
no visible lesions	6	9	7	8	7	5	8	5
diaphragm								
hernia diaphragmatica	-	-	1	-	-	-	-	-
liver								
medial lobe; nodule	-	-	-	-	-	-	-	1
skin / subcutis								
sparsely haired	-	-	-	-	-	2	-	2
stomach								
deposition; yellow	-	-	2	-	-	-	-	-
thymus								
discoloration; red	0	0	-	1	0	-	-	-
spots; red	1	1	-	0	1	-	-	-
spots; red, unilateral	1	0	-	0	0	-	-	-
uterus								
swollen	-	-	-	-	3	3	2	4

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 16: Microscopic observations

Removal Reason(s): ALL	Male				Female			
	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Number of Animals:	10	10	10	10	10	10	10	10
adrenal glands								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
aorta								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
bone marrow, sternum								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
brain								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
coagulating glands								
Examined	10	0	0	10	-	-	-	-
No Visible Lesions	10	-	-	10	-	-	-	-
epididymides								
Examined	10	0	0	10	-	-	-	-
No Visible Lesions	9	-	-	10	-	-	-	-
inflammation; mononuclear, focal	1	-	-	0	-	-	-	-
.... minimal	1	-	-	0	-	-	-	-
esophagus								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
eyes								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	0	10
dystrophy; lenticular	0	-	-	0	0	-	1	0
.... moderate	0	-	-	0	0	-	1	0
heart								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	9	-	-	9	10	-	1	10
inflammation; mononuclear, focal	1	-	-	1	0	-	0	0
.... minimal	1	-	-	1	0	-	0	0
intestine, duodenum								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
intestine, jejunum								
Examined	10	0	0	10	10	0	1	10

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 16: Microscopic observations

Removal Reason(s): ALL	Male				Female			
	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Number of Animals:	10	10	10	10	10	10	10	10
intestine, jejunum (Continued...)								
No Visible Lesions	10	-	-	10	10	-	1	10
intestine, ileum								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
intestine, cecum								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
intestine, colon								
Examined	10	0	0	10	9	0	1	10
No Visible Lesions	10	-	-	10	9	-	1	10
intestine, rectum								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
kidneys								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	8	-	-	8	10	-	0	9
inflammation; mononuclear, (multi)focal	1	-	-	2	0	-	0	0
.... minimal	1	-	-	2	0	-	0	0
mineralization; medullary	0	-	-	0	0	-	1	1
.... minimal	0	-	-	0	0	-	1	1
basophilic tubules	1	-	-	0	0	-	0	1
.... minimal	1	-	-	0	0	-	0	1
liver								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	5	-	-	9	7	-	0	9
inflammation; mononuclear, (multi)focal	4	-	-	1	3	-	0	0
.... minimal	4	-	-	1	3	-	0	0
inflammation; mixed, multifocal	0	-	-	0	0	-	1	0
.... minimal	0	-	-	0	0	-	1	0
vasculitis; chronic, single	1	-	-	0	0	-	0	0
.... mild	1	-	-	0	0	-	0	0
gross finding not confirmed	0	-	-	0	0	-	0	1
lungs								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	8	-	-	7	9	-	1	10
inflammation; mononuclear, focal	2	-	-	2	1	-	0	0

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 16: Microscopic observations

Removal Reason(s): ALL	Male				Female			
	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Number of Animals:	10	10	10	10	10	10	10	10
lungs (Continued...)								
.... minimal	2	-	-	2	1	-	0	0
inflammation; mixed, focal	0	-	-	1	0	-	0	0
.... minimal	0	-	-	1	0	-	0	0
lymph node, axillary								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	9	-	-	10	10	-	1	10
cyst(s)	1	-	-	0	0	-	0	0
lymph node, mesenteric								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
mammary glands								
Examined	-	-	-	-	10	0	0	10
No Visible Lesions	-	-	-	-	10	-	-	10
nerve, peripheral								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
ovaries								
Examined	-	-	-	-	10	0	1	10
No Visible Lesions	-	-	-	-	9	-	1	9
mineralization; focal	-	-	-	-	1	-	0	1
.... minimal	-	-	-	-	1	-	0	1
oviducts								
Examined	-	-	-	-	10	0	1	10
No Visible Lesions	-	-	-	-	10	-	1	10
pancreas								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	9	-	-	9	10	-	1	9
inflammation; mononuclear, focal	1	-	-	0	0	-	0	1
.... minimal	1	-	-	0	0	-	0	1
degeneration; focal	0	-	-	1	0	-	0	0
.... minimal	0	-	-	1	0	-	0	0
parathyroid glands								
Examined	10	0	0	9	10	0	1	9
No Visible Lesions	10	-	-	9	10	-	1	9
patches of peyer								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	8	-	-	9	10	-	1	10

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 16: Microscopic observations

Removal Reason(s): ALL	Male				Female			
	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Number of Animals:	10	10	10	10	10	10	10	10
patches of peyer (Continued...)								
lymphangiectasis; focal	2	-	-	1	0	-	0	0
.... minimal	2	-	-	1	0	-	0	0
pituitary gland								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	8	10	-	1	10
cyst(s)	0	-	-	1	0	-	0	0
remnant(s) rathkes pouch	0	-	-	1	0	-	0	0
prostate gland								
Examined	10	0	0	10	-	-	-	-
No Visible Lesions	9	-	-	8	-	-	-	-
inflammation; mononuclear, focal	1	-	-	2	-	-	-	-
.... minimal	1	-	-	2	-	-	-	-
salivary gland(s), parotis								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	9	-	1	9
inflammation; mixed, focal	0	-	-	0	1	-	0	0
.... minimal	0	-	-	0	1	-	0	0
degeneration; multifocal	0	-	-	0	0	-	0	1
.... mild	0	-	-	0	0	-	0	1
salivary gland(s) sublingual								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
salivary gland(s), submaxillary/mandibular								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
seminal vesicles								
Examined	10	0	0	10	-	-	-	-
No Visible Lesions	10	-	-	10	-	-	-	-
skeletal muscle								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
skin/subcutis								
Examined	10	0	0	10	10	2	1	10
No Visible Lesions	10	-	-	10	10	0	1	8
acanthosis; focal	0	-	-	0	0	2	0	0
.... mild	0	-	-	0	0	2	0	0
encrustation; focal	0	-	-	0	0	1	0	1

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 16: Microscopic observations

Removal Reason(s): ALL	Male				Female			
	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Number of Animals:	10	10	10	10	10	10	10	10
skin/subcutis (Continued...)								
.... minimal	0	-	-	0	0	1	0	1
gross finding not confirmed	0	-	-	0	0	0	0	2
spinal cord								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
spleen								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	9	-	-	9	10	-	1	9
erythropoiesis; extramedullary	1	-	-	1	0	-	0	0
.... minimal	1	-	-	0	0	-	0	0
.... mild	0	-	-	1	0	-	0	0
haematopoiesis; extramedullary	0	-	-	0	0	-	0	1
.... minimal	0	-	-	0	0	-	0	1
stomach								
Examined	10	0	2	10	10	0	1	10
No Visible Lesions	8	-	0	10	9	-	1	9
inflammation; mononuclear, focal	2	-	1	0	1	-	0	1
.... minimal	2	-	1	0	1	-	0	0
.... mild	0	-	0	0	0	-	0	1
gross finding not confirmed	0	-	2	0	0	-	0	0
testes								
Examined	10	0	0	10	-	-	-	-
No Visible Lesions	10	-	-	10	-	-	-	-
thymus								
Examined	10	1	0	10	10	0	1	10
No Visible Lesions	3	0	-	3	5	-	0	9
microhaemorrhage(s)	7	1	-	7	5	-	1	1
starry sky appearance	1	0	-	1	0	-	0	0
thyroid gland								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	9
ectopic thymus	0	-	-	0	0	-	0	1
trachea/bronchi								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	8	-	-	8	8	-	0	9
inflammation; mononuclear, focal	2	-	-	2	2	-	1	1
.... minimal	2	-	-	1	2	-	0	1

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Table 16: Microscopic observations

Removal Reason(s): ALL	Male				Female			
	0% diet	3% diet	6% diet	10% diet	0% diet	3% diet	6% diet	10% diet
Number of Animals:	10	10	10	10	10	10	10	10
trachea/bronchi (Continued...)								
.... mild	0	-	-	1	0	-	1	0
urinary bladder								
Examined	10	0	0	10	10	0	1	10
No Visible Lesions	10	-	-	10	10	-	1	10
uterus								
Examined	-	-	-	-	10	3	3	10
No Visible Lesions	-	-	-	-	7	0	1	6
lumen; dilatation	-	-	-	-	3	3	2	4
.... mild	-	-	-	-	3	3	2	4
inflammation; mixed, focal	-	-	-	-	0	0	0	1
.... mild	-	-	-	-	0	0	0	1
vagina								
Examined	-	-	-	-	10	0	1	10
No Visible Lesions	-	-	-	-	10	-	1	10

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Annexes

Annex 1: GLP Endorsement

ENDORSEMENT OF COMPLIANCE

WITH THE OECD PRINCIPLES OF GOOD LABORATORY PRACTICE

Pursuant to the Netherlands GLP Compliance Monitoring Programme and according to Directive 2004/9/EC the conformity with the OECD Principles of GLP was assessed on 29 September-6 October and 9 December 2015 at

TNO Triskelion BV
Utrechtseweg 48, 3704 HE Zeist
PO Box 844, 3700 AV Zeist

It is herewith confirmed that the afore-mentioned test facility is currently operating in compliance with the OECD Principles of Good Laboratory Practice in the following areas of expertise: Toxicity, mutagenicity, analytical and clinical chemistry, safety pharmacology, kinetics, metabolism and in-vitro studies.

Utrecht, 14 December 2015

(b) (6)

Dr R.M.A. Jaspers
Coordinating/specialist senior inspector

Health Care Inspectorate of the Ministry of Health, Welfare and Sport
Stadsplateau 1, 3521 AZ Utrecht
P.O. Box 2680, 3500 GR Utrecht, The Netherlands

Annex 2: Certificate of analysis of the test substance

[redacted]

Product	: **Vivinal FL**
Product code	: NA (developmental product)
Batchnumber	: MRS02
Date of production	: 02-07-2016
Contact person	: Jan-Willem Boots (R&D)

Description : Human milk oligosaccharide

Typical analysis : Dry matter 97%, moisture 3%, 2'-Fucosyllactose 94%, lactose 1%, glucose 1%, fucose 1%

Chemical/ physical:	**Specification**	**Results**	**Method of analysis**
Total moisture	max. 5%	3%	ISO 760 (modified), Karl Fischer
2'-Fucosyllactose	min. 90%	>94%	FC-method using HPAEC-PAD
3-Fucosyllactose	max. 3%	<1%	FC-method using HPAEC-PAD
Difucosyllactose	max. 3%	<1%	FC-method using HPAEC-PAD
Fucose	max. 2%	<1%	FC-method using HPAEC-PAD
Lactose	max. 2%	<1%	FC-method using HPAEC-PAD
Glucose	max. 2%	<1%	FC-method using HPAEC-PAD
Protein	max. 0.01%	0.002%	Bradford
Sulphated ash	max. 0.2%	0.06%	NEN 6810 (modified)
Nitrite	max. 1 mg/kg	<0.1	ISO 14673-2/IDF 189-2
Nitrate	max. 50 mg/kg	0.2	ISO 14673-2/IDF 189-2
pH (10%)	3.0 - 7.5	3.9	FC-method using NEN 3775

Microbiological:

Aerobic mesophilic count	max. 3000 cfu/g	<1000	FC-method equivalent to ISO 4833
Enterobacteriaceae	absent in 1 g	<1	FC-method, BPW 18h 37°C, SD, VRBG 18-24h 37°C
E. coli	absent in 1 g	<1	FC-method, LMX 25h, Coli ID 24h
Yeasts	max. 30 cfu/g	<1	FC-method equivalent to ISO 6611
Moulds	max. 30 cfu/g	<1	FC-method equivalent to ISO 6611
Presumptive Bacillus cereus	max. 100 cfu/g	<1	FC-method equivalent to ISO 7932
Staphylococcus aureus	absent in 1 g	<1	FC-method, G&C 42h 37°C, PCR
Sulphite reducing clostridia spores	max. 30 cfu/g	<1	FC-method using IJFM 27 (1995) 195-200 Weenk
Clostridium perfringens	absent in 1 g	neg	FC-method, RPM 20h 46°C, confirmation
Salmonella	absent in 1 g	neg	FC-method equivalent to ISO 6579
Cronobacter spp.	absent in 1 g	neg	FC-method equivalent to ISO/TS 22964

Wageningen, 15-07-2016

(b) (6)

PSB-nr: [redacted]

02 AUG. 2016

Dispense nr.: 160161

Jan-Willem Boots

i/o Dianne Delsing

(b) (6)

[redacted]

Annex 3: Cross reference list

20880/02

Sub-chronic (13-week) oral toxicity study with **2'**-Fucosyllactose in rats

Animal Number	Group	Cage	Sex	Animal Number	Group	Cage	Sex
2	Low dose	2	M	1	High dose	1	F
4	Low dose	2	M	3	High dose	1	F
6	Low dose	2	M	5	High dose	1	F
8	Low dose	2	M	7	High dose	1	F
10	Low dose	2	M	9	High dose	1	F
12	Mid dose	4	M	11	Control	3	F
14	Mid dose	4	M	13	Control	3	F
16	Mid dose	4	M	15	Control	3	F
18	Mid dose	4	M	17	Control	3	F
20	Mid dose	4	M	19	Control	3	F
22	High dose	6	M	21	Low dose	5	F
24	High dose	6	M	23	Low dose	5	F
26	High dose	6	M	25	Low dose	5	F
28	High dose	6	M	27	Low dose	5	F
30	High dose	6	M	29	Low dose	5	F
32	Control	8	M	31	Mid dose	7	F
34	Control	8	M	33	Mid dose	7	F
36	Control	8	M	35	Mid dose	7	F
38	Control	8	M	37	Mid dose	7	F
40	Control	8	M	39	Mid dose	7	F
42	Mid dose	10	M	41	Control	9	F
44	Mid dose	10	M	43	Control	9	F
46	Mid dose	10	M	45	Control	9	F
48	Mid dose	10	M	47	Control	9	F
50	Mid dose	10	M	49	Control	9	F
52	High dose	12	M	51	Low dose	11	F
54	High dose	12	M	53	Low dose	11	F
56	High dose	12	M	55	Low dose	11	F
58	High dose	12	M	57	Low dose	11	F
60	High dose	12	M	59	Low dose	11	F
62	Control	14	M	61	Mid dose	13	F
64	Control	14	M	63	Mid dose	13	F
66	Control	14	M	65	Mid dose	13	F
68	Control	14	M	67	Mid dose	13	F
70	Control	14	M	69	Mid dose	13	F
72	Low dose	16	M	71	High dose	15	F
74	Low dose	16	M	73	High dose	15	F
76	Low dose	16	M	75	High dose	15	F
78	Low dose	16	M	77	High dose	15	F
80	Low dose	16	M	79	High dose	15	F

Annex 4 Health certificate

charles river | every step of the way.

Location : Sulzfeld
Telephone : 09761/406-20
Fax : 09761/406-79
Contact person : Madlen Bauer

DQS-zertifiziert nach DIN ISO 9001:2008 Reg.-Nr. 29 10 25 QM

Delivery Account Number 15012 Tel. : 0031888662800

DELIVERY NOTE No. EEW31994 Date 1/11/2016

Invoice Account Number : 15012

Charles River Laboratories, Research Models and Services, Germany GmbH
Sandhofer Weg 7, D-97633 Sulzfeld

TNO TRISKELION BV

UTRECHTSEWEG 48
NL-3704HE ZEIST
NIEDERLANDE

TNO TRISKELION BV
TAV CREDITEURENADMINISTRATIE

POSTBUS 844
NL-3700AJ ZEIST
NIEDERLANDE

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CARRIER : NIEDERLANDE PAGE : 1

PRODUCT CODE	DESCRIPTION	ORDER QUANTITY	DELIVERED QUANTITY
YOUR REFERENCE : 56000045	ORDER DATE : 24/08/2016	REFERENCE CRG :	EWA025299
WIHSIFA	WL.WIST.HAN RATTE ZEITL.VERPAART Crl:WI(Han) verp 18/19.10.16 10-12 w.o. From area : 9	16	16
04F	Filter Karton	4	4

No. of packages : 4 Weight : 7,60 Volume : 0,180

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The goods remain our property until complete payment is done.

Annex 4 Health certificate

charles river

HEALTH REPORT

Printed on : 1/11/2016
Page : 1

TNO TRISKELION BV | 16 | WISTAR HAN | DN N° : EEW31994

Unit N° : 9 | Specie : RAT | Health Status : SPF / VAF

Summary item	Primary Assay	Primary Lab	Most Recent Year Week*	Most Recent Positive / Tested	Past 18 Months Positive / Tested
Viruses					
RPV	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
EMV	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
H1	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
KRV	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
SDAV	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
TMEV (GDVII)	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
REO	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
SEND	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
PVM	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
MAV	a e MFIA	RADS EU	2016-35	0 / 8	0 / 120
LCMV	a d MFIA	RADS EU	2016-35	0 / 8	0 / 96
HANT	a g MFIA	RADS EU	2016-35	0 / 8	0 / 96
Mycoplasma					
M. pulmonis	a e MFIA	RADS EU	2016-43	0 / 16	0 / 344
Bacteria					
Tyzzer's Disease	a e Exam	RADS EU	2016-35	0 / 12	0 / 72
B. bronchiseptica	b e Culture	RADS EU	2016-35	0 / 8	0 / 72
C. kutscheri	a e Culture	RADS EU	2016-35	0 / 8	0 / 72
P. pneumotropica	b e Culture	RADS EU	2016-35	0 / 8	0 / 72
E. coli O.C.	a e Culture	RADS EU	2016-35	0 / 8	0 / 48
Salmonella spp.	a e Culture	RADS EU	2016-35	0 / 8	0 / 72
S. moniliformis	a c PCR	RADS EU	2016-35	0 / 12	0 / 96
Beta Strep. sp., Grp A	c e Culture	RADS EU	2016-35	0 / 8	0 / 72
Beta Strep. sp. - Grp G	c e Culture	RADS EU	2016-35	0 / 8	0 / 72
Strep. pneumoniae	b e Culture	RADS EU	2016-35	0 / 8	0 / 72
H. hepaticus	a e PCR	RADS EU	2016-35	0 / 6	0 / 56
H. bilis	b e PCR	RADS EU	2016-35	0 / 6	0 / 56
Helicobacter sp.	b e PCR	RADS EU	2016-35	0 / 8	0 / 56
CAR Bacillus	a e MFIA	RADS EU	2016-35	0 / 8	0 / 120
Pneumocystis spp.	a d MFIA	RADS EU	2016-43	0 / 16	0 / 344
Parasites					
E. cuniculi	a e MFIA	RADS EU	2016-35	0 / 8	0 / 96
Ectoparasites	a e Exam	RADS EU	2016-35	0 / 8	0 / 72
Helminths	a e Exam	RADS EU	2016-35	0 / 8	0 / 72
Pinworms, Protozoa	a e Exam	RADS EU	2016-35	0 / 8	0 / 72
Lesions observed					
Gross Exam	b g Exam	RADS EU	2016-35	0 / 12	0 / 72

Legend :

Legend:
RADS EU = Research Animal Diagnostic Services Europe Lyon, France
RADS US = Research Animal Diagnostic Services United States Wilmington Massachusetts

COLONY POLICY FOR POSITIVE RESULT: a = immediate termination b = planned future recycle of the colony; c = no action

TESTING SCHEDULE: d = screened every four or five weeks; e = screened every 12 or 13 weeks;

Annex 4 Health certificate

charles river

HEALTH REPORT

Printed on : 1/11/2016
Page : 2

TNO TRISKELION BV | 16 | WISTAR HAN | DN N° : EEW31994

Unit N° : 9 Specie : Health Status :

Summary Item	Primary Assay	Primary Lab	Most Recent Year Week*	Most Recent Positive / Tested	Past 18 Months Positive / Tested

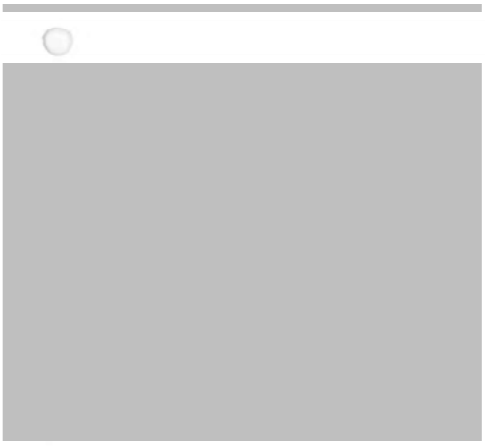
f = screened annually; g = screened quarterly by necropsy examination.

*Sampling date/ Result validation could take until 3 weeks.

Laurence Bonnet Masson , DVM
Health monitoring programme design
laurence.bonnetmasson@wxi.com

(b) (6)

K.Martelet
Operational Manager
Sanitary Control Laboratory



Annex 5: Analysis of the diet

Quality Control Certificate of Analysis

Product:	**VRF1 (P) VRF1 (FG)**
Premix Batch Numbers:	**18482**

Batch Number:	**2619**
Date of Manufacture:	**26.09.2016**
Expiry Date	**25.06.2017**

NUTRIENTS	Unit	Result	Tolerance Limits Min	Tolerance Limits Max	Analysis Error (actual) or (%)	Limit of Quantification
Moisture	%	10.3	9.0	11.5	2.0	0.1 g/100g
Crude Fat (A)	%	4.5	3.8	6.2	16.4	0.1 g/100g
Crude Protein	%	19.8	17.4	20.4	1.9	0.1 g/100g
Crude Fibre	%	4.0	2.8	5.2	14.0	0.1 g/100g
Ash	%	5.8	4.5	7.0	2.7	0.1 g/100g
NFE (by difference)	%	55.6	48.0	60.0	n/a	n/a
Calcium	mg/kg	9950	8000	12000	6.5	5 mg/kg
Phosphorus	mg/kg	6390	4000	8300	7.5	2 mg/kg
Sodium	mg/kg	2710	2500	3500	8	10 mg/kg
Potassium	mg/kg	9160	5700	9700	6.9	50 mg/kg
Copper	mg/kg	18	13	25	18	0.6 mg/kg
Manganese	mg/kg	112	85	185	2.1	0.6 mg/kg
Vitamin A	iu/kg	22000	20000	55000	15	700 iu/kg
Vitamin E	mg/kg	103	80	150	10	1 mg/kg

CONTAMINANTS

Nitrogen Derivative Quality	Unit	Result	Tolerance Limits Min	Tolerance Limits Max	Analysis Error (actual) or (%)	Limit of Detection
Nitrate	mg/kg	57	sum of NO_3 and NO_2 <500		13.8	5.0 mg/kg
Nitrite	mg/kg	Not detected	sum of NO_3 and NO_2 <500		25.0	6.0 mg/kg
Heavy Metal Quality						
Arsenic	mg/kg	0.12	-	1.00	7.7	0.002 mg/kg
Cadmium	mg/kg	0.13		0.25	17.6	0.001 mg/kg
Lead	mg/kg	0.20	-	1.50	17.4	0.005 mg/kg
Mercury	mg/kg	0.002	-	0.10	20.0	0.001 mg/kg

Annex 5: Analysis of the diet

[redacted]

Mycotoxin Quality

B1 Aflatoxin	µg/kg	<0.2	-	-	-	0.2 µg/kg
B2 Aflatoxin	µg/kg	<0.2	-	-	-	0.2 µg/kg
G1 Aflatoxin	µg/kg	<0.2	-	-	-	0.2 µg/kg
G2 Aflatoxin	µg/kg	<0.2	-	-	-	0.2 µg/kg
Total Aflatoxins (by HPLC)	µg/kg	<0.8	-	5.0	25.0	0.8 µg/kg each of B1, B2, G1, G2

Microbiological Quality

Entero Bacteriaceae	cfu/g	<5	-	5.0	-	5 cfu/g
Escherichia Coli	cfu/g	None Detected	-	None Detected	-	5.0 cfu/g
Fungal Units	cfu/g	<10	-	1000	-	10.0 cfu/g
Salmonellae Species	cfu/g	None Detected	-	None Detected	-	Absent in 25g
Total Viable Organisms	cfu/g	<10	-	100000	-	10.0 cfu/g

Miscellaneous Quality

Antibiotic Activity M. luteus S. aureus B. subtilis		Non Detected	-	None	-	-
Selenium	µg/kg	242	-	600	13.8	20.0 µg/kg

Pesticides	Unit	Result	Tolerance Limits Min	Tolerance Limits Max	Analysis Error (actual) or (%)	Limit of Detection
Total P.C.B.	µg/kg	Not Detected	-	<50.0	-	10 µg/kg
Toal D.D.T.	µg/kg	Not Detected	-	sum<50.0	-	1.0 µg/kg
Dieldrin	µg/kg	Not Detected	-	<20.0	-	1.0 µg/kg
Lindane	µg/kg	Not Detected	-	<100	-	1.0 µg/kg
Heptachlor	µg/kg	Not Detected	-	sum<10.0	-	1.0 µg/kg
Malathion	µg/kg	Not Detected	-	<5000	-	20.0 µg/kg

Notes:
The results are in line with expected values.

SDS AUTHORISATION		
Signed	(b) (6)	(b) (6)
Dated	02/11/2016	02/11/2016
Name	Myriam Lunn	Penny Buttling
Position	Quality Services Manager	Senior Nutritionist

[redacted]

[redacted]

Annex 6: Analysis of drinking water

Results of periodical analyses in drinking water collected on the premises of the test facility.

Drinking water was sampled and analysed by the local waterworks (Vitens). The samples were collected on 09-11-2016 (08:03 hr) in room number 05.1.11 at TNO Triskelion, Utrechtseweg 48, Zeist.
The results presented in the table below were reported by Vitens on 14-11-2016

Parameter	Unit	Result
Temperature in situ	°C	23.3
Odour (semi-quantitative)[1,2]		2
Taste (semi-quantitative)[1,2]		0
pH		7.90
Electrical conductivity (20°C)	mS/m	27.4
Turbidity	FTE	0.31
Oxygen	mg/l O_2	10.3
Nitrite	mg/l NO_2	<0.01
Nitrate	mg/l NO_3	8.49
Ammonia	mg/l NH_4	<0.03
Cadmium	µg/l	<0.10
Lead	µg/l	<0.5
Copper	µg/l	84.1
Iron	mg/l	<0.01
Manganese	mg/l	<0.005
Total Organic Carbon (Non Purgeable Organic Carbon)	mg/l C	<0.5
Coli bacteria (37°C)	#/100 ml	<1
Escherichia coli (37°C)	#/100 ml	<1
Aeromonas bacteria (30°C)	#/100 ml	<10
Plate count (22°C)	#/ml	1

[1] Remark: The expiration date for the determination of odour and taste was exceeded. This may have increased the inaccuracy of the measurement.
[2] This observation was evaluated by Vitens as 'No abnormal change'.

Conclusion:
The above parameters meet the requirements of the Dutch Drinking Water Act.

Annex 7: Measurements in all pups

Measurements in all pups on PND 14 and PND 21

On postnatal day 14 litter size, body weight and the sex of all pups were determined (see Table 1 of this Annex), just to have a rough indication of the variability within and between litters.

On postnatal day 21 the pups were weaned and allocated to the different dose groups. Litter size, body weight and the sex of all pups were determined (see Table 2 of this Annex). Allocation was done by manual randomization, using a the Random-Org service list on internet (https://www.Random.org/lists, taking into account body weight, sex of all pups and lineage as presented in Table 2. Body weight of the allocated pups is also presented in Table 4 and Appendix 3 of the main report as body weight on day -4

Table 1 – Pup body weight and sex at postnatal day 14

Mother 1	**Mother 3**	**Mother 5**	**Mother 7**	**Mother 9**	**Mother 11**	**Mother 13**	**Mother 15**
Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)
35.5 (m)	31.7 (m)	29.0 (m)	27.3 (m)	31.6 (m)	33.2 (m)	31.1 (m)	27.7 (m)
34.1 (f)	31.0 (m)	29.3 (m)	26.2 (m)	25.6 (m)	31.5 (m)	29.3 (m)	28.2 (m)
33.9 (f)	30.2 (m)	29.3 (m)	27.7 (m)	27.5 (m)	32.4 (m)	30.6 (m)	26.8 (m)
34.5 (f)	30.3 (m)	32.0 (m)	27.4 (m)	27.7 (m)	32.2 (m)	30.5 (m)	28.3 (m)
33.9 (f)	31.6 (m)	31.2 (m)	27.5 (m)	28.7 (m)	31.7 (m)	28.4 (f)	27.3 (f)
33.2 (f)	28.4 (f)	29.6 (m)	26.7 (m)	28.0 (m)	31.4 (m)	31.6 (f)	28.3 (f)
	30.2 (m)[1]	30.6 (m)	27.8 (m)	29.6 (m)	30.1 (f)	30.3 (f)	27.5 (f)
	30.0 (f)	30.8 (m)	25.9 (f)	28.0 (m)	31.3 (f)	29.3 (f)	27.7 (f)
	29.8 (f)	30.4 (m)	27.1 (f)	28.8 (f)	32.1 (f)	31.6 (f)	27.6 (f)
	30.6 (f)	29.7 (m)	26.6 (f)	29.1 (f)	31.4 (f)	30.4 (f)	27.1 (f)
	29.5 (f)		26.4 (f)	23.7 (f)	30.0 (f)	30.0 (f)	21.6 (f)
			26.7 (f)	26.7 (f)			
				25.6 (f)			

[1] At postnatal day 14 this animals was reported as female. At postnatal day 21 this animals was reported as male. With increased age sex is generally easier to determine in rats and therefore male is considered to be the correct sex of this rat.

Annex 7: Measurements in all pups

Table 1 continued– Pup body weight and sex at postnatal day 14

Mother 17	**Mother 19**	**Mother 21**	**Mother 23**	**Mother 25**	**Mother 27**	**Mother 29**	**Mother 31**
Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and
29.1 (m)	29.4 (m)	34.7 (m)	36.3 (m)	29.5 (m)	29.3 (m)	37.7 (m)	29.7 (m)
29.0 (m)	28.5 (m)	35.5 (m)	35.0 (m)	31.5 (m)	32.8 (m)	38.0 (m)	28.2 (m)
30.2 (m)	29.2 (f)	35.0 (m)	30.7 (m)	30.0 (m)	34.4 (m)	36.9 (m)	29.0 (m)
28.8 (m)	29.9 (f)	33.4 (m)	29.0 (m)	30.2 (m)	32.2 (m)	38.1 (m)	30.4 (m)
21.9 (m)	28.9 (f)	35.5 (m)	30.6 (f)	31.5 (m)	32.6 (m)	35.7 (f)	27.1 (m)
28.9 (f)	29.1 (f)	34.8 (f)	34.3 (f)	29.3 (f)	31.2 (f)	37.5 (f)	28.2 (m)
20.2 (f)	29.4 (f)	34.0 (f)	32.4 (f)	29.8 (f)	30.1 (f)	37.4 (f)	28.6 (m)
27.0 (f)	29.8 (f)	35.3 (f)	32.2 (f)	29.0 (f)	32.4 (f)	35.6 (f)	28.4 (f)
27.2 (f)	29.4 (f)		34.3 (f)	29.7 (f)	32.1 (f)	36.4 (f)	28.0 (f)
27.7 (f)	28.5 (f)		31.5 (f)		30.1 (f)		29.3 (f)
27.8 (f)	28.5 (f)				31.5 (f)		27.0 (f)
30.1 (m)	29.2 (f)						28.4 (f)
							29.5 (f)

Table 2 – Pup body weight and sex at postnatal day 21

Mother 1	**Mother 3**	**Mother 5**	**Mother 7**	**Mother 9**	**Mother 11**	**Mother 13**	**Mother 15**
Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)
54.9 (m)	49.5 (m)	48.5 (m)	45.9 (m)	44.6 (m)	51.7 (m)	48.0 (m)	41.7(m)
48.9 (f)	49.0 (m)	46.1 (m)	47.1 (m)	37.2 (m)	50.6 (m)	46.3 (m)	44.6 (m)
52.0 (f)	50.6 (m)	48.1 (m)	44.1 (m)	40.1 (m)	49.1 (m)	48.9 (m)	42.7 (m)
52.9 (f)	49.7 (m)	48.6 (m)	43.8 (m)	42.3 (m)	49.7 (m)	48.2 (m)	43.3 (m)
52.7 (f)	52.0 (m)	50.5 (m)	45.4 (m)	42.6 (m)	49.0 (m)	46.6 (f)	40.8 (f)
52.1 (f)	45.8 (f)	45.1 (m)	43.0 (m)	41.7 (m)	49.9 (m)	49.9 (f)	41.0 (f)
	48.4 (f)	47.9 (m)	44.5 (m)	45.1 (m)	45.6 (f)	46.8 (f)	41.9 (f)
	47.5 (f)	47.5 (m)	41.3 (f)	41.9 (m)	45.9 (f)	44.9 (f)	32.5 (f)
	51.4 (f)	45.0 (f)	45.8 (f)	43.2 (f)	49.1 (f)	51.0 (f)	40.7 (f)
	47.8 (f)	44.7 (f)	45.8 (f)	37.5 (f)	48.3 (f)	45.3 (f)	42.5 (f)
	49.8 (m)		43.0 (f)	34.7 (f)	45.6 (f)	49.3 (f)	43.7 (f)
			44.0 (f)	41.5 (f)			
				38.9 (f)			

Annex 7: Measurements in all pups

Table 2 continued– Pup body weight and sex at postnatal day 21

Mother 17	**Mother 19**	**Mother 21**	**Mother 23**	**Mother 25**	**Mother 27**	**Mother 29**	**Mother 31**
Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and sex (m/f)	Body weight pups (g) and
45.9 (m)	46.1 (m)	52.4 (m)	57.6 (m)	45.0 (m)	47.5 (m)	56.6 (m)	44.8 (m)
45.5 (m)	45.5 (m)	52.2 (m)	56.2 (m)	50.1 (m)	51.1 (m)	56.5 (m)	46.2 (m)
47.5 (m)	44.7 (f)	53.1 (m)	49.7 (m)	47.7 (m)	52.5 (m)	59.4 (m)	46.0 (m)
45.9 (m)	43.0 (f)	50.3 (m)	45.2 (m)	49.7 (m)	51.2 (m)	56.5 (m)	50.4 (m)
36.9 (m)	46.3 (f)	54.5 (m)	52.8 (f)	50.1 (m)	50.1 (m)	55.7 (f)	45.9 (m)
49.4 (m)	44.8 (f)	51.3 (f)	49.3 (f)	46.7 (f)	49.2 (f)	57.5 (f)	46.8 (m)
47.3 (f)	45.1 (f)	53.2 (f)	51.2 (f)	49.4 (f)	45.4 (f)	57.8 (f)	46.3 (m)
44.2 (f)	46.4 (f)	53.4 (f)	54.4 (f)	43.2 (f)	50.6 (f)	54.1 (f)	46.1 (f)
42.4 (f)	46.3 (f)		55.2 (f)	48.1 (f)	48.8 (f)	55.0 (f)	48.7 (f)
42.7 (f)	46.3 (f)		49.3 (f)		50.0 (f)		47.7 (f)
43.4 (f)	46.4 (f)				49.1 (f)		46.4 (f)
45.1 (f)	44.0 (f)						45.0 (f)
							45.5 (f)

Annex 8: Listing of clinical signs

The clinical signs listed below are derived from the lexicon which is part of the computer programme used for the recording of clinical observations.

RESPIRATION
Sniffing
Grunting
Increased rate
Decreased rate
Irregular
Dyspnea
Shallow
Sneezing
Mouth breathing

GENERAL
Thin
Emaciated
Obese
Weakened
Unconscious
Pale
Red
Jaundice
Cyanosis
Warm
Cold
Dehydrated
Increased muscle tension

MOUTH
Malocclusion of incisors
Lower incisors light color
Lower incisors white
Upper incisors light color
Hemorrhagic discharge
Salivation
Stomatitis
Wart-like lesion(s)
Encrustation(s)
Chewing movement

ABDOMEN
Distension
Tense/firm
Blue/grey
Nodule(s)
Umbilical hernia

FAECES
Increased defecation
Decreased defecation
Hard
Soft
Diarrhea
Pale
Hemorrhagic
Black

BEHAVIOUR
Muscle weakness
Lethargic
Hunched posture
Excessive scratching
Hyperactive
Hypoactive
Aggressive
Stereotypy
Tremors
Convulsions
Ataxia
Circling movements
Vomiting
Vocalization
Chattering
Excessive grooming
Prone position
Myoclonic jerks

SKIN/FUR
Alopecic area(s)
Sparsely haired area(s)
Piloerection
Soiled fur
Depigmented fur
Edema
Abscess(es)
Pimple(s)
Subcutaneous nodule(s)
Erythema
Scaly
Hematoma
Hematoma iatrogenic
Encrustation(s)
Wound(s)
Shaving wound(s)
Scar tissue
Sc. color inj. site
Color ventral of inj. site
Red iatrogenic
Scaly iatrogenic

INJECTION SITE
Small nodule
Small red sc nodule
Redness
Swollen
Warm
Shaving wound/encrustation
Hematoma sc
Red nodule with white core
Red sc nodule with wound

HEAD
Tilted
Local/general swelling
Trimmed whiskers
Erythema between ears

NOSE
Encrustation(s)
Wound
Hemorrhagic discharge
Discharge-other than red
Crooked
Swollen
Itching
Skin protrusion

EYES
Discharge
Encrustation(s)
Blepharospasm
Blepharitis
Redness conjunctivae
Microphthalmia
Macrophthalmia
Exophthalmus
Dark red
Pale
Corneal opacity/keratitis
Cataract
Panophthalmitis
Complete degeneration
Protruding nictitant membrane

EARS
Encrustration(s)
Wound(s)
Ear canal greased
Ear canal hemorrhagic
Hematoma iatrogenic
Necrotizing ear pinna
Ear pinna (partly) gone
Nodule
Swollen
Erythema

PENIS
Prolapse
Purulent discharge
Hemorrhagic discharge
Swollen preputium

PERINEUM
Soiled with urine
Soiled with feces
Soiled with blood
Erythema
Vaginal blood
Vaginal pus
Vaginal occlusion
Membrane present
Prolapsus ani -et recti
Vulva red
Vulva swollen
Vulva nodule

EXTREMITIES (LEG(S))
Encrustation(s)
Wound(s)
Swollen leg
Broken leg
Leg(s) gone
Stiffness
Muscle weakness
Lameness
Hard skin
Pododermatitis
Swollen toe(s)
Toe(s) gone
Nail(s) gone
Popliteal lymph node enlarged

TAIL
Ringtail
Kink
(Partially) discolored
Encrustation(s)
Wound(s)
Scaly
Local thickening
Tip of tail missing
Short and thick

TESTES
Cryptorchidism
Small
Large
Firm
Soft

URETHRA
Urethritis

URINE
Hematuria

Abbreviations: inj. site = injection site sc = subcutaneous

Annex 9: Listing of hematology parameters and methods of analysis

Parameter	Method	Reference
Hemoglobin	Advia 2120i hematology analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5
Packed cell volume	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Calc. from impulse height
Red blood cells	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Impedance
Reticulocytes	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter Fluorescence
White blood cells	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Training manual 04/11/99 chapter 5 Impedance
Differential white blood cell count	Advia 2120i hematology analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Impedance and Absorption
Differential white blood cell count (manual); conducted only if automatic differential count fails	Microscopic examination of stained blood smears according to Pappenheim. Absolute numbers are calculated from total white blood cells and percentage distribution of each cell type	Gorter, E. and W.C. de Graaff, Klinische Diagnostiek, 7th ed. H.E. Stenfert Kroese N.V. Leiden, 1955, the Netherlands, part I, p. 34
Thrombocytes	Advia 2120i hematology analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter Impedance
Prothrombin time	Neoplastine CL PLUS STart-clotanalyzer, Stago citrate plasma	Manufacturers Manual
Mean corpuscular volume (MCV)	Calculated MCV = packed cell volume / red blood cells	
Mean corpuscular hemoglobin (MCH)	Calculated MCH = hemoglobin / red blood cells	
Mean corpuscular hemoglobin concentration (MCHC)	Calculated MCHC = hemoglobin / packed cell volume	

Annex 10: Listing of clinical chemistry parameters and methods of analysis

Parameter	Method
Glucose (plasma)	Olympus AU-400 analyser[1], Olympus reagent Hexokinase
Alkaline phosphatase (ALP)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C.
Alanine aminotransferase (ALAT)/ glutamic-pyruvic transaminase (GPT)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C. without PLP.
Aspartate aminotransferase (ASAT)/ glutamic-oxalacetic transaminase (GOT)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C. without PLP.
γ-Glutamyl transferase (GGT)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C
Total protein	Olympus AU-400 analyser[1], Olympus reagent Biuret
Albumin	Olympus AU-400 analyser[1], Olympus reagent Bromcresol green
Ratio albumin to globulin	Calculated, ratio = albumin / (total protein – albumin)
Urea	Olympus AU-400 analyser[1], Olympus reagent Urease-UV
Creatinine	Olympus AU-400 analyser[2], Roche reagent Enzymatic PAP
Bilirubin (total)	Olympus AU-400 analyser[2], Randox reagent Diazotized sulphanilic acid
Cholesterol (total)	Olympus AU-400 analyser[1], Olympus reagent CHOD-PAP
Triglycerides	Olympus AU-400 analyser[1], Olympus reagent Enzymatic GPO-PAP
Phospholipids	Olympus AU-400 analyser[2], iNstruchemie Reagent Enzymatic
Inorganic phosphate	Olympus AU-400 analyser[1], Olympus reagent Molybdate-UV
Calcium (Ca)	Olympus AU-400 analyser[1], Olympus reagent Arsenazo III
Sodium (Na)	Olympus AU-400 analyser, Olympus reagent I.S.E.
Potassium (K)	Olympus AU-400 analyser[1], Olympus reagent I.S.E.
Chloride (Cl)	Olympus AU-400 analyser[1], Olympus reagent I.S.E.

I.F.C.C. = International Federation of Clinical Chemistry
PLP = pyridoxalphosphate
PAP = phenol-4-aminophenazone
CHOD-PAP = cholesterol oxidase - phenol-4-aminophenazone
GPO-PAP = glycerolphosphate oxidase - phenol-4-aminophenazone
I.S.E. = Ion Selective Electrode

[1] Reference: Manufacturer's manual
[2] Reference: Manufacturer's manual, adapted for the Olympus AU-400 analyse

Annex 11.1: Urinalysis; parameters and methods

Parameter	Method	Reference
Appearance	Visual inspection	
Density	Sysmex refractometer	
Volume (ConcUrin Volume)	Collection in graduated tubes and weighing	
pH, protein, glucose, occult blood (Occ bld), ketones, bilirubin, urobilinogen (Urobili)	Clinitek STATUS Test strips, Siemens	Manufacturer's manual
Sediment: erythro-cytes, leucocytes, epithelial cells, amorph material, crystals, casts, bacteria, sperm cells and worm eggs/ mucus	Microscopic examination after centrifugation	

Annex 11.2: Urinalysis: grading system

Semiquantitative observations

Appearance

Color (range 0-6)
0 yellow
1 light yellow
2 amber
3 dark yellow
4 brown
5 red
6 other

Clarity (range 0-4)
0 clear
1 slightly cloudy
2 cloudy
3 turbid
4 other

Bilirubin (range 0-3) [1]
0 negative <9 µmol/L
1 slight
2 moderate
3 high >100 µmol/L

Occult blood (range 0-3)[1]
0 negative
1 ca. 0 - 25 erythrocytes/µL
2 ca. 25 - 80 erythrocytes/µL
3 ca. 80 - 200 erythrocytes/µL

Glucose (range 0-4) [1]
0 0 – 5.5 mmol/L
1 5.5 -14 mmol/L
2 14 - 28 mmol/L
3 28 - 55 mmol/L
4 > 111 mmol/L

Protein (range 0-4) [1]
0 negative
1 0 – 0.3 g/L
2 0.3 - 1 g/L
3 1-3 g/L
4 > 20 g/L

Ketones (range 0-4) [1]
0 negative
1 0 - 1.5 mmol/L
2 1.5 - 4 mmol/L
3 4 – 8 mmol/L
4 ≥ 16 mmol/L

Urobilinogen
Results in µmol/L

pH
Result from test strips

Microscopy of the sediment

White or red blood cells (range 0-5)
0 0 cells per high powerfield
1 1-2 cells per high powerfield
2 3-10 cells per high powerfield
3 11-20 cells per high powerfield
4 21-50 cells per high powerfield
5 51-100 cells per high powerfield

Epithelial cells, Amorphous material, Crystals, Casts, Bacteria (range 0-5)
0 negative
1 minimal
2 slight
3 moderate
4 high
5 very high

Worm eggs, Sperm cells (range 0-1)
0 negative
1 positive

[1] Concentrations for test strips are approximate only

Annex 12: Analysis of the test substance

Quantitative analysis of **2'**-fucosyllactose in diet for a sub-chronic (13-week) oral toxicity study in rats

Author	Dr. A.J. Kleinnijenhuis
Sponsor	FrieslandCampina Innovation
Triskelion project number	P10197-102
Triskelion study code	20880/02
Date	16 August 2017
Status	Final
Number of pages of this annex	13

Annex 12: Analysis of the test substance

1 Introduction

This annex describes the analytical method used for the quantitative analysis of 2'-fucosyllactose in VRF1 (FG) diet and its validation. In addition data on homogeneity, stability and content of the test substance in diets prepared for study 20880/02 are presented.

2 Experimental

2.1 Test substance

The test substance was 2'-fucosyllactose (2'-FL, Triskelion dispense number 160161, batch number MRS02, storage 2-10 °C in the dark, expiry date 15 July 2018, molecular formula $C_{18}H_{32}O_{15}$). The test substance is a white powder with 94% purity.

2.2 Analysis of the test substance in diet

2.2.1 Principle

After extraction and dilution with milliQ water, diet samples were analyzed using Ultra-Performance Liquid Chromatography – tandem Mass Spectrometry (UPLC-MS/MS).

2.2.2 Validation criteria

Before analysis of study samples, the analytical method was validated by analyzing three spiked samples per dose level, to conform to the following criteria:

- Linearity: the correlation coefficient of the calibration curve should be ≥ 0.996.
- Recovery: the mean recovery of the test substance from diet should be between 85% and 115% at each of the dose levels of the study.
- Repeatability: the relative standard deviation in the percentage recovery should be less than 10% at each of the dose levels of the study.

With respect to specificity: signals should be corrected in case the signal obtained for blank samples was ≥ 5% of the signal obtained for low-dose samples.

2.2.3 Preparation of validation samples

Validation samples with nominal concentrations of approximately 0, 3, 6 and 10 % test substance in diet were prepared by addition of approximately 0, 60, 120 and 200 mg test substance to approximately 2.00, 1.94, 1.88 and 1.80 g diet, respectively, for control, low-dose, mid-dose and high-dose test diet.

All validation samples were prepared as described in section 2.2.4 and analyzed as described in section 2.2.5 of this annex.

2.2.4 Sample preparation

Validation samples were prepared and analyzed in triplicate and study samples were prepared and analyzed in duplicate according to the following method:

Annex 12: Analysis of the test substance

(• Weigh 2.00 +/- 0.01 grams of diet)
• Add 100 ml milliQ water
• Shake 30 minutes at 200 rpm
• Transfer 1 ml to Eppendorf
• Centrifuge 5 minutes at 14000 rpm
• Add 50 µl of the supernatant to 950 µl milliQ water
• Add 20 µl of the diluted sample to 980 µl mobile phase B
• Add 10 µl IS solution (approximately 100 µg/ml trehalose dihydrate in milliQ water)

• Analyze using UPLC-MS/MS.

2.2.5 UPLC-MS/MS conditions

The following UPLC-MS/MS conditions were applied:

LC:	Acquity UPLC		
Column:	Acquity UPLC Glycan BEH amide 130 Å, 1.7 µm, 2.1 x 100 mm.		
Column temperature:	40 °C		
Mobile phase A:	5 mM ammonium formate in milliQ water		
Mobile phase B:	10 mM ammonium formate in acetonitrile/milliQ water 95/5		
Injection volume:	5 µl		
Gradient:	Time	%A	%B
	0	10	90
	0.5	10	90
	4	45	55
	5	45	55
	5.1	10	90
	8	10	90
Flow:	0.5 ml/min		
MS:	Qtrap 6500		
ESI:	negative		
Detection:			
Test substance	486.986 => 325.000 (Quantifier)		
	486.986 => 205.100		
	486.986 => 409.200		
IS	341.000 => 178.900 (Quantifier)		

2.2.6 Calibration samples

On each day that the concentration of the test substance in diet was analyzed 2 stock solutions of 2'-FL were prepared in milliQ water at approximately 1 mg/ml. The stock solutions were diluted to 10 µg/ml. Calibration samples were prepared in an alternating fashion from the 2 diluted stock solutions at concentrations of approximately 0, 0.1, 0.2, 0.5, 1, 2 and 4 or 5 µg/ml by dilution with mobile phase B at end volume 1 ml. The end volume also contained 20 µl 20-fold diluted blank diet extract (in milliQ water) when matrix-matched calibration samples were prepared. Finally 10 µl IS solution was added.

Annex 12: Analysis of the test substance

2.3 Determination of homogeneity, stability and content of the test substance in diet

2.3.1 Homogeneity

The homogeneity of the test substance was assessed in the batch of diets, prepared for study 20880/02 on 01 December 2016. Five samples of each test diet, taken at left top, right top, middle, left bottom and right bottom of the container, and 1 sample of the control diet were analyzed in duplicate.

For each concentration level, a one-way analysis of variance (Anova) was performed using the sample location (1-5) as grouping factor. An associated F-value with probability $p < 0.01$ was considered to be significant (i.e. the mean concentrations differ significantly at the five locations in the container). The test substance was considered to be homogeneously distributed in the diet if $p \geq 0.01$ and/or if the relative standard deviation (RSD) between the mean concentrations at the five locations was ≤ 5%.

2.3.2 Stability

The stability of the test substance in diet was assessed in the batch of diets, prepared for study 20880/02 on 01 December 2016. The samples were stored in the animal room for 4 days and in the freezer (< -18 °C) for ≥ 5 weeks. One sample of each test diet and one sample of the control diet were analyzed in duplicate.

For each concentration level, a one-way analysis of variance (Anova) was performed using time as grouping factor. An associated F-value with probability $p < 0.01$ was considered to be significant (i.e. the mean concentrations differ significantly before and after storage). The test substance was considered to be stable in diet if $p \geq 0.01$ and/or if the mean concentration after storage was within 90-110% of the mean concentration at $t = 0$.

2.3.3 Content

The content of the test substance was determined in the batches of diets, prepared for study 20880/02 on 01 December 2016, 03 January 2017 and 02 February 2017.

The content of the test substance in diet was considered to be "close to intended" if the mean measured concentration was between 90 and 110% of the intended concentration.

Annex 12: Analysis of the test substance

3 Results and discussion

The following series were analyzed:

Subject	Date	Accepted Y/N
Validation 1	19 and 28 October 2016	Y [1]
Homogeneity / content 1	01 December 2016	Y
Stability 4 days	05 December 2016	Y
Content 2 / Content 1 confirmation	03-04 January 2017	Y [2]
Content 3 / Stability ≥ 5 weeks / Validation 2	02 February 2017	Y

[1]The series of 19 October 2016 was rejected due to high response shift, as documented in the study file.

[2]Prior to the accepted series, 5 series were rejected due to multiple reasons, as documented in the study file. The last series of 6 series was accepted.

3.1 Validation of the method

Linearity:
A typical calibration graph of 2'-FL is presented in Figure 1 of this annex and a typical chromatogram of a calibration solution is shown in Figure 2. All calibration graphs had a correlation coefficient of > 0.996 and were therefore considered to be linear. The calibration curves which were recorded in this study had correlation coefficients of 0.998 (validation 1), 0.998 (homogeneity / content 1), 1.000 (stability 4 days), 1.000 (content 2) and 1.000 (content 3, stability ≥ 5 weeks, validation 2). The first two calibration curves were recorded using calibration samples in solvent and the remaining were matrix-matched calibration curves. During the "stability 4 days" run calibration samples with and without matrix were prepared and analyzed in order to compare the resulting calibration curve equations.

Specificity:
Chromatograms of a blank diet sample and a low-dose validation sample are shown in Figures 3 and 4, respectively. The chromatograms of the blank diet showed a minor peak at the position of the test substance. In most cases the signal obtained for blank samples was < 5% of the signal obtained for low-dose samples. Through implementation of matrix-matched calibration solutions the signals for study samples were corrected for the signal obtained for blank samples.

Recovery:
The mean recoveries ranged from 95.6% to 115% , see Table 1 of this annex. All mean recovery values met the validation criterion set for recovery (namely, mean recovery between 85% and 115%).

Repeatability:
The relative standard deviations (RSD) in the mean recoveries ranged from 0.9% to 4.9%, see Table 1 of this annex, which met the criterion set for the RSD in the percentage recovery (namely RSD ≤ 10%).

Annex 12: Analysis of the test substance

3.2 Homogeneity and content of the test substance in diet

3.2.1 Homogeneity

The results of the homogeneity analyses are presented in Tables 2a and 2b of this annex. The RSD between the mean concentrations at three different locations was < 5% for all dose levels and/or p was ≥ 0.01. Therefore the test substance was considered to be homogeneously distributed in the diets.

3.2.2 Stability

The results of the stability experiments are presented in Tables 3 and 4 of this annex. After storage in the animal room for 4 days and after storage at < -18 °C for ≥ 5 weeks (9 weeks), the relative difference in test substance concentration was lower than 10%. Therefore, 2'-FL was considered to be stable under the experimental conditions.

3.2.3 Content

In Table 5 of this annex, the determined concentrations of the test substance in diets, prepared on 01 December 2016, 03 January 2017 and 02 February 2017 are presented, as well as the relative differences from the intended concentrations. The concentration of the test substance was close to intended (90-110%) for each batch at each dose level. Therefore the content of the test substance was considered to have been close to the intended concentration.

Annex 12: Analysis of the test substance

Tables

Table 1: validation of the analytical method for 2'-FL in diet.

Intended concentration of **2'**-FL (%)	Added amount of **2'**-FL (mg)	Theoretical end concentration (ng/ml)	Experimental end concentration (ng/ml)	Recovery (%)	Mean recovery (%)	RSD (%)
0 [1]	0	-	-	-	-	-
	0					
	0	-	-	-		
0 [2]	0	-	-	-	-	-
	0	-	-	-		
	0	-	-	-		
3 [1]	61.29	613	719	117	115	3.6
	59.63	596	698	117		
	60.75	608	669	110		
3 [2]	59.91	599	569	94.9	95.6	0.9
	61.43	614	586	95.3		
	61.08	611	590	96.6		
6 [1]	120.04	1200	1281	107	105	3.1
	120.55	1206	1227	102		
	121.79	1218	1313	108		
6 [2]	120.50	1205	1219	101	103	1.6
	122.25	1222	1263	103		
	121.65	1216	1270	104		
10 [1]	199.60	1996	1897	95.0	99.9	4.9
	202.86	2029	2027	99.9		
	198.16	1982	2076	105		
10 [2]	199.35	1994	1918	96.2	100	3.5
	201.54	2015	2068	103		
	200.34	2003	2038	102		

[1]These analyses were performed on 28 October 2016. The results were calculated using calibration samples prepared in solvent.

[2]These analyses were performed on 02 February 2017. The results were calculated using matrix-matched calibration samples.

Annex 12: Analysis of the test substance

Table 2a: homogeneity of 2'-FL in diets prepared on 01 December 2016.[1]

Intended concentration of **2'**-FL (%)	Sample code	Determined end concentration **2'**-FL (ng/ml)		Mean determined end concentration **2'**-FL (ng/ml) [2]	Overall mean	F-probability	RSD (%)
		I	II				
0	20880/02-01	-	-	-	-	-	-
3	20880/02-02	839	807	823	789	0.081	3.5
	20880/02-03	777	802	789			
	20880/02-04	813	770	791			
	20880/02-05	807	787	797			
	20880/02-06	749	741	745			
6	20880/02-07	1374	1326	1350	1371	0.822	1.9
	20880/02-08	1404	1340	1372			
	20880/02-09	1486	1343	1415			
	20880/02-10	1315	1409	1362			
	20880/02-11	1366	1345	1355			
10	20880/02-12	2145	2073	2109	2170	0.511	2.8
	20880/02-13	2199	2256	2228			
	20880/02-14	2132	2068	2100			
	20880/02-15	2085	2334	2209			
	20880/02-16	2173	2236	2205			

[1]These samples were prepared and analyzed on 01 December 2016. The results were calculated using calibration samples prepared in solvent. The test substance was found to be homogeneously distributed in the test diets, but the determined content deviated > 10% from the intended content for the low- and mid-dose level. It was noticed that the calibration curve in solvent exhibited non-linear behavior in the lower-concentration range. Therefore it was decided to compare matrix-matched and solvent calibration curves in the subsequent run (stability 4 days). After the latter run it was found that the matrix-matched calibration curve was linear in the lower-concentration range, in contrast to the solvent calibration curve. It is proposed that the presence of diet components chromatographically enhances the analyte signal. In Table 2b the homogeneity results are presented when these would be calculated using an intercept and slope corrected for the presence of matrix. The intercept and slope ratios (matrix-matched calibration curve divided by solvent calibration curve) in the "stability 4 days" run were used to correct for the presence of matrix by multiplying the intercept and slope of the solvent calibration curve by the aforementioned intercept ratio and slope ratio, respectively. To confirm the corrected content of the homogeneity samples one sample from each dose level was reanalyzed in a run with a matrix-matched calibration curve, see Table 5.

[2]The theoretical end concentrations were 0, 600, 1200 and 2000 ng/ml for the control, low-dose, mid-dose and high-dose group, respectively.

Annex 12: Analysis of the test substance

Table 2b: homogeneity of 2'-FL in diets prepared on 01 December 2016.[1]

Intended concentration of **2'**-FL (%)	Sample code	Determined end concentration **2'**-FL (ng/ml)		Mean determined end concentration **2'**-FL (ng/ml) [2]	Overall mean	F-probability	RSD (%)
		I	II				
0	20880/02-01	-	-	-	-	-	-
3	20880/02-02	675	645	660	628	0.081	4.2
	20880/02-03	617	640	628			
	20880/02-04	651	610	630			
	20880/02-05	645	626	636			
	20880/02-06	590	583	587			
6	20880/02-07	1181	1135	1158	1178	0.822	2.1
	20880/02-08	1209	1148	1179			
	20880/02-09	1287	1152	1219			
	20880/02-10	1125	1214	1169			
	20880/02-11	1173	1153	1163			
10	20880/02-12	1909	1841	1875	1933	0.511	3.0
	20880/02-13	1960	2014	1987			
	20880/02-14	1896	1837	1866			
	20880/02-15	1852	2087	1970			
	20880/02-16	1936	1994	1965			

[1]These samples were prepared and analyzed on 01 December 2016. The results were calculated using an intercept and slope corrected for the presence of matrix.

[2]The theoretical end concentrations were 0, 600, 1200 and 2000 ng/ml for the control, low-dose, mid-dose and high-dose group, respectively.

Annex 12: Analysis of the test substance

Table 3: stability of 2'-FL in diet, after storage in the animal room for 4 days.

Intended concentration of **2'**-FL (%)	Storage time	Sample code	Determined end concentration **2'**-FL (ng/ml)		Mean determined end concentration **2'**-FL (ng/ml) [4]	F-probability	Relative difference (%)
			I	II			
0	t = 0 [1]	Mean of homogeneity [3]			-	-	-
	t = 4 days [2]	20880/02-17	-	-	-		
3	t = 0 [1]	Mean of homogeneity [3]			628	0.015	-9.8
	t = 4 days [2]	20880/02-18	566	568	567		
6	t = 0 [1]	Mean of homogeneity [3]			1178	0.080	-5.7
	t = 4 days [2]	20880/02-19	1105	1116	1110		
10	t = 0 [1]	Mean of homogeneity [3]			1933	0.147	+4.3
	t = 4 days [2]	20880/02-20	1995	2035	2015		

[1]These samples were prepared and analyzed on 01 December 2016.
[2]These samples were prepared on 01 December 2016 and stored in the animal room until they were analyzed on 05 December 2016.
[3]See Table 2b.
[4]The theoretical end concentrations were 0, 600, 1200 and 2000 ng/ml for the control, low-dose, mid-dose and high-dose group, respectively.

Table 4: stability of 2'-FL in diet, after storage at < -18 °C for 63 days.

Intended concentration of **2'**-FL (%)	Storage time	Sample code	Determined end concentration **2'**-FL (ng/ml)		Mean determined end concentration **2'**-FL (ng/ml) [4]	F-probability	Relative difference (%)
			I	II			
0	t = 0 [1]	Mean of homogeneity [3]			-	-	-
	t ≥ 5 weeks [2]	20880/02-01	-	-	-		
3	t = 0 [1]	Mean of homogeneity [3]			628	0.021	-9.7
	t ≥ 5 weeks [2]	20880/02-05	545	589	567		
6	t = 0 [1]	Mean of homogeneity [3]			1178	0.798	+0.8
	t ≥ 5 weeks [2]	20880/02-10	1186	1188	1187		
10	t = 0 [1]	Mean of homogeneity [3]			1933	0.416	-2.8
	t ≥ 5 weeks [2]	20880/02-15	1813	1943	1878		

[1]These samples were prepared and analyzed on 01 December 2016.
[2]These samples were prepared on 01 December 2016 and stored at < -18 °C until they were analyzed on 02 February 2017.
[3]See Table 2b.
[4]The theoretical end concentrations were 0, 600, 1200 and 2000 ng/ml for the control, low-dose, mid-dose and high-dose group, respectively.

Annex 12: Analysis of the test substance

Table 5: content of 2'-FL in test diet.

Preparation date	*Intended concentration of **2'**-FL (%)*	*Sample code*	*Determined end concentration **2'**-FL (ng/ml)*		*Mean determined end concentration **2'**-FL (ng/ml)* [5]	*Relative difference (%)*
			I	*II*		
01 December 2016 [1]	*0*	*20880/02-01, see Table 2b*			-	-
	3	*20880/02-02 to 06, see Table 2b*			*628*	*+4.7*
	6	*20880/02-05 to 11, see Table 2b*			*1178*	*-1.9*
	10	*20880/02-12 to 16, see Table 2b*			*1933*	*-3.4*
01 December 2016 [2]	*0*	*20880/02-01*	-	-	-	-
	3	*20880/02-03*	*567*	*586*	*577*	*-3.9*
	6	*20880/02-08*	*1165*	*1203*	*1184*	*-1.3*
	10	*20880/02-13*	*2058*	*2078*	*2068*	*+3.4*
03 January 2017 [3]	*0*	*20880/02-21*	-	-	-	-
	3	*20880/02-22*	*599*	*589*	*594*	*-1.0*
	6	*20880/02-23*	*1191*	*1162*	*1176*	*-2.0*
	10	*20880/02-24*	*1961*	*2098*	*2030*	*+1.5*
02 February 2017 [4]	*0*	*20880/02-25*	-	-	-	-
	3	*20880/02-26*	*603*	*603*	*603*	*+0.5*
	6	*20880/02-27*	*1270*	*1248*	*1259*	*+4.9*
	10	*20880/02-28*	*2042*	*1945*	*1994*	*-0.3*

[1]These samples were prepared and analyzed on 01 December 2016.
[2]To confirm their content these samples were reanalyzed on 03-04 January 2017 (after storage at < -18 °C).
[3]These samples were prepared and analyzed on 03-04 January 2017.
[4]These samples were prepared and analyzed on 02 February 2017.
[5]The theoretical end concentrations were 0, 600, 1200 and 2000 ng/ml for the control, low-dose, mid-dose and high-dose group, respectively.

Annex 12: Analysis of the test substance

Figures

Figure 1: Typical calibration graph of 2'-FL: Ratio peak area analyte / IS versus concentration 2'-FL (ng/ml).

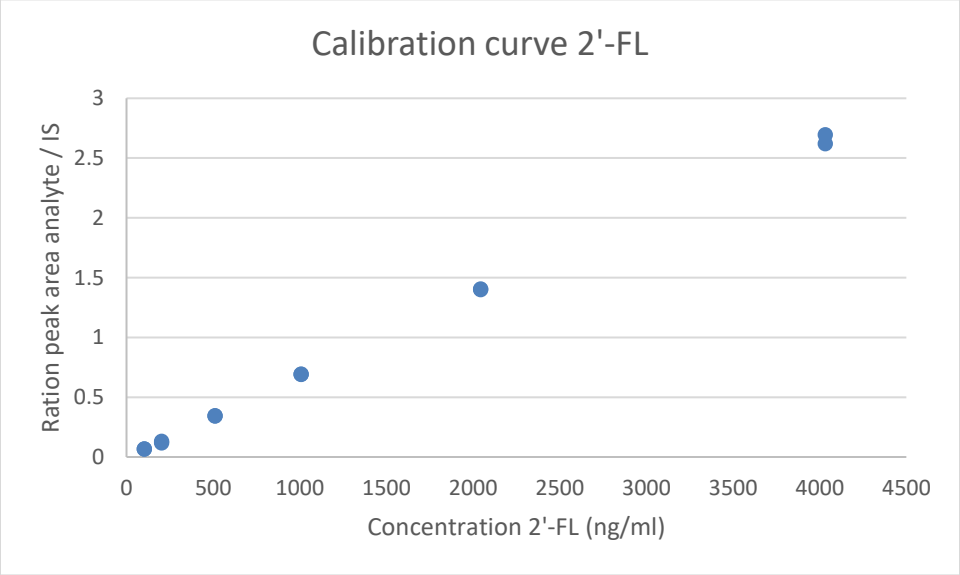
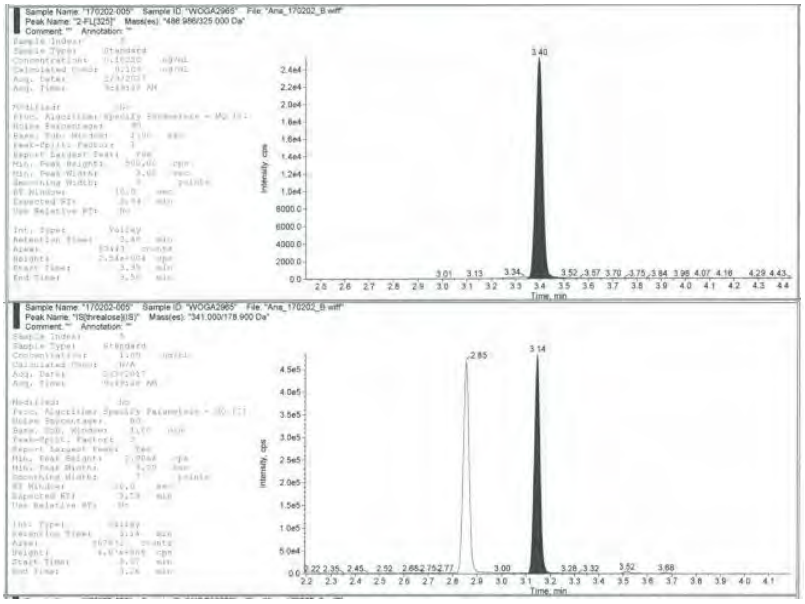


Figure 2: UPLC-MS/MS chromatograms of a calibration sample containing 102.2 ng/ml 2'-FL. Top: test substance, bottom: internal standard trehalose. The test substance eluted after 3.40 minutes and the internal standard after 3.14 minutes.



Annex 12: Analysis of the test substance

Figure 3: UPLC-MS/MS chromatograms of a blank validation sample. Top: test substance, bottom: internal standard trehalose.

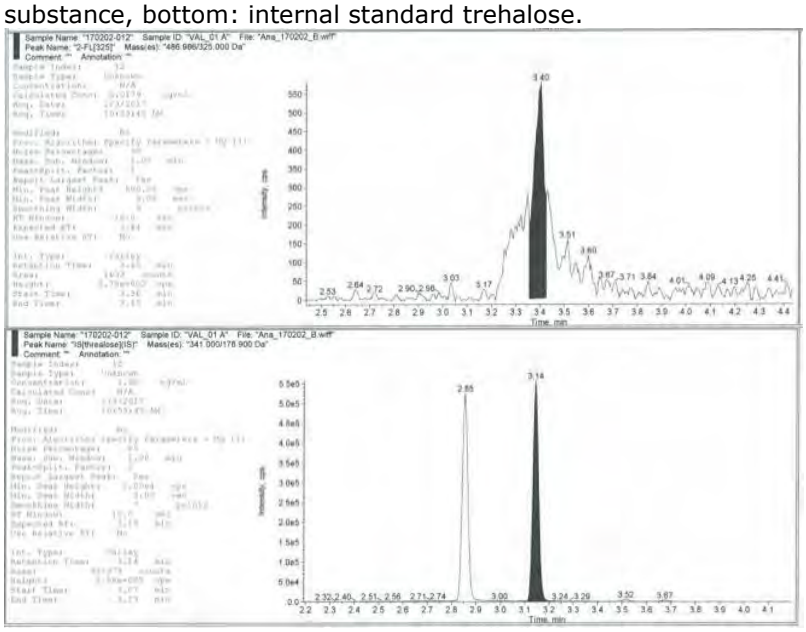
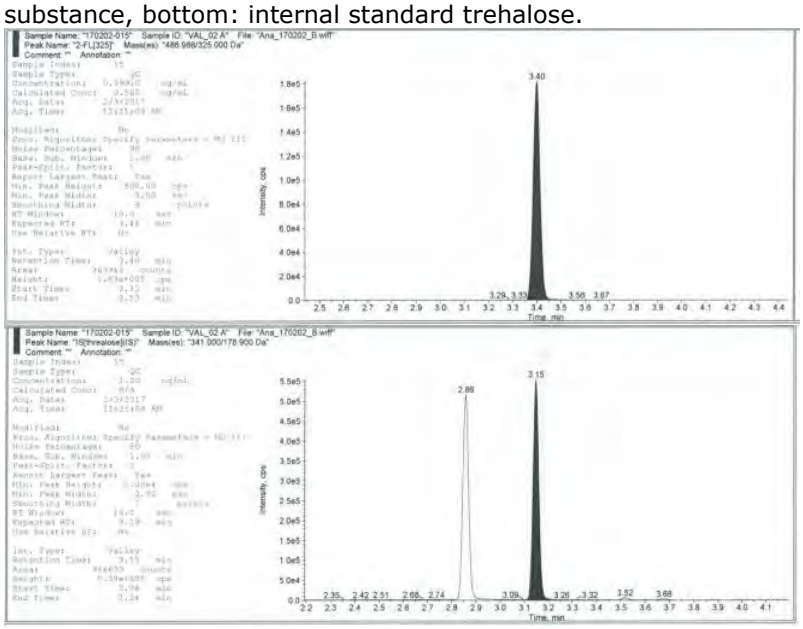


Figure 4: UPLC-MS/MS chromatograms of a low-dose validation sample. Top: test substance, bottom: internal standard trehalose.



Annex 13

Neurobehavioral testing: detailed clinical observations, Functional Observational Battery and Motor Activity Assessment

1 Experimental procedures

Neurobehavioral testing was conducted on all rats of all groups.
During neurobehavioral testing, the group identification on the cages was masked in order not to disclose the treatment of the animals.

Detailed clinical observations

In addition to the daily general clinical observations (clinical signs), detailed clinical observations were conducted in the experimental room (no. 5.1.08) outside the home cage one day after the initiation of treatment and once weekly thereafter up to and including week 13. Detailed clinical observations were part of the Functional Observational Battery test in week 12 of the study. Signs noted included but were not limited to changes in skin and fur, piloerection, changes in the eyes, gait (including posture), and presence of clonic or tonic movements, stereotypies and bizarre behavior.

Female no. 33 of the mid-dose group was found dead on day 24 of the study (see section 5.3 Clinical observations of the main report for more information).

Functional Observational Battery (FOB) and Motor Activity Assessment (MAA)

Functional Observational Battery (FOB) tests and spontaneous Motor Activity Assessment (MAA) were performed at the end of the study period in week 12. On the morning of testing (at least one hour prior to the start of the observations) the selected animals were placed individually in macrolon cages in a waiting area in examination room 05.2.24. After testing the animals were returned to the experimental room (no. 5.1.08).

FOB:
The FOB used in our laboratory is adapted from the WHO/IPCS Functional Observational Battery that was used in the Collaborative Study on Neurotoxicity Assessment sponsored by the International Programme on Chemical Safety of the World Health Organization. Details on the conduct of observations included in this battery and operational definitions of the different scores for each item are given in the FOB-manual entitled "Functional Observational Battery. Operational Definitions" (Lammers, 2000) which is attached to this Annex.

Unlike the daily, general clinical observations (intended to detect all abnormalities, signs of ill health or reactions to treatment), the FOB is a series of non-invasive observational and interactive measures designed to assess the neurobehavioral and functional integrity of the rat.

Annex 13: Neurobehavioral testing

The measures included according to functional domain are as follows:

Domain	Behavioral end-point
Autonomic	lacrimation (R), salivation (R), pupil response to light (Q), palpebral closure (R), piloerection (Q), defaecation (C), urination (C)
Neuromuscular	gait (D,R), mobility (R), forelimb and hindlimb gripstrength (I), landing foot splay (I), righting reflex (R)
Sensorimotor	response (R) to tail pinch, click, touch and approach of a visual object
Convulsive	clonic and tonic movements (D)
Excitability	ease of removal (R), handling reactivity (R), arousal (R), vocalizations (Q)
Activity	rearing (C), posture (D)
Physiological	body temperature (I)

Abbreviations: R=rank order data Q=quantal data C=count data
D=descriptive rank order data I=interval or continuous data

First, measurements were carried out in the cage. The rat's posture, palpebral closure and the possible presence of clonic and tonic convulsions were recorded. Then the rat was removed from the cage and the ease of removal and handling were rated. Palpebral closure and any lacrimation or salivation were also rated, and the presence or absence of piloerection and vocalizations was recorded. In addition, other signs, such as changes in skin and fur, exophthalmus, crustiness around the eyes, bite marks on the tail or paws, missing toe nails or emaciation (shallow stomach, protruding spinal vertebrae) were recorded. The rat was then placed in an open arena (77 *l* x 55 *w* x 7 *h* cm) and observed for 3 minutes. Rears (both supported and unsupported) were counted. At the same time, gait characteristics were recorded and ranked, the ease with which the rat locomoted was ranked, and arousal was assessed and recorded. Further, the occurrence of clonic and/or tonic convulsions, stereotypies and bizarre behavior was recorded. At the end of the observation period, the number of fecal boluses and urine pools were recorded.

Following this observation period, reflex testing was conducted. Reflex testing consisted of recording the rat's responses to the approach of a pencil, a touch of a pencil to the rump, a click stimulus, tail pinch, and the constriction of the pupil to light. Aerial righting was rated next. Forelimb and hindlimb gripstrength were measured. Three valid determinations (from a maximum of five attempts) were taken for each gripstrength measure. The rectal temperature was taken with the rat restrained by hand. Finally, the hindlimb feet were painted lightly and landing foot splay was measured.

Motor activity:
Motor activity was assessed following FOB testing. Changes in spontaneous motor activity were assessed using an automated quantitative microprocessor-based video image analysis system. Rats were placed individually in open roofed cages measuring 48.8 *l* x 44.7 *w* x 50 *h* cm on the insides and equipped with a video camera suspended above the test cage. The position of the rat was continuously monitored throughout the test session. Spontaneous motor activity was expressed as the total distance run in a 30 minute test period. In addition, habituation of activity was evaluated. To this end, each session was divided into 5 time blocks of 6 minutes each. Motor activity tests were recorded on a DVD recorder, in order to enable re-analysis of motor activity tests should that be necessary for technical reasons. However, re-analysis was not necessary. Therefore, recordings will be deleted after submission of the final report. Squads of up to eight animals were monitored simultaneously. Dose groups were evenly

distributed for motor activity test cage and for time as much as possible. Motor activity testing of a squad was conducted immediately after functional observations for that squad had finished.

2 Statistical analysis of the results

Parameters assessed during Functional Observational Battery and Motor Activity Assessment were measured on different measurement scales (e.g. continuous, rank, categorical) and evaluated as follows:

- Continuous measures: one-way analysis of variance, followed by Dunnett's post-hoc group comparisons in case of a significant result.
- Rank order data: Kruskal-Wallis non-parametric analysis of variance, followed by multiple comparison tests in case of a significant result.
- Categorical data: Pearson's chi-square analysis, followed by multiple comparison tests in case of a significant result.
- Total distance moved: one-way analysis of variance, followed by Dunnett's post-hoc group comparisons in case of a significant result.
- Habituation of activity: repeated measures analysis of variance on time blocks.

Tests were performed as two-sided tests with results taken as significant where the probability of the results was <0.05 or <0.01.

3 Results and discussion

Detailed clinical observations and Functional Observational Battery (FOB)

Remarkable observations and additional (i.e. not standardized) observations recorded during the detailed clinical observations or during the Functional Observational Battery test at the end of the study period, are summarized in Appendix I of this annex. Results of all standardized observations of individual animals recorded during Functional Observational Battery testing are given in Appendix II of this annex. Group mean data are summarized in Tables I-IV of this annex. Frequency tables were not prepared for the standardized quantal or descriptive measures for which all animals in all groups had the same score, or for which no abnormalities were observed.

No treatment-related effects were observed from detailed clinical observations or from functional observations in any of the dose groups during the study period.

Statistical analysis showed a significant increase in the mean landing footsplay of males of the low-dose group when compared to the control group ($p<0.05$). This group difference was not considered to be toxicologically relevant, for the increase in gripstrength was only observed in males of the lowest dose group, no dose-response relationship could be established and the effect was not accompanied by effects on other parameters from the same functional domain.

Further, some abnormalities (tilted head, slightly tiptoe walking, dermal wounds, skin encrustations, sparsely haired skin, kinktail and a broken toenail) were observed in some animals of different groups in various weeks of the study (see Appendix I). Based on the incidence and on the distribution among the dose groups, these findings were considered not to be related to treatment.

Annex 13: Neurobehavioral testing

Motor Activity Assessment (MAA)

Motor activity data of individual animals are presented in Appendix III, and group mean data are presented in Table V of this annex.

No treatment-related effects were observed from motor activity assessment in any of the dose groups during the 30-minute test period.

4 Conclusion

The results of the neurobehavioral observations and motor activity assessment did not indicate any neurotoxic potential of 2'-Fucosyllactose in rats.

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

TABLE I: GROUP DATA

---------- SEX=MALE TEST=FOB ----------

GROUP	PC_N	PALPC	PC_SEM	RR_N	REAR	RR_SEM	AR_N	AROUS	AR_SEM
Control	10	2.60	0.48	10	11.40	1.42	10	4.00	0.00
Low-dose	10	2.80	0.49	10	8.20	1.15	10	4.00	0.00
Mid-dose	10	2.60	0.48	10	10.60	1.03	10	4.00	0.00
High-dose	10	2.80	0.49	10	14.20	2.43	10	4.10	0.10

GROUP	RE_N	REMOV	RE_SEM	HA_N	HAND	HA_SEM	PH_N	PALPH	PH_SEM
Control	10	2.20	0.13	10	2.00	0.00	10	1.00	0.00
Low-dose	10	2.00	0.00	10	2.00	0.00	10	1.00	0.00
Mid-dose	10	2.10	0.10	10	2.00	0.00	10	1.00	0.00
High-dose	10	2.10	0.10	10	2.00	0.00	10	1.00	0.00

GROUP	UR_N	URIN	UR_SEM	FA_N	FAEC	FA_SEM	SA_N	SALIV	SA_SEM
Control	10	5.20	1.43	10	0.00	0.00	10	1.00	0.00
Low-dose	10	3.20	1.18	10	0.00	0.00	10	1.00	0.00
Mid-dose	10	5.10	2.09	10	0.00	0.00	10	1.00	0.00
High-dose	10	4.60	1.49	10	0.20	0.20	10	1.00	0.00

GROUP	LA_N	LACR	LA_SEM	GS_N	GAITSC	GS_SEM	MO_N	MOBIL	MO_SEM
Control	10	1.00	0.00	10	1.00	0.00	10	1.00	0.00
Low-dose	10	1.00	0.00	10	1.00	0.00	10	1.00	0.00
Mid-dose	10	1.00	0.00	10	1.00	0.00	10	1.00	0.00
High-dose	10	1.00	0.00	10	1.00	0.00	10	1.00	0.00

GROUP	RI_N	RIGHT	RI_SEM	FG_N	FGRPM	FG_SEM	HG_N	HGRPM	HG_SEM
Control	10	1.00	0.00	10	1576	56.1	10	827	60.8
Low-dose	10	1.00	0.00	10	1662	76.5	10	866	50.6
Mid-dose	10	1.00	0.00	10	1648	58.5	10	862	50.2
High-dose	10	1.00	0.00	10	1524	84.8	10	823	28.3

GROUP	SP_N	SPLAYM	SP_SEM	AP_N	APPR	AP_SEM	TO_N	TOUCH	TO_SEM
Control	10	79.50	5.14	10	2.00	0.00	10	2.00	0.00
Low-dose	10	104.75*	4.77	10	2.00	0.00	10	2.00	0.00
Mid-dose	10	97.15	6.57	10	2.00	0.00	10	2.10	0.10
High-dose	10	92.35	7.68	10	2.00	0.00	10	2.00	0.00

GROUP	CL_N	CLICK	CL_SEM	TA_N	TAIL	TA_SEM	TE_N	TEMP	TE_SEM
Control	10	3.00	0.00	10	4.00	0.00	10	37.80	0.09
Low-dose	10	3.00	0.00	10	3.80	0.20	10	37.59	0.06
Mid-dose	10	2.90	0.10	10	4.00	0.00	10	38.01	0.09
High-dose	10	3.00	0.00	10	4.00	0.15	9	37.99	0.15

Statistics:
Continuous measures: Anova, Dunnett's test
Rank order data: Kruskal-Wallis, multiple comparisons
**=P≤0.05; **=P≤0.01*

PC/PALPC : Palpebral closure in homecage (mean rank score)
RR/REAR : Rears (mean number)
AR/AROUS : Arousal (mean rank score)
RE/REMOV : Ease of removal (mean rank score)
HA/HAND : Handling (mean rank score)
PH/PALPH : Palpebral closure during handling (mean rank score)
UR/URIN : Urine spots (mean number)
FA/FAEC : Fecal boli (mean number)
SA/SALIV : Salivation (mean rank score)
LA/LACR : Lacrimation (mean rank score)
GS/GAITSC: Gait score (mean rank score)
MO/MOBIL : Mobility (mean rank score)
RI/RIGHT : Righting reflex (mean rank score)
FG/FGRPM : Mean forelimb gripstrength (g)
HG/HGRPM : Mean hindlimb gripstrength (g)
SP/SPLAYM: Mean landing footsplay (mm)
AP/APPR : Approach response (mean rank score)
TO/TOUCH : Touch response (mean rank score)
CL/CLICK : Click response (mean rank score)
TA/TAIL : Tail pinch response (mean rank score)
TE/TEMP : Mean body temperature (deg. C)
_N : Number of subjects
_SEM : Standard Error of the Mean

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

TABLE I: GROUP DATA

---------- SEX=FEMALE TEST=FOB ----------

GROUP	PC_N	PALPC	PC_SEM	RR_N	REAR	RR_SEM	AR_N	AROUS	AR_SEM
Control	10	1.90	0.46	10	20.80	2.43	10	4.20	0.13
Low-dose	10	1.30	0.30	10	19.00	1.31	10	4.10	0.10
Mid-dose	9	1.00	0.00	9	18.11	1.46	9	4.00	0.00
High-dose	10	1.70	0.40	10	21.10	2.16	10	4.10	0.10

GROUP	RE_N	REMOV	RE_SEM	HA_N	HAND	HA_SEM	PH_N	PALPH	PH_SEM
Control	10	2.00	0.00	10	2.00	0.00	10	1.00	0.00
Low-dose	10	2.00	0.00	10	2.00	0.00	10	1.00	0.00
Mid-dose	9	2.22	0.15	9	2.11	0.11	9	1.00	0.00
High-dose	10	2.10	0.10	10	2.00	0.00	10	1.00	0.00

GROUP	UR_N	URIN	UR_SEM	FA_N	FAEC	FA_SEM	SA_N	SALIV	SA_SEM
Control	10	2.70	1.23	10	0.00	0.00	10	1.00	0.00
Low-dose	10	0.70	0.60	10	0.10	0.10	10	1.00	0.00
Mid-dose	9	2.44	0.88	9	0.00	0.00	9	1.00	0.00
High-dose	10	2.70	2.09	10	0.00	0.00	10	1.00	0.00

GROUP	LA_N	LACR	LA_SEM	GS_N	GAITSC	GS_SEM	MO_N	MOBIL	MO_SEM
Control	10	1.00	0.00	10	1.30	0.15	10	1.00	0.00
Low-dose	10	1.00	0.00	10	1.20	0.13	10	1.00	0.00
Mid-dose	9	1.00	0.00	9	1.00	0.00	9	1.00	0.00
High-dose	10	1.00	0.00	10	1.00	0.00	10	1.00	0.00

GROUP	RI_N	RIGHT	RI_SEM	FG_N	FGRPM	FG_SEM	HG_N	HGRPM	HG_SEM
Control	10	1.00	0.00	10	1340	67.7	10	592	25.3
Low-dose	10	1.00	0.00	10	1376	63.5	10	651	35.1
Mid-dose	9	1.00	0.00	9	1349	50.7	9	634	35.4
High-dose	10	1.00	0.00	10	1315	53.0	10	642	31.9

GROUP	SP_N	SPLAYM	SP_SEM	AP_N	APPR	AP_SEM	TO_N	TOUCH	TO_SEM
Control	10	94.85	6.51	10	2.00	0.00	10	2.00	0.00
Low-dose	10	97.85	9.48	10	2.00	0.00	10	2.00	0.00
Mid-dose	9	91.94	7.35	9	2.00	0.00	9	2.00	0.00
High-dose	10	99.85	7.16	10	2.00	0.00	10	2.00	0.00

GROUP	CL_N	CLICK	CL_SEM	TA_N	TAIL	TA_SEM	TE_N	TEMP	TE_SEM
Control	10	2.90	0.10	10	3.40	0.16	10	38.54	0.15
Low-dose	10	2.90	0.10	10	3.40	0.22	10	38.61	0.07
Mid-dose	9	2.78	0.15	9	3.22	0.22	9	38.60	0.12
High-dose	10	2.60	0.16	10	3.50	0.17	10	38.72	0.11

Statistics:
Continuous measures: Anova, Dunnett's test
Rank order data: Kruskal-Wallis, multiple comparisons
**=P≤0.05; **=P≤0.01*

PC/PALPC	: Palpebral closure in homecage	(mean rank score)
RR/REAR	: Rears	(mean number)
AR/AROUS	: Arousal	(mean rank score)
RE/REMOV	: Ease of removal	(mean rank score)
HA/HAND	: Handling	(mean rank score)
PH/PALPH	: Palpebral closure during handling	(mean rank score)
UR/URIN	: Urine spots	(mean number)
FA/FAEC	: Fecal boli	(mean number)
SA/SALIV	: Salivation	(mean rank score)
LA/LACR	: Lacrimation	(mean rank score)
GS/GAITSC	: Gait score	(mean rank score)
MO/MOBIL	: Mobility	(mean rank score)
RI/RIGHT	: Righting reflex	(mean rank score)
FG/FGRPM	: Mean forelimb gripstrength	(g)
HG/HGRPM	: Mean hindlimb gripstrength	(g)
SP/SPLAYM	: Mean landing footsplay	(mm)
AP/APPR	: Approach response	(mean rank score)
TO/TOUCH	: Touch response	(mean rank score)
CL/CLICK	: Click response	(mean rank score)
TA/TAIL	: Tail pinch response	(mean rank score)
TE/TEMP	: Mean body temperature	(deg. C)
_N	: Number of subjects	
_SEM	: Standard Error of the Mean	

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

TABLE II: FREQUENCY TABLE FOR VARIABLE HOMECAGE POSTURE

---------- SEX=MALE TEST=FOB ----------

GROUP HOMECAGE POSTURE (CATEGORIES)

Frequency	1	1+2	2	3	Total
Control	3	2	0	5	10
Low-dose	3	1	0	6	10
Mid-dose	4	1	1	4	10
High-dose	0	3	1	6	10
Total	10	7	2	21	40

---------- SEX=FEMALE TEST=FOB ----------

GROUP HOMECAGE POSTURE (CATEGORIES)

Frequency	1	1+2	2	3	Total
Control	2	1	4	3	10
Low-dose	1	7	1	1	10
Mid-dose	4	1	4	0	9
High-dose	4	2	2	2	10
Total	11	11	11	6	39

Statistics: Pearson chi-square analysis
**=P≤0.05; **=P≤0.01*

HOMECAGE POSTURE (CATEGORIES):

1) sitting or standing normally
2) rearing, i.e. front paws are off the floor of the cage
3) asleep and/or lying on side and/or curled

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

TABLE III: FREQUENCY TABLE FOR VARIABLE GAIT ABNORMALITIES

---------- SEX=MALE TEST=FOB ----------

GROUP	GAIT SCORE (CATEGORIES)	
Frequency	0	Total
Control	10	10
Low-dose	10	10
Mid-dose	10	10
High-dose	10	10
Total	40	40

---------- SEX=FEMALE TEST=FOB ----------

GROUP	GAIT SCORE (CATEGORIES)		
Frequency	0	5	Total
Control	7	3	10
Low-dose	8	2	10
Mid-dose	9	0	9
High-dose	10	0	10
Total	34	5	39

Statistics: Pearson chi-square analysis
**=P≤0.05; **=P≤0.01*

GAIT DESCRIPTION (CATEGORIES):

0) no gait abnormality
5) walks on toes - this refers to walking with the heel of the hind feet off the surface. We have seen this under "normal" conditions, especially in rats who are somewhat excitable.

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

TABLE IV: FREQUENCY TABLE FOR VARIABLE VOCALIZATIONS

---------- SEX=MALE TEST=FOB ----------

GROUP VOCALIZATIONS (0=NO, 1/2=YES)

Frequency	0	1	Total
Control	8	2	10
Low-dose	9	1	10
Mid-dose	8	2	10
High-dose	9	1	10
Total	34	6	40

---------- SEX=FEMALE TEST=FOB ----------

GROUP VOCALIZATIONS (0=NO, 1/2=YES)

Frequency	0	1	2	Total
Control	8	1	1	10
Low-dose	10	0	0	10
Mid-dose	7	1	1	9
High-dose	8	2	0	10
Total	33	4	2	39

Statistics: Pearson chi-square analysis
**=P≤0.05; **=P≤0.01*

VOCALIZATIONS (0=NO, 1/2=YES):

0) None
1) Vocalizations during either removal from the home cage or handling
2) Vocalizations during removal from the home cage and handling

Annex 13: Neurobehavioral testing

MOTOR ACTIVITY ASSESSMENT

TABLE V: GROUP DATA

---------- SEX=MALE ZONE=ARENA TEST=MAA ----------

GROUP	N	INT_1	I1_SEM	INT_2	I2_SEM	INT_3	I3_SEM
Control	10	962	55	768	70	468	79
Low-dose	10	963	109	688	72	513	95
Mid-dose	10	847	60	591	59	416	45
High-dose	10	909	121	684	53	339	87

GROUP	N	INT_4	I4_SEM	INT_5	I5_SEM	TOTDM	TOT_SEM
Control	10	362	79	253	71	2812	248
Low-dose	10	455	90	348	86	2967	354
Mid-dose	10	283	42	274	67	2412	135
High-dose	10	304	89	267	79	2502	322

---------- SEX=FEMALE ZONE=ARENA TEST=MAA ----------

GROUP	N	INT_1	I1_SEM	INT_2	I2_SEM	INT_3	I3_SEM
Control	10	1501	125	937	116	580	72
Low-dose	10	1503	93	967	52	632	88
Mid-dose	9	1333	102	877	61	682	52
High-dose	10	1313	67	891	59	574	54

GROUP	N	INT_4	I4_SEM	INT_5	I5_SEM	TOTDM	TOT_SEM
Control	10	393	64	381	62	3792	382
Low-dose	10	461	82	394	92	3956	314
Mid-dose	9	569	106	331	72	3792	256
High-dose	10	470	49	309	79	3556	183

Statistics:
*Total Distance Moved: Anova, Dunnett's test; *=P≤0.05; **=P≤0.01*
Habituation of activity: repeated measures Anova; #=P≤0.05; ##=P≤0.01

INT_1/I1: distance moved (cm) in interval 1
INT_2/I2: distance moved (cm) in interval 2
INT_3/I3: distance moved (cm) in interval 3
INT_4/I4: distance moved (cm) in interval 4
INT_5/I5: distance moved (cm) in interval 5
TOTDM : total distance moved (cm)
_N : Number of subjects
_SEM : Standard Error of the Mean

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX I: BEHAVIOURAL OBSERVATIONS RECORDED DURING THE WEEKLY DETAILED CLINICAL OBSERVATIONS OR DURING THE FUNCTIONAL OBSERVATIONAL BATTERY (FOB)[1] IN WEEK 12 OF THE STUDY

Anomalous/additional observations	Control	Low-dose	Mid-dose	High-dose
Tilted head				♂22 week 6-13
(Slightly) tiptoe walking	♀13 week 12 ♀15 week 7,9 ♀17 week 12 ♀41 week 9 ♀43 week 3,4,6,8,12	♀23 week 9,10 ♀25 week 12 ♀51 week 6,11 ♀59 week 12	♀31 week 13 ♀39 week 11,13 ♀67 week 13	♀09 week 6 ♀73 week 5,10,13
Dermal wounds			♂12 week 5	♂54 week 2
Skin encrustations	♀41 week 2 ♀49 week 5	♂10 week 6,7 ♂78 week 5 ♂80 week 4-6 ♀53 week 5-10,12 ♀59 week 7,11-13	♂12 week 6 ♀33 week 4	♂54 week 1,3 ♂58 week 5,6 ♀01 week 3 ♀03 week 3-5,10 ♀05 week 1 ♀73 week 5
Sparsely haired skin	♀45 week 5,12,13 ♀49 week 12	♂76 week 12 ♀53 week 11-13		♂52 week 12,13 ♂58 week 8-10 ♀03 week 5 ♀05 week 6-13 ♀07 week 9-13 ♀75 week 12
Kinktail	♂36 week 1-13 ♂62 week 3-13		♂18 week 1-13	♂22 week 4-13 ♂60 week 11
Broken toenail during gripstrength measurements	♂38 week 12			

[1] The complete results of the standardized observations recorded during FOB testing in week 12 of the study are presented in Appendix II of this Annex.

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=MALE TEST=FOB GROUP=Control ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
32	3	4	8	4	2	2	1
34	1+2	1	17	4	2	2	1
36	3	4	8	4	2	2	1
38	1	1	17	4	2	2	1
40	1	2	18	4	2	2	1
62	1	1	12	4	2	2	1
64	1+2	1	11	4	3	2	1
66	3	4	9	4	2	2	1
68	3	4	9	4	2	2	1
70	3	4	5	4	3	2	1

---------- SEX=MALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
2	1	1	6	4	2	2	1
4	3	4	6	4	2	2	1
6	3	4	3	4	2	2	1
8	1+2	1	11	4	2	2	1
10	3	4	6	4	2	2	1
72	1	1	15	4	2	2	1
74	3	4	10	4	2	2	1
76	3	4	7	4	2	2	1
78	3	4	12	4	2	2	1
80	1	1	6	4	2	2	1

---------- SEX=MALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
12	1	1	13	4	2	2	1
14	3	4	10	4	2	2	1
16	3	4	13	4	2	2	1
18	1+2	1	11	4	2	2	1
20	1	1	8	4	2	2	1
42	1	2	13	4	2	2	1
44	2	4	6	4	2	2	1
46	3	4	16	4	2	2	1
48	3	4	10	4	2	2	1
50	1	1	6	4	3	2	1

---------- SEX=MALE TEST=FOB GROUP=High-dose ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
22	2	1	32	5	2	2	1
24	3	4	16	4	3	2	1
26	3	4	9	4	2	2	1
28	3	4	5	4	2	2	1
30	3	4	14	4	2	2	1
52	1+2	1	8	4	2	2	1
54	1+2	1	20	4	2	2	1
56	3	4	15	4	2	2	1
58	1+2	1	14	4	2	2	1
60	3	4	9	4	2	2	1

POST : Homecage posture (categories)
PALPC: Palpebral closure in homecage (rank score)
REAR : Number of rears
AROUS: Arousal (rank score)
REMOV: Ease of removal (rank score)
HAND : Handling reactivity (rank score)
PALPH: Palpebral closure during handling (rank score)

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=MALE TEST=FOB GROUP=Control ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
32	0	0	0	0	9	0
34	0	0	0	0	1	0
36	0	0	0	0	3	0
38	0	0	0	0	8	0
40	0	0	0	0	13	0
62	0	0	0	0	1	0
64	0	0	0	0	0	0
66	0	0	0	0	8	0
68	0	0	0	0	8	0
70	0	0	0	0	1	0

---------- SEX=MALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
2	0	0	0	0	0	0
4	0	0	0	0	1	0
6	0	0	0	0	0	0
8	0	0	0	0	7	0
10	0	0	0	0	4	0
72	0	0	0	0	2	0
74	0	0	0	0	11	0
76	0	0	0	0	6	0
78	0	0	0	0	0	0
80	0	0	0	0	1	0

---------- SEX=MALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
12	0	0	0	0	9	0
14	0	0	0	0	0	0
16	0	0	0	0	0	0
18	0	0	0	0	0	0
20	0	0	0	0	11	0
42	0	0	0	0	16	0
44	0	0	0	0	0	0
46	0	0	0	0	14	0
48	0	0	0	0	0	0
50	0	0	0	0	1	0

---------- SEX=MALE TEST=FOB GROUP=High-dose ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
22	0	0	0	0	8	0
24	0	0	0	0	5	0
26	0	0	0	0	0	0
28	0	0	0	0	2	0
30	0	0	0	0	3	2
52	0	0	0	0	0	0
54	0	0	0	0	15	0
56	0	0	0	0	6	0
58	0	0	0	0	7	0
60	0	0	0	0	0	0

CLONC: Clonic movements in homecage (categories)
CLONO: Clonic movements in open field (categories)
TONC : Tonic movements in homecage (categories)
TONO : Tonic movements in open field (categories)
URIN : Number of urine spots
FAEC : Number of fecal boli

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=MALE TEST=FOB GROUP=Control ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
32	1	1	1	0	1	0	0
34	1	1	1	0	0	0	0
36	1	1	1	0	0	0	0
38	1	1	1	0	0	0	0
40	1	1	1	0	0	0	0
62	1	1	1	0	0	0	0
64	1	1	1	0	1	0	0
66	1	1	1	0	0	0	0
68	1	1	1	0	0	0	0
70	1	1	1	0	0	0	0

---------- SEX=MALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
2	1	1	1	0	0	0	0
4	1	1	1	0	0	0	0
6	1	1	1	0	0	0	0
8	1	1	1	0	1	0	0
10	1	1	1	0	0	0	0
72	1	1	1	0	0	0	0
74	1	1	1	0	0	0	0
76	1	1	1	0	0	0	0
78	1	1	1	0	0	0	0
80	1	1	1	0	0	0	0

---------- SEX=MALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
12	1	1	1	0	0	0	0
14	1	1	1	0	0	0	0
16	1	1	1	0	0	0	0
18	1	1	1	0	1	0	0
20	1	1	1	0	0	0	0
42	1	1	1	0	0	0	0
44	1	1	1	0	0	0	0
46	1	1	1	0	0	0	0
48	1	1	1	0	0	0	0
50	1	1	1	0	1	0	0

---------- SEX=MALE TEST=FOB GROUP=High-dose ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
22	1	1	1	0	0	0	0
24	1	1	1	0	1	0	0
26	1	1	1	0	0	0	0
28	1	1	1	0	0	0	0
30	1	1	1	0	0	0	0
52	1	1	1	0	0	0	0
54	1	1	1	0	0	0	0
56	1	1	1	0	0	0	0
58	1	1	1	0	0	0	0
60	1	1	1	0	0	0	0

SALIV : Salivation (rank score)
LACR : Lacrimation (rank score)
PUPIL : Pupil response (0=no, 1=yes)
PILO : Piloerection (0=no, 1=yes)
VOCAL : Vocalizations (0=no, 1/2=yes)
STEREO: Stereotypies (0=no, 1=yes)
BIZBEH: Bizarre behavior (0=no, 1=yes)

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=MALE TEST=FOB GROUP=Control ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
32	0	1	1	1	85.5	1605	1101
34	0	1	1	1	72.0	1242	688
36	0	1	1	1	57.0	1555	644
38	0	1	1	1	87.5	1786	750
40	0	1	1	1	79.0	1345	632
62	0	1	1	1	59.0	1544	721
64	0	1	1	1	65.5	1731	797
66	0	1	1	1	99.5	1525	1200
68	0	1	1	1	84.5	1656	925
70	0	1	1	1	105.5	1775	811

---------- SEX=MALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
2	0	1	1	1	120.0	1676	1115
4	0	1	1	1	104.5	1908	853
6	0	1	1	1	92.5	1183	754
8	0	1	1	1	133.0	1634	645
10	0	1	1	1	93.5	1672	984
72	0	1	1	1	122.0	1740	1051
74	0	1	1	1	88.0	2003	816
76	0	1	1	1	98.0	1769	972
78	0	1	1	1	94.5	1344	665
80	0	1	1	1	101.5	1687	803

---------- SEX=MALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
12	0	1	1	1	118.5	1578	1133
14	0	1	1	1	74.0	1786	743
16	0	1	1	1	65.5	1338	746
18	0	1	1	1	121.5	1560	865
20	0	1	1	1	109.0	1424	892
42	0	1	1	1	102.0	1700	782
44	0	1	1	1	120.5	1829	778
46	0	1	1	1	74.0	1698	1067
48	0	1	1	1	96.5	1621	628
50	0	1	1	1	90.0	1949	983

---------- SEX=MALE TEST=FOB GROUP=High-dose ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
22	0	1	1	1	81.0	1299	755
24	0	1	1	1	84.0	1921	825
26	0	1	1	1	121.0	1694	921
28	0	1	1	1	70.0	1269	955
30	0	1	1	1	96.0	1168	751
52	0	1	1	1	79.5	1415	947
54	0	1	1	1	98.0	1809	821
56	0	1	1	1	70.0	1321	698
58	0	1	1	1	146.0	1533	781
60	0	1	1	1	78.0	1813	774

GAIT : Gait abnormalities (categories)
GAITSC: Gait score (rank score)
MOBIL : Mobility score (rank score)
RIGHT : Righting reflex (rank score)
SPLAYM: Mean landing footsplay (mm)
FGRPM : Mean forelimb gripstrength (g)
HGRPM : Mean hindlimb gripstrength (g)

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=MALE TEST=FOB GROUP=Control ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
32	2	2	3	4	37.8
34	2	2	3	4	38.3
36	2	2	3	4	37.5
38	2	2	3	4	38.3
40	2	2	3	4	37.5
62	2	2	3	4	37.9
64	2	2	3	4	37.7
66	2	2	3	4	37.6
68	2	2	3	4	37.8
70	2	2	3	4	37.6

---------- SEX=MALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
2	2	2	3	4	37.4
4	2	2	3	4	37.6
6	2	2	3	3	37.3
8	2	2	3	5	37.4
10	2	2	3	3	37.5
72	2	2	3	4	38.0
74	2	2	3	3	37.7
76	2	2	3	4	37.6
78	2	2	3	4	37.7
80	2	2	3	4	37.7

---------- SEX=MALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
12	2	2	3	4	38.1
14	2	2	3	4	38.5
16	2	2	3	4	38.1
18	2	2	3	4	38.2
20	2	2	3	4	37.4
42	2	2	3	4	37.8
44	2	2	3	4	38.1
46	2	2	2	4	38.1
48	2	2	3	4	37.8
50	2	3	3	4	38.0

---------- SEX=MALE TEST=FOB GROUP=High-dose ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
22	2	2	3	4	38.5
24	2	2	3	4	37.7
26	2	2	3	4	37.5
28	2	2	3	5	NM[2]
30	2	2	3	4	37.7
52	2	2	3	4	38.4
54	2	2	3	4	37.4
56	2	2	3	3	37.9
58	2	2	3	4	38.3
60	2	2	3	4	38.5

APPR : Approach response (rank score)
TOUCH : Touch response (rank score)
CLICK : Click response (rank score)
TAIL : Tail pinch response (rank score)
TEMP : Body temperature (deg. C)

[2] *NM: Not Measured. Erroneously, the body temperature of this male was not recorded.*

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=FEMALE TEST=FOB GROUP=Control ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
11	2	1	18	4	2	2	1
13	1	1	18	4	2	2	1
15	2	1	21	4	2	2	1
17	1+2	1	28	5	2	2	1
19	3	4	18	4	2	2	1
41	2	1	16	4	2	2	1
43	2	1	39	5	2	2	1
45	3	4	16	4	2	2	1
47	3	4	22	4	2	2	1
49	1	1	12	4	2	2	1

---------- SEX=FEMALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
21	1+2	1	16	4	2	2	1
23	1+2	1	16	4	2	2	1
25	1+2	1	24	5	2	2	1
27	2	1	19	4	2	2	1
29	1+2	1	26	4	2	2	1
51	1+2	1	14	4	2	2	1
53	1+2	1	20	4	2	2	1
55	1	1	23	4	2	2	1
57	3	4	17	4	2	2	1
59	1+2	1	15	4	2	2	1

---------- SEX=FEMALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
31	1	1	14	4	2	2	1
35	1	1	19	4	2	2	1
37	2	1	19	4	2	2	1
39	1	1	18	4	2	2	1
61	2	1	19	4	2	2	1
63	2	1	18	4	3	3	1
65	1	1	15	4	2	2	1
67	1+2	1	28	4	3	2	1
69	2	1	13	4	2	2	1

---------- SEX=FEMALE TEST=FOB GROUP=High-dose ----------

ANIMAL	POST	PALPC	REAR	AROUS	REMOV	HAND	PALPH
1	1+2	1	27	4	2	2	1
3	3	4	18	4	2	2	1
5	1	1	16	4	2	2	1
7	1+2	1	22	4	3	2	1
9	3	4	14	4	2	2	1
71	2	1	26	4	2	2	1
73	1	1	19	4	2	2	1
75	2	1	36	5	2	2	1
77	1	2	18	4	2	2	1
79	1	1	15	4	2	2	1

POST : Homecage posture (categories)
PALPC: Palpebral closure in homecage (rank score)
REAR : Number of rears
AROUS: Arousal (rank score)
REMOV: Ease of removal (rank score)
HAND : Handling reactivity (rank score)
PALPH: Palpebral closure during handling (rank score)

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=FEMALE TEST=FOB GROUP=Control ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
11	0	0	0	0	0	0
13	0	0	0	0	0	0
15	0	0	0	0	0	0
17	0	0	0	0	2	0
19	0	0	0	0	4	0
41	0	0	0	0	0	0
43	0	0	0	0	12	0
45	0	0	0	0	6	0
47	0	0	0	0	3	0
49	0	0	0	0	0	0

---------- SEX=FEMALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
21	0	0	0	0	0	0
23	0	0	0	0	0	0
25	0	0	0	0	0	0
27	0	0	0	0	0	0
29	0	0	0	0	0	0
51	0	0	0	0	0	0
53	0	0	0	0	6	0
55	0	0	0	0	0	0
57	0	0	0	0	1	1
59	0	0	0	0	0	0

---------- SEX=FEMALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
31	0	0	0	0	0	0
35	0	0	0	0	2	0
37	0	0	0	0	0	0
39	0	0	0	0	8	0
61	0	0	0	0	4	0
63	0	0	0	0	4	0
65	0	0	0	0	0	0
67	0	0	0	0	3	0
69	0	0	0	0	1	0

---------- SEX=FEMALE TEST=FOB GROUP=High-dose ----------

ANIMAL	CLONC	CLONO	TONC	TONO	URIN	FAEC
1	0	0	0	0	1	0
3	0	0	0	0	0	0
5	0	0	0	0	0	0
7	0	0	0	0	0	0
9	0	0	0	0	0	0
71	0	0	0	0	0	0
73	0	0	0	0	21	0
75	0	0	0	0	5	0
77	0	0	0	0	0	0
79	0	0	0	0	0	0

CLONC: Clonic movements in homecage (categories)
CLONO: Clonic movements in open field (categories)
TONC : Tonic movements in homecage (categories)
TONO : Tonic movements in open field (categories)
URIN : Number of urine spots
FAEC : Number of fecal boli

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=FEMALE TEST=FOB GROUP=Control ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
11	1	1	1	0	0	0	0
13	1	1	1	0	0	0	0
15	1	1	1	0	0	0	0
17	1	1	1	0	2	0	0
19	1	1	1	0	0	0	0
41	1	1	1	0	0	0	0
43	1	1	1	0	0	0	0
45	1	1	1	0	1	0	0
47	1	1	1	0	0	0	0
49	1	1	1	0	0	0	0

---------- SEX=FEMALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
21	1	1	1	0	0	0	0
23	1	1	1	0	0	0	0
25	1	1	1	0	0	0	0
27	1	1	1	0	0	0	0
29	1	1	1	0	0	0	0
51	1	1	1	0	0	0	0
53	1	1	1	0	0	0	0
55	1	1	1	0	0	0	0
57	1	1	1	0	0	0	0
59	1	1	1	0	0	0	0

---------- SEX=FEMALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
31	1	1	1	0	0	0	0
35	1	1	1	0	0	0	0
37	1	1	1	0	0	0	0
39	1	1	1	0	0	0	0
61	1	1	1	0	0	0	0
63	1	1	1	0	2	0	0
65	1	1	1	0	0	0	0
67	1	1	1	0	1	0	0
69	1	1	1	0	0	0	0

---------- SEX=FEMALE TEST=FOB GROUP=High-dose ----------

ANIMAL	SALIV	LACR	PUPIL	PILO	VOCAL	STEREO	BIZBEH
1	1	1	1	0	0	0	0
3	1	1	1	0	0	0	0
5	1	1	1	0	0	0	0
7	1	1	1	0	1	0	0
9	1	1	1	0	1	0	0
71	1	1	1	0	0	0	0
73	1	1	1	0	0	0	0
75	1	1	1	0	0	0	0
77	1	1	1	0	0	0	0
79	1	1	1	0	0	0	0

SALIV : Salivation (rank score)
LACR : Lacrimation (rank score)
PUPIL : Pupil response (0=no, 1=yes)
PILO : Piloerection (0=no, 1=yes)
VOCAL : Vocalizations (0=no, 1/2=yes)
STEREO: Stereotypies (0=no, 1=yes)
BIZBEH: Bizarre behavior (0=no, 1=yes)

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=FEMALE TEST=FOB GROUP=Control ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
11	0	1	1	1	119.0	1374	695
13	5	2	1	1	74.5	1316	576
15	0	1	1	1	106.0	1200	550
17	5	2	1	1	62.5	1031	641
19	0	1	1	1	81.0	1076	520
41	0	1	1	1	114.5	1592	714
43	5	2	1	1	70.0	1589	503
45	0	1	1	1	105.5	1641	665
47	0	1	1	1	106.5	1343	505
49	0	1	1	1	109.0	1241	553

---------- SEX=FEMALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
21	0	1	1	1	129.0	1537	667
23	0	1	1	1	90.0	1206	649
25	5	2	1	1	61.0	1117	538
27	0	1	1	1	74.0	1441	809
29	0	1	1	1	116.0	1404	560
51	0	1	1	1	68.5	1624	777
53	0	1	1	1	137.5	1687	562
55	0	1	1	1	123.0	1117	717
57	0	1	1	1	118.0	1348	745
59	5	2	1	1	61.5	1279[3]	486

---------- SEX=FEMALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
31	0	1	1	1	91.5	1161	637
35	0	1	1	1	58.5	1153	571
37	0	1	1	1	101.0	1434	650
39	0	1	1	1	111.0	1464	708
61	0	1	1	1	76.5	1351	673
63	0	1	1	1	60.0	1433	409
65	0	1	1	1	118.5	1427	803
67	0	1	1	1	107.5	1554	643
69	0	1	1	1	103.0	1160	616

---------- SEX=FEMALE TEST=FOB GROUP=High-dose ----------

ANIMAL	GAIT	GAITSC	MOBIL	RIGHT	SPLAYM	FGRPM	HGRPM
1	0	1	1	1	53.0	1183	741
3	0	1	1	1	98.5	1354	667
5	0	1	1	1	120.0	1164	667
7	0	1	1	1	73.0	1328	796
9	0	1	1	1	102.0	1537	610
71	0	1	1	1	97.0	1029	508
73	0	1	1	1	119.0	1575	450
75	0	1	1	1	99.5	1328	665
77	0	1	1	1	129.0	1402	652
79	0	1	1	1	107.5	1252	660

GAIT : Gait abnormalities (categories)
GAITSC: Gait score (rank score)
MOBIL : Mobility score (rank score)
RIGHT : Righting reflex (rank score)
SPLAYM: Mean landing footsplay (mm)
FGRPM : Mean forelimb gripstrength (g)
HGRPM : Mean hindlimb gripstrength (g)

[3] *This female did not hold the t-bar firmly during gripstrength measurements. In this case, the mean forelimb gripstrength was determined from only 2 valid measurements instead of 3.*

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY

APPENDIX II: DATA PER INDIVIDUAL

---------- SEX=FEMALE TEST=FOB GROUP=Control ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
11	2	2	3	3	38.6
13	2	2	3	4	38.5
15	2	2	3	3	38.4
17	2	2	2	4	39.1
19	2	2	3	3	39.2
41	2	2	3	3	38.5
43	2	2	3	3	39.0
45	2	2	3	3	37.8
47	2	2	3	4	38.5
49	2	2	3	4	37.8

---------- SEX=FEMALE TEST=FOB GROUP=Low-dose ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
21	2	2	3	3	38.7
23	2	2	3	3	38.8
25	2	2	2	4	38.4
27	2	2	3	3	38.8
29	2	2	3	2	38.8
51	2	2	3	4	38.4
53	2	2	3	4	38.9
55	2	2	3	3	38.3
57	2	2	3	4	38.7
59	2	2	3	4	38.3

---------- SEX=FEMALE TEST=FOB GROUP=Mid-dose ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
31	2	2	3	3	38.7
35	2	2	2	3	38.4
37	2	2	2	4	39.2
39	2	2	3	3	39.0
61	2	2	3	4	38.7
63	2	2	3	4	38.5
65	2	2	3	3	38.1
67	2	2	3	2	38.7
69	2	2	3	3	38.1

---------- SEX=FEMALE TEST=FOB GROUP=High-dose ----------

ANIMAL	APPR	TOUCH	CLICK	TAIL	TEMP
1	2	2	2	3	38.7
3	2	2	3	4	38.9
5	2	2	3	3	38.5
7	2	2	2	4	39.1
9	2	2	3	4	39.1
71	2	2	3	3	38.8
73	2	2	3	3	38.8
75	2	2	2	4	38.9
77	2	2	2	4	38.5
79	2	2	3	3	37.9

APPR : Approach response (rank score)
TOUCH : Touch response (rank score)
CLICK : Click response (rank score)
TAIL : Tail pinch response (rank score)
TEMP : Body temperature (deg. C)

Annex 13: Neurobehavioral testing

MOTOR ACTIVITY ASSESSMENT

APPENDIX III: DATA PER INDIVIDUAL

---------- SEX=MALE ZONE=ARENA TEST=MAA GROUP=CONTROL ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
32	696	666	498	353	259	2472
34	1064	457	59	303	191	2075
36	960	1045	454	564	93	3116
38	712	449	495	3	0	1659
40	1040	854	655	231	275	3054
62	1082	640	491	321	267	2801
64	1080	775	661	278	293	3086
66	1137	815	915	948	785	4599
68	749	865	245	235	363	2456
70	1099	1111	207	379	3	2800

---------- SEX=MALE ZONE=ARENA TEST=MAA GROUP=LOW-DOSE ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
2	1384	881	824	467	445	4001
4	792	284	188	147	538	1950
6	905	687	402	553	57	2604
8	552	416	124	3	5	1100
10	1172	762	463	525	78	3001
72	1480	859	980	873	615	4806
74	1237	1064	519	693	638	4150
76	953	635	262	91	405	2347
78	543	704	463	668	44	2421
80	613	583	906	530	657	3288

---------- SEX=MALE ZONE=ARENA TEST=MAA GROUP=MID-DOSE ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
12	1193	621	479	233	110	2635
14	993	369	225	336	256	2178
16	885	808	400	327	180	2600
18	961	387	137	17	15	1518
20	580	755	561	431	215	2542
42	709	446	355	106	671	2287
44	585	863	549	411	602	3011
46	922	723	546	335	349	2874
48	847	538	469	365	167	2385
50	801	403	438	266	177	2085

---------- SEX=MALE ZONE=ARENA TEST=MAA GROUP=High-dose ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
22	1555	567	826	530	511	3990
24	992	566	277	581	444	2859
26	359	863	6	3	0	1232
28	697	608	331	13	3	1653
30	959	691	205	193	14	2062
52	914	777	685	524	293	3192
54	987	818	580	604	565	3555
56	1292	705	19	582	615	3213
58	1035	902	174	7	177	2295
60	302	342	282	0	43	970

INT_1-INT_5: distance moved (cm) per 6-min interval
TOTDM : total distance moved (cm)

Annex 13: Neurobehavioral testing

MOTOR ACTIVITY ASSESSMENT

APPENDIX III: DATA PER INDIVIDUAL

---------- SEX=FEMALE ZONE=ARENA TEST=MAA GROUP=CONTROL ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
11	1722	655	419	517	13	3326
13	2030	1543	1065	625	588	5850
15	1252	932	615	409	352	3560
17	1237	748	306	156	323	2770
19	1751	1152	667	424	589	4583
41	917	412	386	419	87	2222
43	2008	1403	838	613	539	5401
45	1144	706	481	245	464	3040
47	1188	656	531	0	422	2797
49	1764	1162	489	523	437	4375

---------- SEX=FEMALE ZONE=ARENA TEST=MAA GROUP=LOW-DOSE ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
21	1353	800	252	12	132	2548
23	1597	1062	878	361	141	4038
25	1522	882	690	503	259	3855
27	994	753	282	447	4	2480
29	2032	1113	564	687	231	4627
51	1768	972	732	556	852	4880
53	1312	1132	685	647	459	4236
55	1652	822	529	462	450	3914
57	1224	885	512	83	617	3320
59	1571	1252	1194	850	795	5663

---------- SEX=FEMALE ZONE=ARENA TEST=MAA GROUP=MID-DOSE ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
31	1786	1021	662	1002	470	4941
35	1111	817	726	71	7	2732
37	1579	669	608	720	364	3940
39	1598	943	666	346	9	3561
61	1174	771	521	611	368	3445
63	1445	907	950	555	347	4203
65	1279	914	803	666	289	3950
67	1247	1227	772	954	442	4643
69	777	624	429	195	687	2712

---------- SEX=FEMALE ZONE=ARENA TEST=MAA GROUP=HIGH-DOSE ----------

ANIMAL	INT_1	INT_2	INT_3	INT_4	INT_5	TOTDM
1	1667	1171	750	610	480	4678
3	912	931	865	607	316	3631
5	1297	876	680	690	676	4219
7	1478	1000	420	457	184	3539
9	1500	981	676	547	141	3845
71	1308	713	416	323	764	3523
73	1177	816	528	561	193	3275
75	1368	1012	370	305	0	3056
77	1275	918	410	230	200	3033
79	1145	486	626	366	140	2763

INT_1-INT_5: distance moved (cm) per 6-min interval
TOTDM : total distance moved (cm)

Annex 13: Neurobehavioral testing

FUNCTIONAL OBSERVATIONAL BATTERY[4]

OPERATIONAL DEFINITIONS

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August, 2000

[4] The Functional Observational Battery described herein is based on that used in the Collaborative Study on Neurotoxicity Assessment sponsored by the International Programme on Chemical Safety of the World Health Organization. This manual is adapted from that originally developed for the WHO/IPCS study and prepared by Dr. V. Moser, NSI Technology Services Corp. under contract to the Health Effects Research Laboratory, U.S. Environmental Protection Agency, April 1989.

Annex 13: Neurobehavioral testing

INTRODUCTION

The WHO/IPCS Functional Observational Battery (FOB) is a series of non-invasive observational and interactive measures designed to assess the neurobehavioral and functional integrity of the rat (see Table below).

Several types of data are generated in the FOB including continuous (e.g. body weight), rank order (e.g. gait score), count (e.g. number of boluses), descriptive (e.g. type of gait), and quantal (e.g. presence or absence of piloerection) types of measurements. Statistically, these types of data are handled differently, and the distinction must be clear when performing the FOB.

Summary of Measures in the FOB

Home cage and Open field	Manipulative	Physiologic
Posture (D)[a]	Ease of removal (R)	Body temperature (I)
Convulsions, tremors (D)	Handling reactivity (R)	Body weight (I)
Palpebral closure (R)	Palpebral closure (R)	
Lacrimation (R)	Approach response (R)	
Piloerection (Q)	Click response (R)	
Salivation (R)	Tail pinch response (R)	
Vocalizations (Q)	Touch response (R)	
Rearing (C)	Righting reflex (R)	
Urination (C)	Landing foot splay (I)	
Defaecation (C)	Forelimb grip strength (I)	
Gait (D,R)	Hindlimb grip strength (I)	
Arousal (R)	Pupil response (Q)	
Mobility (R)		
Stereotypy (D)		
Bizarre behavior (D)		

[a] *D=descriptive data* *R=rank order data* *Q=quantal data*
C=count data *I=interval or continuous data*

Annex 13: Neurobehavioral testing

OPERATIONAL DEFINITIONS AND SCORING CRITERIA

FOR INDIVIDUAL FOB MEASURES

CAGESIDE OBSERVATIONS

Home Cage Posture

The posture of the rat in the home cage at the moment that the observer approaches it (it may change postures in the few seconds during the observation period). Possible descriptors are:

1. sitting or standing normally
2. rearing, i.e. front paws are off the floor of the cage
3. asleep and/or lying on side and/or curled
4. flattened on belly and/or limbs extended
5. lying on side and/or limbs in air (may be rigid)
6. crouched or hunched over
7. head bobbing, up and down and/or side to side

Note that only 1, 2, and 3 are "normal" postures, i.e. are most commonly seen. Note also, that this is the only measure in the FOB were "abnormal" is distinguished from "normal". This distinction is made because there are many behaviors that a population of rats normally display, and as a consequence many different descriptions may be appropriate. More than one description is possible for this type of data and hence it may be necessary to combine terms to accurately describe an observed posture.

Involuntary Motor Movements

Involuntary motor movements are comprised of either clonus, a form of movement marked by alternate contraction and relaxation of muscles, or tonus, a state of continuous muscular contraction. Clonic and tonic movements can occur together, and more than one type of movement may be present. The various possible movements are as follows:

Clonus:

0. none
1. repetitive movements of mouth and jaws - a smacking of the lips which resembles chewing behavior
2. (normal) quivers of limbs, and/or ears, and/or head, and/or skin - refers to the fine twitches or shivers that often are seen in "normal" animals. If you are not familiar with this type of movement, think of the muscular actions of a horse with a fly on his back, or when you shiver from the cold.
3. mild tremors - fine tremors, or rhythmical and rapid contractions and relaxations of the muscles. Tremor may involve the whole body or be restricted only to the limbs.

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4. severe, and/or whole body tremors - a more severe form of '3', which usually encompasses the whole body but may just involve the limbs.

5. myoclonic jerks - rapid contractions and relaxations of the muscles. As opposed to tremors, these are not rhythmical but are more sporadic.

6. clonic convulsions - violent spasms, with the muscles alternately contracting and relaxing. These may be considered as a severe combination of '4' and '5', above.

7. wet dog shakes - rhythmic shaking resembling a wet dog shaking, beginning from the head and progressing down the body.

Tonus

These contractions may last from a second to minutes

0. none

1. contraction of extensors such that limbs are rigid and extended

2. opisthotonus - head and body rigidly arched backwards, i.e. a tetanic spasm in which the spine and extremities are bent backwards

3. emprosthotonus - head and body rigidly extended forward, i.e. a tetanic contraction of the flexor muscles, curving the back and bending the body forward

4. explosive jumps into the air with all feet leaving the surface

5. severe clonic and tonic convulsions resulting in dyspnea, postictal depression, or death – resembling grand mal-seizures seen in humans.

Vocalizations

Vocalizations are scored if the animal 'peeps' or otherwise vocalizes during removal from the home cage and/or during handling.

0. none

1. vocalizations during either removal from the home cage or handling.

2. vocalizations during removal from the home cage and handling.

If vocalizations are spontaneous or unprovoked, i.e. vocalizations which are not elicited by handling or other stimulation, they should be scored under the "other" category described below. These may occur any time during FOB testing (also in the open field).

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Palpebral Closure

Palpebral closure is a rating of the degree of closure of the eyelids, both in the home cage and while the rat is being handled. Note that any of these rankings may occur in normal rats, depending on the state of wakefulness at the time of testing. Chemically-induced ptosis, or drooping eyelids, may or may not be reversed by handling or otherwise stimulating the rat, depending on the chemical used. Palpebral closure is ranked as follows:

1. eyelids wide open
2. eyelids slightly drooping
3. eyelids drooping approximately halfway
4. eyelids completely shut

Ease of Removal

The rat is removed from the cage by holding the rat under the shoulders (not by the tail). The rat is handled gently and always supported under the shoulders.

Ease of removal is a rating of the rat's reactivity to being removed from its home cage. Examples for the scoring of this measure are given below, but the descriptions for each are not all-inclusive. The observer should think of this as a progression from '1' (very easy) to '6' (extremely difficult), with '2' through '5' being graded steps in between.

1. very easy - rat does not move, may sit quietly, allowing the observer to pick it up with no resistance
2. easy - rat is still easy to pick up, but shows some slight reactions such as vocalizing and/or slowly walking from one side of the cage to the other
3. moderately difficult - rat may rear and follow the observer's hand, and/or move more quickly form one side of the cage to the other, making it somewhat difficult to grasp the rat from behind the shoulders
4. rat freezes - this is a familiar reaction of a rat that is evidenced by pronounced flinch or muscle contractions. Though the rat may still be fairly easy to remove, this reaction receives a higher reactivity score. This reaction may also be accompanied by vocalizations.
5. difficult - rat may dart around the cage, and/or kick energetically, and/or rear often, making it difficult for the observer to get a firm hold on the rat. Rat may or may not vocalize.
6. very difficult - the rat may show aggressiveness in the form of tail and/or throat rattles, and/or vocalizations. The rat may actually lunge at the hand, as opposed to the avoidance behaviors shown in '3', '4', and '5'.

Reactivity to Being Handled

Reactivity to being handled is a subjective measure of the rat's reactions while being held in the observer's hand. The scoring criteria range from '1' (the rat is docile) to '4' (the rat is hyperreactive). This should not be considered a rating of how well the observer can handle rats.

1. low - rat shows no resistance to being held, and is quiet in the observer's hand

2. moderately low - there is a slight resistance, such as occasional squirming and/or vocalizations

3. moderately high - the rat may be tense, and/or freeze, and/or vocalize, and/or squirm more vigorously

4. high - rat may be difficult to hold, and/or may be squirming and/or twisting vigorously, and/or attempting to bite and/or vocalizing

Lacrimation

Lacrimation is evidenced by wetness around the eyes, and is scored '1' to '3'. The tears may be clear, or red-tinged (termed chromodacryorrhea). If the latter is seen, this is recorded as a comment to the score. In some strains of rats, red porphyrin deposits are fairly common.

1. none

2. slight

3. severe

Salivation

Salivation is evidenced by wetness around the mouth, and may include the nose. It is scored '1' to '3'. Crustiness around the mouth and/or nose should be recorded as a comment to the score.

1. none

2. slight

3. severe

Piloerection

Piloerection refers to the body hairs standing on end. It can be differentiated from a scruffy or ungroomed coat by stroking the back of the rat in a rostral to caudal direction. Piloerection will still be apparent after stroking.

0. absent

1. present

Annex 13: Neurobehavioral testing

OPEN FIELD OBSERVATIONS

Open-field measurements are made while the rat is in a 77x55x7 cm open field in which it is free to move about. A stopwatch is used to time the observation period.

The rat is placed in the center of the open field. The surface is covered with clean absorbent paper, which is replaced after each rat is tested.

Vertically Directed Movement: Rears

A rear occurs when the front legs of the rat are lifted completely off the surface. This is a measure of the ability of the rat to place its weight on its haunches. Note that the rat does not necessarily have to raise itself up to a stretched position. Note also that grooming episodes may be counted as rears by this definition. Rears also occur when the rat places its front paws or legs on the side or lip of the open field. Additional rears are counted after each time that one or both front paws are placed on the surface, however briefly. The amount of rearing is highly dependent on the strain of rat, and habituates quickly with repeated testing.

Gait Description and Gait Scoring

Gait characteristics are described both categorically and ranked. If there is any gait other than "normal" (i.e. Gait description = 0), there will then be a score of greater than '1' for the gait severity score. Note, too, that "normal" rats may show slight gait alterations, such as tiptoe walking or ataxia (sometimes seen in large rats). While the gait descriptions numbered '1' to '5' actually describe gait, or movement, '6' and '7' also describe body posture, which can be used either in addition to, or instead of, a gait.

If the rat did not move during the entire observation period, it may be gently prodded in order to observe its gait. If the rat still does not move, testing should proceed since gait features may be evaluated when sensorimotor reactivity is tested or landing foot splay is measured. If the rat does not move under any circumstance, one may consider that to be a rating of '4' (since it is too impaired to move) and a gait of '6' to '7' (whichever is appropriate to describe the body posture).

Gait descriptions are as follows:

0. none

1. ataxia, and/or excessive sway, and/or rocking, and/or lurching - any sort of unsteady locomotion. These may appear to be but are not always problems with equilibrium and balance

2. hindlimbs show exaggerated and/or overcompensated movements, and/or drag, and/or are splayed - this describes abnormalities which primarily involve the hindlimbs, although there are several different types of gait which may fall into this category

3. feet markedly point outwards from body - this refers primarily to placement of the hind feet, not the hindlimbs

4. forelimbs drag, and/or show abnormal positioning, and/or are unable to support weight – whereas '2' refers to abnormalities dealing with the hindlimbs, this refers primarily to problems with the forelimbs - in movement, placement, or ability to support the rat's own weight

5. walks on toes - this refers to walking with the heel of the hind feet off the surface. We have seen this under "normal" conditions, especially in rats who are somewhat excitable

6. hunched or crouched body position - this is a hunched over, curved body position which may be seen with any of the above gaits

7. body drags and/or is flattened against surface - this body position, in contrast to '6', is one in which the body is flat and the stomach may be dragging the surface. This may also be seen with any of the above gaits.

The severity of gait abnormalities are scored as:

1. normal, i.e. no abnormal gait

2. slightly abnormal

3. moderately abnormal

4. severely abnormal

Mobility Score

The mobility score is a measure of the degree to which an abnormal gait interferes with the animal's ability to get around in the open field. It is a ranking of how well the animal gets about despite whatever gait changes are seen. An animal with a normal gait score of 1 will also have a normal mobility score of 1. However, an animal showing a gait disturbance may show a slight to severe mobility problem independent of the severity of gait abnormality. A rat with a peripheral neuropathy, for example, may show virtual paralysis of the hindlegs and receive a '4' (i.e. severely abnormal) on the gait severity score, but show only a slight or moderate impairment in getting about the open field.

Mobility is scored as:

1. normal

2. slightly impaired

3. somewhat impaired

4. totally impaired

Arousal

Arousal is a ranking of the level of unprovoked activity and alertness in the open field during the observation period. The observer may think of this as the attentiveness or vigilance of the rat, which is not to be assumed to be only locomotion or motor activity. For instance, a rat that is very tense and makes only quick darting motions, with otherwise little overall motor activity, might receive a rank of '5'. The distinction is important to make, since this measure is not meant to replace motor activity tests using automated devices.

Arousal is scored as:

1. very low - rat may be in a stupor and/or coma, and/or be prostrate

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2. low - rat may be somewhat sluggish, and/or showing some head and body movement, but not very alert or attentive

3. somewhat low - rat may be slightly sluggish, and/or have some exploratory movements with periods of immobility

4. normal - rat is alert, and may spend the full observation time showing exploratory behavior. Note that this is not the only rating that a "normal" rat could show; in fact, this activity may habituate and arousal scores often decrease with repeated testing.

5. somewhat high - rat shows slight excitement, and/or tenseness, and/or is excited, and/or shows sudden darting and/or freezing

6. very high - rat is very alert, and/or is very excited and/or tense, and/or shows sudden bouts of running or quick body movements.

Stereotypy

Stereotypy is defined as the pronounced repetition of specific gestures or movements, i.e. it is the presence of excessive or repetitive behaviors that appear purposeless. Examples include, but are not limited to, circling in tight circles, stereotypic grooming whose duration continues well beyond the normal grooming action, persistent pacing especially in one particular direction or around the perimeter of the open field, repetitive sniffing at one area, or head weaving back and forth. The behaviors themselves are normal; e.g. all rats walk around in a circle or occasionally groom. It is rather the frequency and persistence of these behaviors that distinguish them as being stereotypic.

0. absent

1. present

Bizarre Behavior

This classification includes any unusual behavior that is not normally seen in rats - this is the distinction between bizarre and stereotypic behaviors. Examples include, but are not limited to, self- mutilation (or evidence of, e.g. missing digits or bite marks on the tail), retropulsion (marked backwards movements), Straub tail (tail is stiff and is held in a vertical position), writhing (a twisting motion or spasmodic pulling in of the abdominal muscles), or flopping (motions similar to a fish on the ground).

0. absent

1. present

Annex 13: Neurobehavioral testing

Defecation and Urination

Excretion, the number of fecal boluses and urine pools on the absorbent paper, is counted at the end of the observation period. If diarrhoea is present, 'D' is listed instead of giving a number under defecation. Likewise, if there is a very large pool of urine, indicative of polyuria, 'X' is listed under urination.

Any change in colour, presence of mucous or other observations concerning the elimination products, is recorded as a comment.

STIMULUS REACTIVITY MEASUREMENTS

All the reactivity tests are intended to rate the sensory responses to stimuli of different modalities – however, since the motor output is the response being assessed, this has a large motor component as well.

These tests are carried out while the rat is freely moving in the open field. The rat may have to be positioned properly in order to perform the test. For instance, it may be difficult to perform the approach response if the rat is facing a corner.

It is important to remember that the responses are rank-order. Thus, two responses may differ, but being on the same level of degree of excitability, thereby earning the same rating. In all the responses, a '1' indicates no reaction to the stimulus, and a '5' indicates an extreme, hyperreactive response.

Approach Response

The rat is approached at nose-level with the end of a blunt object, such as a pen or pencil, and it is held approximately 3 cm from the face for 4 seconds. This allows the rat time to make a response.

The approach response is ranked '1' through '5' as follows:

1. no reaction
2. some slight reaction - rat may slowly approach the object and/or sniff it and/or turn away. Rat may vocalize with little or no movement
3. somewhat more reaction - the rat may freeze or flinch, i.e. actual muscle contractions. Rat may or may not vocalize
4. moderate reaction - more energetic response than '2' or '3'. Rat may quickly approach the object, and/or jump. Rat may or may not vocalize
5. exaggerated reaction - rat may jump, and/or bite at the object, and/or attack the object (or the observer's hand). Rat may or may not vocalize.

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Touch Response

This is performed after the approach response. Coming in from the side, the rump of the rat is touched gently with a blunt object, such as a pen or pencil. The touch should be brief (1-2 seconds) and deliberate (but not forceful enough to knock the rat over).

Touch response scoring includes:

1. no reaction
2. some slight reaction - rat may slowly turn just the head or the body, and/or walk away. Rat may vocalize with little or no movement
3. somewhat more reaction - the rat may freeze or flinch, i.e. actual muscle contractions. Rat may or may not vocalize
4. moderate reaction - more energetic response than '2' or '3'. Rat may quickly turn, and/or jump. Rat may or may not vocalize
5. exaggerated reaction - rat may jump or turn quickly, and/or attack, and/or bite at the object or the observer's hand. Rat may or may not vocalize.

Click Response

A metal clicker is positioned approximately 5 cm above the back of the rat and a sudden sound is made. It is avoided to have the clicker in the rat's field of vision.

The click response is scored as follows:

1. no reaction
2. some slight reaction - evidence that the noise was heard, such as an ear flick and/or turning the head towards the sound. Rat may vocalize with little or no movement.
3. somewhat more reaction - the rat may freeze or flinch, i.e. actual muscle contractions. Rat may or may not vocalize.
4. moderate reaction - more energetic response than '2' or '3'. Rat may jump, and/or turn around. Rat may or may not vocalize.
5. exaggerated reaction - rat may twist and/or jump quickly, and/or bite at the object, and/or attack the object (or the observer's hand). Rat may or may not vocalize.

Tail Pinch Response

This test is performed last. Metal tweezers are used to squeeze the tail approximately 2-3 cm from the tip. This distance may vary slightly, depending on the size of the rat - the very tip of the tail is not used since it is relatively insensitive.

Annex 13: Neurobehavioral testing

The tail pinch response is scored as follows:

1. no reaction
2. some slight reaction - rat may slowly turn and/or walk away and/or sniff at the stimulus. Rat may vocalize with little or no movement
3. somewhat more reaction - the rat may freeze or flinch, i.e. actual muscle concentrations. Rat may or may not vocalize
4. moderate reaction - more energetic response than '2' or '3'. Rat may jump, and/or turn around.Rat may or may not vocalize
5. exaggerated reaction - rat may jump and/or turn quickly, and/or bite at the stimulus, and/or attack the stimulus (or the observer's hand). Rat may or may not vocalize.

OTHER INTERACTIVE TESTS

Pupil Response

The animal is brought into a darkened part of the testing room. A narrow beam of light (e.g. from a penlight flashlight or other suitable source) is brought in from the side of the rat's head. Constriction of the pupil is noted with a '1', and '0' indicates lack of response. Even if the pupil is difficult to see, the contraction itself is usually visible. If the pupil is already markedly constricted, "miosis" is indicated as a comment. Likewise, if the pupil appears markedly dilated, "mydriasis". is indicated. The pupil response could be absent, however, without either of these states being obvios.

0. absent
1. present

Righting Reflex

Rat is held supine, with the observer's hands under the back and shoulders to support it, then dropped from approximately 30 cm on to a 1-2 cm thick polyurethane pad. The rat should flip over and land on its feet. The observer scores the ease of landing. Note, if the rat is paralysed or severely affected, this test and the landing foot splay test are not carried out, when injury to the rat might occur because of debilitation.

The righting reflex is scored as follows:

1. normal, i.e. rat lands on its feet
2. slightly uncoordinated
3. lands on side
4. lands on back - this score should not be obtained often, since this would indicate a totally impaired rat who could be injured by the test procedure. It is hoped that the doses used would not be severely intoxicating, but if the occasion arises, judgement should be used to decide whether to test all the rats who are so affected.

Annex 13: Neurobehavioral testing

Forelimb and Hindlimb Gripstrength

Grip strength is measured using commercially available strain gauges with T-bars for the rat to grab. The force at which the rat releases its hold on the screen or T-bar is the measure of grip strength.

For forelimb grip strength, the rat is held until it grabs the screen or bar, then pulled back smoothly and quickly until the rat's grip is broken. A slight pause may be necessary to insure that the rat's digits are properly curled around the mesh or bar before beginning the pulling motion.

For the hindlimb grip strength, the hind feet of the rat are placed on the bar and the rat is pulled gently by the tail until the rat engages the bar. A slight pause may be necessary to assure that the rat's digits are properly curled around the mesh or bar before beginning the pulling motion. The rat is pulled backwards smoothly and quickly until the rat's grip is broken.

For both measures, several trials may be needed to get two or three valid readings.

Body Temperature

Body temperature is measured using a rectal probe.

Landing Foot Splay

The fourth digit pads (on the outer portion of the foot) are dabbed with (non-toxic) paint. The rat is held in a prone position (i.e. the legs should not be dangling) and dropped twice from approximately 40 cm onto a piece of paper. The observer immediately indicates the paint spots where the rat landed. Sometime later, the distance between the centers of the marks is measured and record on the data sheet. The average of the two readings is used.

Comments

This is a catchall category for all other findings or observations which are not adequately described above. These items may or may not be a consequence of the chemical treatment. This includes torn toe nails, broken teeth, soiled fur, fur discoloration, convulsions at any time other than in the home cage or on the open field, crustiness around the face or eyes, red pigmented excretions from eyes, exophthalmus, increased or decreased muscle tone, bite marks, emaciation, hunched posture, vocalization on handling or death.

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TRISKELION
RESEARCH FOR BETTER LIVING

STUDY PLAN

P20880/02

Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

DATE	18 October 2016
AUTHOR	A.E. Wallinga, PhD
SPONSOR	Friesland Campina Innovation Bronland 20 6708 WH Wageningen The Netherlands
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Annex 14: Study plan and amendments

[redacted]

[redacted]

Approval of the Study Plan

[redacted]

Study director

[redacted] (b) (6)

18 oct 2016

A.E. Wallinga, PhD

[redacted]

Program manager

[redacted] (b) (6)

18 10 2016

M.J. Appel, PhD, ERT

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Sponsor

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18 oct 2016

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[redacted]

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[redacted]

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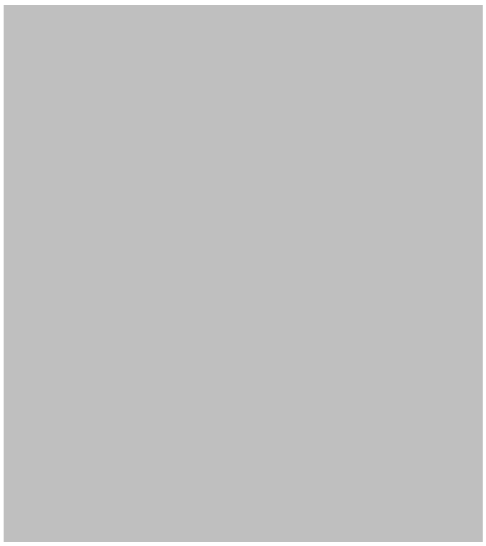
Abbreviations

AWB	Animal Welfare Body
GD	Gestation Day
GLP	Good Laboratory Practice
OECD	Organization for Economic Co-operation and Development
QA	Quality Assurance
QAU	Quality Assurance Unit
SPF	Specific pathogen free



Annex 14: Study plan and amendments

1 General

1.1 Study Sponsor

Sponsor:	Friesland Campina Innovation Bronland 20 6708 WH Wageningen The Netherlands
Monitor:	D. Delsing, PhD
Phone:	+31(0)6 5359 8111
Email:	dianne.delsing@frieslandcampina.com

1.2 Test facility

Triskelion B.V.	www.triskelion.nl
Postal address:	P.O. Box 844 3700 AV Zeist The Netherlands
Location:	Utrechtseweg 48 3704 HE Zeist The Netherlands
Phone:	+31 88 866 2800
Study director:	A.E. Wallinga, PhD alinde.wallinga@triskelion.nl Phone: +31 88 866 6767
Scientific contributor(s):	A.J. Kleinnijenhuis (Test substance analyses in diet) M. Otto (Neurobehavioral testing) M.V.W. Wijnands, PhD, DVM (Pathology)

1.3 Good Laboratory Practice and Quality Assurance

All study activities performed by Triskelion will be conducted according to the Organisation for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice (GLP), as revised in 1997, Paris, ENV/MC/CHEM(98)17.
The OECD principles of GLP are accepted by Regulatory Authorities throughout the European Community, USA and Japan. Chemical analysis for the verification of the test substance identity and properties will not be performed in this study.

The QAU of Triskelion will audit the study plan, the conduct of the study, the raw data and the report. Experimental activities not audited in this study will be audited in other studies. The statement of the QAU will specify the items, the dates of audits and the dates of reports to management and to the study director. This statement will also show dates of audits of other studies for study activities not audited in the present study. Representatives of the sponsor or regulatory authorities may conduct additional inspections of the test facility and/or the raw data.

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1.4 Proposed time schedule

Arrival of the time-mated females:	2 November 2016
Allocation offspring to experimental groups:	Preferably 30 November – 4 December 2016
Start of the treatment (day 0):	5 December 2016
Termination of the in-life phase:	6 March (males) and 7 March (females) 2017
Interim data (Email)[1]:	Within about two weeks after termination of the in-life phase
Unaudited draft report:	30 June 2017[2]
Final report:	15 August 2017, provided that the sponsor's comments on the draft report are timely available. If no comments of the sponsor are received, the final report will be issued about four months after issuing the draft report.

[1] Containing available, unaudited data.
[2] Provided that there will be no major extension of pathological examinations.

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2 Introduction

2.1 Objective

The objective of this study is to provide data on the safety of a 2'-Fucosyllactose. For this purpose the test substance will be examined in a sub-chronic oral toxicity study in rats of both sexes.
Because the test substance is intended for use in infant formula, the study will be conducted with juvenile rats. Time-mated female Wistar rats will be obtained. 2'-Fucosyllactose will be administered to their offspring starting shortly after weaning (the dams will not be exposed to the test substance). The test substance will be incorporated at constant concentrations in the diet and fed to the rats during 13 weeks. The study is intended to provide information on the major toxic effects, indicate target organs and provide an estimate of a no-observed-adverse-effect level of exposure (NOAEL).

2.2 Applicable guidelines

This study plan has been drafted in accordance with the following guideline(s):

- OECD Guideline for the Testing of Chemicals 408. Repeated dose 90-day oral toxicity study in rodents, adopted 21st September 1998.
- B.26. Sub chronic oral toxicity test. Repeated dose 90-day oral toxicity study in rodents. Annex 5D to Commission Directive 2001/59/EC, Official Journal of the European Communities, L225, 21.8.2001.

2.3 Animal welfare

The welfare of the animals will be maintained in accordance with the general principles governing the use of animals in experiments of the European Communities (Directive 2010/63/EU) and Dutch legislation (The revised Experiments on Animals Act, 2014). This includes licensing of the project by the Central Committee on Animal Experimentation (project license 3660) and approval of the study by the Triskelion Animal Welfare Body (AWB number TRIS-185).
To reduce the number of animals used for research, any remaining live animals may be used for training purposes.

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3 Amendments and deviations

Intended changes to the authorized study plan will be documented in study plan amendments. Unintended deviations from the study plan will be documented in the study file and in the final report.

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4 Materials and methods

4.1 Safety measures

In handling the test substance, no other precautions need to be taken than those described in the General Safety Instructions of the testing facility. These measures include wearing a mask, gloves and protective clothing when handling the test substance, or during the preparation and handling of the experimental diets.

4.2 Test substance

2'-Fucosyllactose has the following characteristics:

Name[1,2]	: 2'-Fucosyllactose
Chemical name[1]	: 2'-FL
Chemical formula[1]	: $C_{18}H_{32}O_{15}$
CAS Reg No. [1]	: 41263-94-9
Batch number[1]	: MRS02
Appearance[1]	: White powder
Purity[1]	: 94%
Storage conditions[1]	: 2 – 10 °C, protected from light
Quantity	: 20 kg
Date of receipt	: 19 July 2016
Expiry date[1]	: 15 July 2018
Supplier	: Sponsor
Triskelion Dispense number	: 160161

[1] Information provided by the sponsor
[2] Certificate(s) of analysis, if provided by the sponsor, will be included in the report

Remaining test substance will be retained for at least one month after issuing the final report of the study and then returned to the sponsor.

4.3 Test system

The study will be conducted with albino rats. The rat will be used because this species is considered suitable for this type of study, and is usually required by regulatory agencies. The Han rat strain will be used because it is routinely used at the test facility for this type of studies.

Time-mated females

16 Time-mated female Wistar Han IGS rats (Crl:WI(Han)) will be obtained from a colony maintained under SPF conditions at Charles River Deutschland, Sulzfeld, Germany. The time-mated female rats will be at least 10 weeks of age and around gestation day (GD)15 of pregnancy when arriving at the test facility. These female rats will not be exposed to the test substance.
Upon arrival, the time-mated female rats will be taken to a quarantine room and checked for overt signs of ill health and anomalies. During the quarantine period, serological investigation of the microbiological status will be conducted in a few randomly chosen rats of the batch

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delivered. If the results of serology are satisfactory, the rats will be transferred to their definitive room (or the quarantine room will be cleared for use as experimental room) and acclimatized to the laboratory conditions.

Offspring
For the 13-week study, allocated male and female offspring of the 16 time-mated females will be used. The allocated male and female offspring will preferably be between 21-24 days old at the commencement of the treatment period (rationale: the test substance is intended to be a component of nutrition for infants). Details on the selection and allocation of these rats are given under 'Animal allocation' in § 4.7.
The body weight variation at initiation of treatment should not exceed ±20% of the mean weight for each sex.

4.4 Experimental design with respect to time-mated female rats

16 Time-mated females will arrive around gestation day (GD)15 of pregnancy the test facility. These female rats will not be exposed to the test substance. Details on the test system are described in § 4.3.

Identification
The study will be identified as study 20880/02. After arrival in the test facility, the time-mated females will be identified by a transient mark on their tail. Each cage will be provided with a card showing the animal identification number, and the study code.

Animal husbandry
Conditions of the experimental room are described in § 4.9.1 'Animal room'. The time-mated females will be housed individually in macrolon cages with wood shavings (Lignocel) as bedding material and strips of paper (Enviro-dri) as bedding material.
Food and drinking water will be provided *ad libitum* from the arrival of the time-mated female rats until sacrifice. From their arrival, the time-mated female rats will receive a cereal-based (closed formula) rodent diet (VRF1 (FG)) from a commercial supplier (SDS Special Diets Services, Witham, England). Further details on the rodent diet and on the drinking water supplied are given in § 4.9.3.

General animal health
All time-mated females will be observed daily. All abnormalities or signs of ill health will be recorded. Any animal showing signs of severe health problems, particularly if death appears imminent, will be humanely killed.

Sacrifice
Shortly after weaning and allocation of the pups to the experimental groups, the dams will be killed by exsanguination from the abdominal aorta under CO_2/O_2 anesthesia or may be used for training purposes.

4.5 Administration of the test substance

The test substance will be administered to allocated male and female offspring, at constant concentrations in the diet for 13 consecutive weeks, 7 days per week (the animals will be kept

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on their test diet until overnight fasting prior to necropsy). Different dose groups will be fed diets containing different concentrations of the test substance in the diet. The oral route will be used because this is an anticipated route of exposure.
Details on the preparation, storage and refreshing of the experimental diets are given under 'Food and drinking water' in §4.9.3.

4.6 Experimental design, groups and dose levels

The study will comprise four groups of 10 males and 10 females each, viz. one control group kept on control diet and three test groups receiving different levels of 2'-Fucosyllactose added to this diet. The test substance will be added to the diet as indicated below:

Group	Color code	2'-Fucosyllactose	Number of males/ females
1 Control	white	0%	10 / 10
2 Low-dose	Blue	3 %[1]	10 / 10
3 Mid-dose	green	6 %[1]	10 / 10
4 High-dose	Red	10 %[1]	10 / 10

[1] These dose levels were selected in consultation with the sponsor, based on the results of a 14 day dose range finding study (20880/01).

4.7 Animal allocation and start of the treatment

On postnatal day (PN) 14 litter size and the sex of all pups will be determined. Also, pup weights will be measured, just to have a rough indication of the variability within and between litters.
On PN 21 the pups will be weaned and allocated to the different dosing groups. Hereto pups will be identified by a transient mark on their tail and individual pup weight will be measured. Subsequently, pups will be assigned to the different dosing groups, such that, as far as possible, each group will contain one male and one female pup of each litter.
The pups will be allocated by manual randomization to the experimental groups (see §4.6), taking into account body weight. Because not all dams may deliver on the same day, the allocation procedure may take several days. The treatment will be started after all groups are complete.
The remaining (surplus) pups will be killed by exsanguination from the abdominal aorta under CO_2/O_2 anesthesia or may be used for training purposes.
During the study, additional serological investigations of the microbiological status may be conducted if considered necessary.

4.8 Identification

The study will be identified as study 20880/02. Prior to initiation of treatment, the allocated rats will be identified by a transient mark on their tail. After allocation, the rats will be identified by a subcutaneous transponder with a unique identification number. Each cage will be provided with a colored card (see § 4.6 for color codes) showing the animal identification numbers, the cage number, the group code and the study code.

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4.9 Animal husbandry

4.9.1 Animal room

The animals will be housed under conventional conditions in one room. No other test system will be housed in the same room during the study. The room will be ventilated with about 10 air changes per hour and will be maintained at a temperature of 20-24°C and a relative humidity of at least 45% and not exceeding 65% other than during short periods (e.g. due to room cleaning). Lighting will be artificial with a sequence of 12 hours light and 12 hours dark.

4.9.2 Caging

After weaning at postnatal day 21 days of age, the animals will be kept in macrolon cages with wood shavings (Lignocel) as bedding material, and strips of paper (Enviro-dri) and a wooden block as environmental enrichment. They will be housed in groups of five, separated by sex. If necessary (e.g. because of conditional decline), animals in ill health may be housed individually. Towards the end of the study, the animals will temporarily be kept individually for collection of urine, FOB testing and motor activity assessment.

4.9.3 Food and drinking water

Food and drinking water will be provided *ad libitum* from the arrival of the time-mated female rats until the end of the study, unless precluded by the performance of certain laboratory investigations (see § 4.10).
The rats will receive a cereal-based (closed formula) rodent diet (VRF1 (FG)) from a commercial supplier (SDS Special Diets Services, Witham, England). Each batch of diet is analyzed by the supplier for nutrients and contaminants. The certificate of analysis pertaining to the batch(es) used in this study will be included in the study report.
From the start of treatment, controls will be kept on powdered VRF1 (FG) diet without test substance and the animals of the test groups will be kept on experimental diets prepared by mixing powdered VRF1 (FG) diet with the appropriate amounts of test substance (see § 4.6). The diets will be mixed in a mechanical blender.
Fresh batches of the experimental diets will be prepared about once per month and stored in a freezer (<-18°C) in plastic bags in portions sufficient for three to four days. The diets will be provided in stainless steel cans, covered by a perforated stainless steel plate to prevent spillage. The food in the cans will be replaced twice per week with fresh portions from the freezer.
Each cage will be supplied with domestic mains tap-water suitable for human consumption (quality guidelines according to Dutch legislation based on EC Council Directive 98/83/EC). The water will be given in polypropylene bottles, which will be cleaned weekly and filled as needed. Results of the routine physical, chemical and microbiological examination of drinking water as conducted by the supplier are made available to the test facility. In addition, the supplier periodically (twice per year) analyses water samples taken at the premises for a limited number of physical, chemical and microbiological variables. The results of the samples taken during or close to the conduct of this study will be given in the report.

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4.10 Observations, analyses and measurements

4.10.1 Analysis of the experimental diets

Analyses to determine the stability, homogeneity and content of the test substance in the diet will be conducted using a LC-MS method.
Before analysis of study samples, the analytical method will be validated to conform to the following acceptance criteria:

- Linearity: the correlation coefficient of the calibration curves should ≥ 0.996;
- Recovery: the mean recovery of the test substance from diet should be between 85% and 115% at each of the tested concentrations.
- Repeatability: the relative standard deviation in the percentage recovery of three spiked diet samples per concentration level should be ≤10%.

Specificity: the signal obtained for samples will be corrected for the signal obtained for blank samples in case the signal obtained for blank samples is ≥ 5% of the signal obtained for low-dose samples.

From each batch of diets prepared in the study, samples will be taken of all test diets and the control diet. Test diet samples might be temporarily stored at < -18°C prior to analysis.
The following analyses will be conducted during the study:

- In the first batch of prepared diets: Homogeneity and content of the test substance at each dose level (5 samples per dose level, one control sample).
- In two additional batches of diets: Content of the test substance at each dose level (one sample per dose level and one control sample).
- Stability of the test substance under experimental conditions (one sample per dose level and one control sample, after storage for about 4 days in the animal room and after storage for at least 5 weeks in the freezer (< -18 °C).

4.10.2 General clinical observations

Each animal will be observed daily in the morning hours by cage-side observations and, if necessary, handled to detect signs of toxicity. All cages will be checked again in the afternoon for dead or moribund animals to minimize loss of animals from the study. All abnormalities, signs of ill health or reactions to treatment will be recorded (see Annex 2). Any animal showing signs of severe debility or intoxication, particularly if death appears imminent, will be humanely killed to prevent loss of tissues by cannibalism or autolytic degeneration.

4.10.3 Neurobehavioral testing: detailed clinical observations, FOB and motor activity

Neurobehavioral testing will be conducted on all rats of all groups. During neurobehavioral testing, the group identification on the cages will be masked in order not to disclose the treatment of the animals.

Detailed clinical examinations

Detailed clinical observations will be conducted outside the home cage starting shortly after the initiation of the treatment and once weekly thereafter up to and including week 13. Signs noted will include but not be limited to changes in skin and fur, piloerection, changes in the eyes, gait (including posture), and presence of clonic or tonic movements, stereotypies and bizarre behavior.

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Functional Observational Battery (FOB) and spontaneous motor activity

FOB and motor activity testing will be performed in or about week 12 or 13 of the study. The FOB used in our laboratory is adapted from the WHO/IPCS Functional Observational Battery that was used in the Collaborative Study on Neurotoxicity Assessment sponsored by the International Programme on Chemical Safety of the World Health Organization. Details on the conduct of observations included in this battery and operational definitions of the different scores for each item are given in the FOB-manual entitled "Functional Observational Battery. Operational Definitions" (Lammers, 2000) which will be included in the report.

FOB testing

In addition to the daily, general clinical observations described in the previous section (intended to detect all abnormalities, signs of ill health or reactions to treatment), the FOB is a series of non-invasive observational and interactive measures designed to assess the neurobehavioral and functional integrity of the rat. The measures included according to functional domain are as follows:

Domain	Behavioral End-point
Autonomic	lacrimation (R), salivation (R), pupil response to light (Q), palpebral closure (R), piloerection (Q), defecation (C), urination (C)
Neuromuscular	gait (D,R), mobility (R), forelimb and hind limb grip strength (I), landing foot splay (I), righting reflex (R)
Sensorimotor	response (R) to tail pinch, click, touch and approach of a visual object
Convulsive	clonic and tonic movements (D)
Excitability	ease of removal (R), handling reactivity (R), arousal (R), vocalizations (Q)
Activity	rearing (C), posture (D)
Physiological	body temperature (I)

Abbreviations: D=descriptive rank R=rank order data C=count data
Q=quantal data I=interval or continuous data

At least one hour prior to the start of the observations, the animals will be placed individually in macrolon cages in a waiting room next to the examination room or in a waiting area in the examination room. First, measurements will be carried out in the cage. The rat's posture, palpebral closure and the possible presence of clonic and tonic convulsions will be recorded. Then the rat will be removed from the cage and the ease of removal and handling will be rated. Palpebral closure and any lacrimation or salivation will also be rated, and the presence or absence of piloerection and vocalizations will be recorded. In addition, other signs, such as changes in skin and fur, exophthalmus, crustiness around the eyes, bite marks on the tail or paws, missing toe nails or emaciation (shallow stomach, protruding spinal vertebrae) will be recorded. The rat will then be placed in an open arena (77 l x 55 w x 7 h cm) and observed for 3 minutes. Rears (both supported and unsupported) will be counted. At the same time, gait characteristics will be recorded and ranked, the ease with which the rat locomotes will be ranked, and arousal will be assessed and recorded. Further, the occurrence of clonic and/or tonic convulsions, stereotypies and bizarre behavior will be recorded. At the end of the observation period, the number of fecal boluses and urine pools will be recorded.

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Following this observation period, reflex testing will be conducted. Reflex testing consists of recording the rat's responses to the approach of a pencil, a touch of a pencil to the rump, a click stimulus, tail pinch, and the constriction of the pupil to light. Aerial righting will be rated next. Forelimb and hind limb grip strength will be measured. Three valid determinations (from a maximum of five attempts) will be taken for each grip strength measure. The rectal temperature will be taken with the rat restrained by hand. Finally, the hind limb feet will be painted lightly and landing foot splay will be measured.

Motor activity measurement

Motor activity will be assessed following FOB testing. Changes in spontaneous motor activity will be assessed using an automated quantitative microprocessor-based video image analysis system. Rats will be placed individually in open roofed cages measuring 48.8 l x 44.7 w x 50 h cm on the insides and equipped with a video camera suspended above the test cage. The position of the rat will be continuously monitored throughout the test session. Spontaneous motor activity will be expressed as the total distance run in a 30 minute test period. In addition, habituation of activity will be evaluated. Each session will be divided into 5 time blocks of 6 minutes each. Motor activity tests will be recorded on DVD. Recordings will be used only for re-analysis of motor activity tests should that be necessary for technical reasons. If re-analysis of motor activity tests is not necessary, the DVDs will be removed from the study dossier after submission of the final report. Squads of up to eight animals can be monitored simultaneously. Dose groups will be evenly distributed over motor activity test cages and over time as good as possible. Motor activity testing of a squad will be conducted immediately after functional observations for that squad have finished.

4.10.4 Body weight

Of each rat body weight will be recorded weaning, and at initiation of treatment (day 0), and once per week thereafter. The animals will be weighed prior to scheduled necropsy in order to calculate the correct organ to body weight ratios.

4.10.5 Food consumption

Food consumption will be measured per cage by weighing the feeders. The consumption will be measured over successive 3- or 4 day periods throughout the treatment period for all animals in the cage. The results will be expressed in g per animal per day.

4.10.6 Water consumption

Water consumption will be measured per cage, by weighing the drinking bottles daily, during 5-day periods in or about weeks 1, 6 and 12. The results will be expressed in g per animal per day.

4.10.7 Intake of the test substance

The intake of the test substance per kg body weight per day will be calculated from the nominal dietary concentration, the food consumption and the body weight.

4.10.8 Ophthalmoscopic examination

Ophthalmoscopic observations will be made shortly after the start of treatment in all allocated rats and in or about the last week of the treatment period in all rats of the control group (1)

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and the high dose group (4). If treatment-related ocular changes are observed in the high-dose group, eye examinations will be extended to the animals of the low- and mid-dose groups (2 and 3). Eye examination will be carried out using an ophthalmoscope after induction of mydriasis by a solution of atropine sulphate.

4.10.9 Hematology

Hematology will be conducted on all surviving animals. At necropsy, blood samples will be taken from the abdominal aorta of the rats whilst under CO_2/O_2 anesthesia. The rats will be fasted overnight before necropsy (water will be freely available). EDTA or citrate (for prothrombin time) will be used as anticoagulant. Blood samples will be discarded after analysis. In each sample the following determinations will be carried out according to the methods listed in Annex 3.

- hemoglobin (Hb)
- packed cell volume (PCV)
- red blood cells (RBC)
- reticulocytes
- total white blood cells (WBC)
- differential white blood cells
- prothrombin time
- thrombocytes

The following parameters will be calculated:

- mean corpuscular volume (MCV)
- mean corpuscular hemoglobin (MCH)
- mean corpuscular hemoglobin concentration (MCHC)

4.10.10 Clinical chemistry

Clinical chemistry will be conducted on all surviving animals. At necropsy, blood samples will be taken from the abdominal aorta of the rats whilst under CO_2/O_2 anesthesia. The rats will be fasted overnight before necropsy (water will be freely available). The blood will be collected in heparinized plastic tubes and plasma will be prepared by centrifugation. Plasma samples will be discarded after analysis. The measurements listed below will be made in the plasma according to the methods given in Annex 4.

- alkaline phosphatase activity (ALP)
- aspartate aminotransferase activity (ASAT)
- alanine aminotransferase activity (ALAT)
- gamma glutamyl transferase activity (GGT)
- total protein
- albumin
- ratio albumin to globulin (calculated)
- urea
- creatinine
- (fasting) glucose
- bilirubin (total)
- cholesterol (total)
- triglycerides
- phospholipids
- calcium (Ca)
- sodium (Na)
- potassium (K)
- chloride (Cl)
- inorganic phosphate (PO4)

4.10.11 Renal concentration test and urinalysis

In or about week 13, all surviving rats will be deprived of water for 24 hours and of food during the last 16 hours of this period. During the last 16 hours of deprivation, the rats will be

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individually kept in metabolism cages and urine will be collected. Urine samples will be discarded after analysis.
The following determinations will be carried out in individual samples according to the methods listed in Annex 5:

- volume[1]
- density[1]
- appearance
- pH
- glucose
- microscopy of the urinary sediment[2]
- occult blood
- ketones
- protein
- bilirubin
- urobilinogen

[1] To investigate the concentrating ability of the kidneys
[2] Red blood cells, white blood cells, epithelial cells, amorphous material, crystals, casts, bacteria, worm eggs, sperm cells.

4.10.12 Pathology

4.10.13 Sacrifice, organ weights and macroscopic examination

Sacrifice of the time-mated females is described in § 4.4. 'Time-mated females'. Sacrifice of the surplus pups is described in § 4.7. 'Allocation and start of the treatment'.

Early in week 14, after overnight fasting (water will be freely available), the surviving animals will be killed on two successive working days, in such a sequence that the average time of killing is approximately the same for each group. The animals will be killed by exsanguination from the abdominal aorta under CO_2/O_2 anesthesia and then examined grossly for pathological changes. A thorough necropsy will also be performed on animals that die intercurrently (if not precluded by cannibalism or autolysis) or that have to be killed because they are moribund.

Organ weights
At scheduled necropsy, the following organs will be weighed (paired organs together) as soon as possible after dissection to avoid drying, and the relative organ weights (g/kg body weight) will be calculated on the basis of the terminal body weight of the animals.

- adrenals
- brain
- epididymides
- heart
- kidneys
- liver
- ovaries
- prostate
- seminal vesicles (with coagulating glands)
- spleen
- testes
- thymus
- uterus

Tissue preservation
Samples of the following tissues and organs of all animals will be preserved in a neutral aqueous phosphate-buffered 4% solution of formaldehyde.

- adrenals
- aorta
- axillary lymph nodes
- brain[1]
- oviducts (=fallopian tubes)
- pancreas
- parathyroid
- parotid salivary glands

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caecum	pituitary
colon	prostate
duodenum	rectum
epididymides	seminal vesicles+ coagulating glands
esophagus	skeletal muscle (thigh)
exorbital lachrymal glands*	skin (flank)
eyes	spinal cord[2]
femur with joint*	spleen
GALT (gut associated lymphoid tissue, including Peyer's patches)	sternum with bone marrow
heart	stomach[3]
ileum	sublingual salivary glands
jejunum	submaxillary salivary glands
kidneys[4]	testes
liver[5]	thymus
lungs	thyroid
mammary gland (females)	trachea/bronchi
mandibular (cervical) lymph nodes*	urinary bladder
mesenteric lymph nodes	uterus (with cervix)
nerve-peripheral (sciatic)	vagina
ovaries	all gross lesions

The carcass containing any remaining tissues will also be retained in formalin, but will be discarded after completion of the histopathological examination.

* The tissues marked with * will be preserved but not processed for histopathological examination, unless histopathological examination is considered necessary on the basis of gross observations.
1 Three levels will be examined microscopically (brain stem, cerebrum, cerebellum).
2 Retained in vertebral column, at least three levels will be examined microscopically (cervical, mid-thoracic and lumbar).
3 Non glandular ('forestomach') and glandular (fundus, pyorus) parts will be examined microscopically.

Histopathological examination

The tissues to be examined microscopically will be embedded in paraffin wax, sectioned and stained with hematoxylin and eosin. Special stains may be employed on selected tissues to aid in making a diagnosis at the discretion of the study pathologist.
Histopathological examination (by light microscopy) will be performed on all tissues and organs listed above - except those marked with an asterisk - of all animals of the control group and the high-dose group, and of all animals of the intermediate-dose groups that die during the study or are killed in extremis. Gross lesions will be examined in rats of all dose groups. Histopathology will be subjected to a peer review system.
If treatment-related changes are observed in a specific organ or tissue in the high-dose group, histopathology on this organ or tissue will be extended to the intermediate-dose groups after consultation of the sponsor.

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4.11 Statistical analysis of the results

The statistical procedures for analysis of data in the 13-week study are described below. Other statistical tests may be performed when considered appropriate.

- Body weight data collected after initiation of treatment: "AnCova & Dunnett's Test" with automatic data transformation. Day 0 body weight data are used as covariate unless removed during data preprocessing. The "AnCova & Dunnett's Test" is an automatic decision tree consisting of:
  (1) Data preprocessing tests. These tests start with transformation "None". First, suitability of the covariate is checked (criteria: sufficient cases, at least 2; variability of covariate non-zero; covariate effects sufficiently parallel over the groups, significance level parallelism test 0.01). Next, normality of data distribution (Shapiro-Wilks test; significance level 0.05) and homogeneity of variances (Levene test; significance level 0.05) are checked. If any of these three checks fail they are repeated using Log transformation.
  If checks on log-transformed, covariate-adjusted data fail, the covariate is removed and the normality and homogeneity checks are repeated. If these checks pass on transformations "None" or "Log", data are analyzed without covariate. If they fail, data are rank-transformed and the covariate is reinstated.
  (2) A group test assessing whether or not group means are all equal (one-way analysis of covariance [Ancova], or one-way analysis of variance [Anova] if the covariate is removed). If the group test shows no significant non-homogeneity of group means ($p \geq 0.05$), group summary tables do not show whether or not a covariate is used in the analysis.
  (3) Post-hoc analysis. If the group test shows significant ($p<0.05$) non-homogeneity of group means, pairwise comparisons with the control group are conducted by Dunnett's multiple comparison test (significance levels 0.01 and 0.05).
- Pretreatment body weight data, body weight changes, clinical pathology (hematology, clinical chemistry, urinary volume and specific gravity) and organ weight data: "Generalized Anova Test" with automatic data transformation. This test is an automatic decision tree consisting of:
  (1) Data preprocessing tests. First, normality of data distribution (Shapiro-Wilks test) and homogeneity of variances (Levene test) are checked (initial transformation "None"). If any of these checks fail ($p<0.05$) they are repeated using Log transformation. If checks on log-transformed data fail, data are rank-transformed.
  (2) A group test assessing whether or not group means are all equal (parametric for untransformed or log-transformed data: one-way analysis of variance [Anova]; non-parametric for rank transformed data: Kruskal-Wallis test).
  (3) Post-hoc analysis. If the group test shows significant ($p<0.05$) non-homogeneity of group means, pairwise comparisons with the control group are conducted by Dunnett's multiple comparison test (parametric after Anova, non-parametric after Kruskal-Wallis; significance levels 0.01 and 0.05).
- Food/ water consumption: Dunnett's multiple comparison test.
- Semi quantitative urinalysis results: "Kruskal-Wallis & Dunnett Test" with "Rank" as data transformation method. In this test data are first rank-transformed and then analyzed by the Kruskal-Wallis test. If Kruskal-Wallis shows significant ($p<0.05$) non-homogeneity of group means, pairwise comparisons with the control group are conducted by Dunnett's multiple comparison test on the ranks of the data (significance levels 0.01 and 0.05).
- Functional observational battery: one-way analysis of variance followed by Dunnett's multiple comparison tests (continuous data), Kruskal-Wallis non-parametric analysis of

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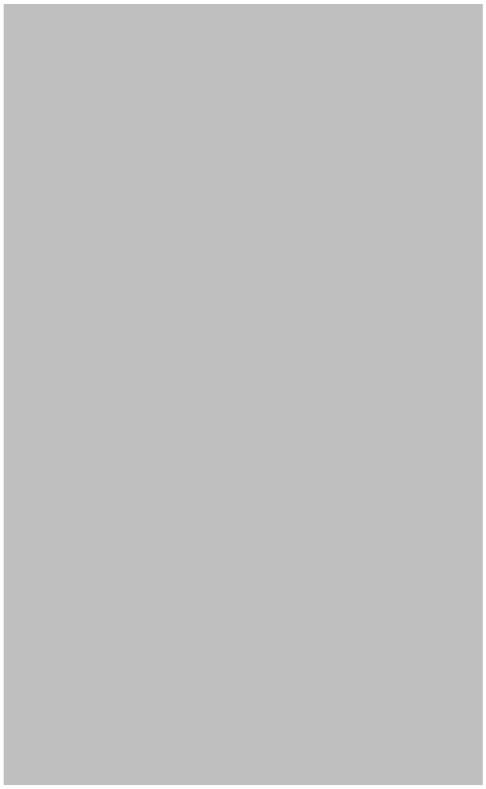
variance followed by multiple comparison tests (rank order data) or Pearson chi-square analysis (categorical data).

- Motor activity data: total distance moved: one-way analysis of variance followed by Dunnett's multiple comparison tests; habituation of activity: repeated measures analysis of variance on time blocks (each session consists of 5 time blocks of 6 minutes each).
- Incidences of histopathological changes: Fisher's exact probability test.



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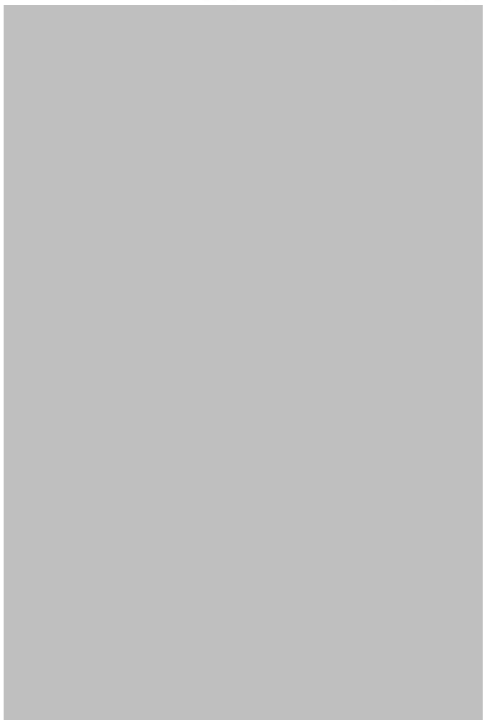
5 Reporting

The final report will specify:

- Summary
- The objective of the study
- The characterization and administration of the test substance
- The test facility
- Responsible personnel
- The time frame of the study
- The test system
- Observations and measurements
- Materials and methods
- Statistical methods
- Deviations from the study plan
- Results
- Evaluation of the results
- Discussion and conclusions
- Location and retention periods of documents and materials related to the study
- A statement by the QAU
- A statement on GLP compliance signed by the study director.

Should any doubt arise from the publication of the Triskelion report in an electronic form, the authorized printed version shall be considered authentic.



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[redacted]

[redacted]

6 Archiving

The following study specific materials will be archived for 5 years:
- Raw data (or true copies if unstable)
- Tissue specimens and paraffin blocks
- A reference sample of the test substance if its nature allows this

The following study specific materials will be archived for 15 years
- Original study plan and final report, and any amendments thereof
- Microscopic slides

General raw data will be retained for at least 25 years, after which they may be destroyed without further notice. These may include, but are not necessarily limited to:
- Facility-based documents
- System calibration and quality control data
- General registrations potentially used for more than one study

At the end of the archiving period, the reference sample, tissue specimens and paraffin blocks will be discarded,
The sponsor will be asked whether the study plan, final report, amendments, raw data, including microscopic slides, and correspondence should be discarded, retained for an additional period, or transferred to the archives of the sponsor.

All materials will be retained in the archives of TNO, Utrechtseweg 48, 3704 HE Zeist, The Netherlands. The archiving period starts on the cover date of the final report.

[redacted]

[redacted]

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Annex 1 Distribution list

Sponsor:
- D. Delsing (study monitor): signed PDF copy by e-mail[1]

Test facility:
- Archives (signed original for study file)[1]
- Study director[2]
- Animal welfare officer[2]
- Animal facility[2]
- Laboratory determinations[2]
- Finance, Planning & Control[2]
- (Histo)pathology[2]
- Neurobehavioral observations[2]
- Operational managers[2]
- Pathology[2]
- Project assistant[2]
- Test material custodian[2]
- Test substance-carrier analyses[2]
- Quality Assurance[2]

[1] Sent by study director
[2] Copies to be distributed by TNO archives

Annex 14: Study plan and amendments

Annex 2 Listing of clinical signs

The clinical signs listed below are derived from the lexicon which is part of the computer programme used for the recording of clinical observations.

RESPIRATION
Sniffing
Grunting
Increased rate
Decreased rate
Irregular
Dyspnea
Shallow
Sneezing
Mouth breathing

GENERAL
Thin
Emaciated
Obese
Weakened
Unconscious
Pale
Red
Jaundice
Cyanosis
Warm
Cold
Dehydrated
Increased muscle tension

MOUTH
Malocclusion of incisors
Lower incisors light color
Lower incisors white
Upper incisors light color
Hemorrhagic discharge
Salivation
Stomatitis
Wart-like lesion(s)
Encrustation(s)
Chewing movement

ABDOMEN
Distension
Tense/firm
Blue/grey
Nodule(s)
Umbilical hernia

FAECES
Increased defecation
Decreased defecation
Hard
Soft
Diarrhea
Pale
Hemorrhagic
Black

BEHAVIOUR
Muscle weakness
Lethargic
Hunched posture
Excessive scratching
Hyperactive
Hypoactive
Aggressive
Stereotypy
Tremors
Convulsions
Ataxia
Circling movements
Vomiting
Vocalization
Chattering
Excessive grooming
Prone position
Myoclonic jerks

SKIN/FUR
Alopecic area(s)
Sparsely haired area(s)
Piloerection
Soiled fur
Depigmented fur
Edema
Abscess(es)
Pimple(s)
Subcutaneous nodule(s)
Erythema
Scaly
Hematoma
Hematoma iatrogenic
Encrustation(s)
Wound(s)
Shaving wound(s)
Scar tissue
Sc. color inj. site
Color ventral of inj. site
Red iatrogenic
Scaly iatrogenic

INJECTION SITE
Small nodule
Small red sc nodule
Redness
Swollen
Warm
Shaving wound/encrustation
Hematoma sc
Red nodule with white core
Red sc nodule with wound

HEAD
Tilted
Local/general swelling
Trimmed whiskers
Erythema between ears

NOSE
Encrustation(s)
Wound
Hemorrhagic discharge
Discharge-other than red
Crooked
Swollen
Itching
Skin protrusion

EYES
Discharge
Encrustation(s)
Blepharospasm
Blepharitis
Redness conjunctivae
Microphthalmia
Macrophthalmia
Exophthalmus
Dark red
Pale
Corneal opacity/keratitis
Cataract
Panophthalmitis
Complete degeneration
Protruding nictitant membrane

EARS
Encrustration(s)
Wound(s)
Ear canal greased
Ear canal hemorrhagic
Hematoma iatrogenic
Necrotizing ear pinna
Ear pinna (partly) gone
Nodule
Swollen
Erythema

PENIS
Prolapse
Purulent discharge
Hemorrhagic discharge
Swollen preputium

PERINEUM
Soiled with urine
Soiled with feces
Soiled with blood
Erythema
Vaginal blood
Vaginal pus
Vaginal occlusion
Membrane present
Prolapsus ani -et recti
Vulva red
Vulva swollen
Vulva nodule

EXTREMITIES (LEG(S))
Encrustation(s)
Wound(s)
Swollen leg
Broken leg
Leg(s) gone
Stiffness
Muscle weakness
Lameness
Hard skin
Pododermatitis
Swollen toe(s)
Toe(s) gone
Nail(s) gone
Popliteal lymph node enlarged

TAIL
Ringtail
Kink
(Partially) discolored
Encrustation(s)
Wound(s)
Scaly
Local thickening
Tip of tail missing
Short and thick

TESTES
Cryptorchidism
Small
Large
Firm
Soft

URETHRA
Urethritis

URINE
Hematuria

Abbreviations: inj. site = injection site sc = subcutaneous

[redacted]

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Annex 3 Hematology parameters and methods of analysis

Parameter	Method	Reference
Hemoglobin	Advia 2120i hematology analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5
Packed cell volume	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Calc. from impulse height
Red blood cells	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Impedance
Reticulocytes	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Fluorescence
White blood cells	Advia 2120i hematology Analyzer, Siemens Nederland N.V.	Training manual 04/11/99 chapter 5 Impedance
Differential white blood cell count	Advia 2120i hematology analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Impedance and Absorption
Differential white blood cell count (manual); conducted only if automatic differential count fails	Microscopic examination of stained blood smears according to Pappenheim. Absolute numbers are calculated from total white blood cells and percentage distribution of each cell type	Gorter, E. and W.C. de Graaff, Klinische Diagnostiek, 7th ed. H.E. Stenfert Kroese N.V. Leiden, 1955, the Netherlands, part I, p. 34
Thrombocytes	Advia 2120i hematology analyzer, Siemens Nederland N.V.	Manufacturers manual 04/11/99 chapter 5 Impedance
Prothrombin time	Neoplastine CL PLUS STart-clotanalyzer, Stago citrate plasma	Manufacturers Manual
Mean corpuscular volume (MCV)	Calculated MCV = $\frac{\text{packed cell volume}}{\text{red blood cells}}$	
Mean corpuscular hemoglobin (MCH)	Calculated MCH = $\frac{\text{hemoglobin}}{\text{red blood cells}}$	
Mean corpuscular hemoglobin concentration (MCHC)	Calculated MCHC = $\frac{\text{hemoglobin}}{\text{packed cell volume}}$	

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Annex 4 Clinical chemistry parameters and methods of analysis

Parameter	Method
Glucose (plasma)	Olympus AU-400 analyser[1], Olympus reagent Hexokinase
Alkaline phosphatase (ALP)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C.
Alanine aminotransferase (ALAT)/ glutamic-pyruvic transaminase (GPT)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C. without PLP.
Aspartate aminotransferase (ASAT)/ glutamic-oxalacetic transaminase (GOT)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C. without PLP.
γ-Glutamyl transferase (GGT)	Olympus AU-400 analyser[1], Olympus reagent according to I.F.C.C
Total protein	Olympus AU-400 analyser[1], Olympus reagent Biuret
Albumin	Olympus AU-400 analyser[1], Olympus reagent Bromcresol green
Ratio albumin to globulin	Calculated, ratio = albumin / (total protein – albumin)
Urea	Olympus AU-400 analyser[1], Olympus reagent Urease-UV
Creatinine	Olympus AU-400 analyser[2], Roche reagent Enzymatic PAP
Bilirubin (total)	Olympus AU-400 analyser[2], Randox reagent Diazotized sulphanilic acid
Cholesterol (total)	Olympus AU-400 analyser[1], Olympus reagent CHOD-PAP
Triglycerides	Olympus AU-400 analyser[1], Olympus reagent Enzymatic GPO-PAP
Phospholipids	Olympus AU-400 analyser[2], iNstruchemie Reagent Enzymatic
Inorganic phosphate	Olympus AU-400 analyser[1], Olympus reagent Molybdate-UV
Calcium (Ca)	Olympus AU-400 analyser[1], Olympus reagent Arsenazo III
Sodium (Na)	Olympus AU-400 analyser, Olympus reagent I.S.E.
Potassium (K)	Olympus AU-400 analyser[1], Olympus reagent I.S.E.
Chloride (Cl)	Olympus AU-400 analyser[1], Olympus reagent I.S.E.

I.F.C.C. = International Federation of Clinical Chemistry
PLP = pyridoxalphosphate
PAP = phenol-4-aminophenazone
CHOD-PAP = cholesterol oxidase - phenol-4-aminophenazone
GPO-PAP = glycerolphosphate oxidase - phenol-4-aminophenazone
I.S.E. = Ion Selective Electrode

[1] Reference: Manufacturer's manual
[2] Reference: Manufacturer's manual, adapted for the Olympus AU-400 analyzer

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Annex 5 Urinalysis; parameters and methods

Parameter	Method	Reference
Appearance	Visual inspection	
Density	Sysmex refractometer	
Volume (ConcUrin Volume)	Collection in graduated tubes	
pH, protein, glucose, occult blood (Occ bld), ketones, bilirubin, urobilinogen (Urobili)	Clinitek STATUS Test strips, Siemens	Manufacturer's manual
Sediment: erythrocytes, leucocytes, epithelial cells, amorph material, crystals, casts, bacteria, sperm cells and worm eggs	Microscopic examination after centrifugation	

Annex 14: Study plan and amendments

TRISKELION
RESEARCH FOR BETTER LIVING

Study plan amendment

Study plan no: P20880/02	**Amendment no: 1**

Title of study: Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Date amendment: 29-11-2016 (dd-mm-yyyy)	**Study director:** A.E. Wallinga

Planned change 1:
§ 4.10.13: At scheduled necropsy, caecum (full and empty) will also be weighed as soon as possible after dissection to avoid drying, and the relative organ weight (g/kg body weight) will calculated, for both the full and the empty caecum, on the basis of the terminal body weight of the animals.

Reason for change:
Erroneously, weighing the caecum (full and empty) after dissection was not included in the study plan.

Planned change 2:
Removed from § 4.10.13: [4] and [5].

Reason for change:
Superscript [4] (right after kidneys) and superscript [5] (right after liver) do not refer to any footnotes and are therefore be removed from the study plan.

Planned change 3:
Addition of the words 'of the results' to § 4.10.13, page 18 :
*The tissues marked with * will be preserved but not processed for histopathological examination, unless histopathological examination is considered necessary on the basis of the results of gross observations.

Reason for change:
For further clarification the words 'of the results' are added to the sentence.

Annex 14: Study plan and amendments

TRISKELION
RESEARCH FOR BETTER LIVING

Planned change 4:
§ 4.7: 2 Two female and two male surplus animals will be kept in the animal room as sentinel animals but will not be included in the study.

Reason for change:
Erroneously, the sentinel animals were not mentioned in the study plan.

Study Director[1]

Signature: (b) (6) Date: 29 nov 2016 (dd-mm-yyyy)

Sponsor

Name company:
Friesland Campina
Innovation

Signatur (b) (6)

Date: 08-12-2016 (dd-mm-yyyy)

Name contact person:
D. Delsing

[1] *In case of change of SD: current and new SD sign the amendment, by unexpected absence of the current SD management signs the amendment.*

[redacted]

Annex 14: Study plan and amendments

[redacted]

TRISKELION
RESEARCH FOR BETTER LIVING

Study plan amendment

Study plan no: P20880/02	Amendment no: 2

Title of study: Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Date amendment: 27-02-2017 (dd-mm-yyyy)

Study director: A.E. Wallinga

Planned change 1:
In § 2.3 'Animal welfare' the second sentence should read:
This includes licensing of the project by the Central Committee on Animal Experimentation (project license 2016602) and approval of the study by the Triskelion Animal Welfare Body (AWB number TRIS-185).

Reason for change:
Triskelion B.V. has acquired a new general project license on animal experiments. Therefore the current animal study is administratively transferred from project license number 3660 to project license number 2016602.

Study Director[1]

Signature (b) (6) Date 27-02-2017 (dd-mm-yyyy)

Sponsor

Name company:
Friesland Campina Innovation

Signature (b) (6)

Date: 06-03-2017 (dd-mm-yyyy)

Name contact person:
D. Delsing

[1] *In case of change of SD: current and new SD sign the amendment, by unexpected absence of the current SD management signs the amendment.*

[redacted]

[redacted]

Annex 14: Study plan and amendments

TRISKELION
RESEARCH FOR BETTER LIVING

Study plan amendment

Study plan no: P20880/02	Amendment no: 3

Title of study: Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Date amendment: 09-08-2017 (dd-mm-yyyy)

Study director: A.E. Wallinga

Planned change 1:
To be added to § 4.10.1 'Analysis of the experimental diets':
The homogeneous distribution and achieved concentration of the test item in the VRF1(FG) Rat feed batches of diet prepared for this study will be analyzed according to a validated LC-MS method and the following acceptance criteria:

-Homogeneity:

- For each concentration level, a one-way analysis of variance (Anova) was performed using the sample location (1-5) as grouping factor. An associated F-value with probability $p < 0.01$ was considered to be significant (i.e. the mean concentrations differ significantly at the five locations in the container).

- The test substance is considered homogeneously distributed in the diet if $p \geq 0.01$ and or if the relative standard deviation (RSD) between the mean concentrations at the five locations is ≤5%.

-Stability:

- For each concentration level, a one-way analysis of variance (Anova) was performed using time as grouping factor. An associated F-value with probability $p < 0.01$ was considered to be significant (i.e. the mean concentrations differ significantly before and after storage).

- The test substance was considered to be stable in diet if $p \geq 0.01$ and/or if the mean concentration after storage was within 90-110% of the mean concentration at $t = 0$.

-Content:

- The content of the test substance in the diet is considered to be 'close to intended' if the mean measured concentration is between 90 and 110% of the intended concentration.

Annex 14: Study plan and amendments

2 mistake in template
1/2 a.t.w.
09-aug-2017

TRISKELION
RESEARCH FOR BETTER LIVING

Reason for change:
Acceptance criteria as specified in SOP TRIS/GEN/310 were followed, however these criteria were not described in the study plan.

Study Director[1]

Signature: (b) (6) Date: 09 aug 2017 (dd-mm-yyyy)

Sponsor

Name company:
Friesland Campina
Innovation

Signature:

(b) (6)

Na
D.

Date: 14/8/17 (dd-mm-yyyy)

[1] *In case of change of SD: current and new SD sign the amendment, by unexpected absence of the current SD management signs the amendment.*

Appendices

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

0% diet Sex: Male	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
32	DEAD Killed scheduled	91
34	DEAD Killed scheduled	91
36	SKIN Encrustation(s)	7 to 27
	TAIL Kink	9 to 91
	DEAD Killed scheduled	91
38	DEAD Killed scheduled	91
40	DEAD Killed scheduled	91
62	TAIL Kink	44 to 91
	DEAD Killed scheduled	91
64	DEAD Killed scheduled	91
66	DEAD Killed scheduled	91
68	DEAD Killed scheduled	91
70	DEAD Killed scheduled	91

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

3% diet Sex: Male	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
2	DEAD Killed scheduled	91
4	DEAD Killed scheduled	91
6	DEAD Killed scheduled	91
8	DEAD Killed scheduled	91
10	SKIN Encrustation(s)	35 to 48
	DEAD Killed scheduled	91
72	SKIN Encrustation(s)	18 to 24
	DEAD Killed scheduled	91
74	DEAD Killed scheduled	91
76	DEAD Killed scheduled	91
	SKIN Sparsely haired area(s)	91
78	SKIN Encrustation(s)	4 to 17,35 to 41
	DEAD Killed scheduled	91
80	SKIN Encrustation(s)	0 to 3,35 to 54
	DEAD Killed scheduled	91

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

6% diet Sex: Male	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
12	SKIN Encrustation(s)	18 to 48
	DEAD Killed scheduled	91
14	DEAD Killed scheduled	91
16	DEAD Killed scheduled	91
18	TAIL Kink	9 to 91
	DEAD Killed scheduled	91
20	DEAD Killed scheduled	91
42	DEAD Killed scheduled	91
44	DEAD Killed scheduled	91
46	DEAD Killed scheduled	91
48	DEAD Killed scheduled	91
50	DEAD Killed scheduled	91

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

10% diet Sex: Male	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
22	HEAD Tilted	43 to 91
	TAIL Kink	44 to 91
	DEAD Killed scheduled	91
24	DEAD Killed scheduled	91
26	DEAD Killed scheduled	91
28	DEAD Killed scheduled	91
30	DEAD Killed scheduled	91
52	DEAD Killed scheduled	91
54	SKIN Wound(s)	0 to 3,35 to 38
	SKIN Encrustation(s)	4 to 20,39 to 48
	DEAD Killed scheduled	91
56	DEAD Killed scheduled	91
58	SKIN Encrustation(s)	28 to 54
	SKIN Sparsely haired area(s)	49 to 83
	DEAD Killed scheduled	91
60	DEAD Killed scheduled	91

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

0% diet Sex: Female	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
11	DEAD Killed scheduled	92
13	DEAD Killed scheduled	92
15	SKIN Encrustation(s)	7 to 10,14 to 17
	DEAD Killed scheduled	92
17	DEAD Killed scheduled	92
19	DEAD Killed scheduled	92
41	SKIN Encrustation(s)	4 to 24
	SKIN Sparsely haired area(s)	50 to 73
	DEAD Killed scheduled	92
43	SKIN Encrustation(s)	0 to 4
	DEAD Killed scheduled	92
45	SKIN Encrustation(s)	4 to 34
	DEAD Killed scheduled	92
47	DEAD Killed scheduled	92
49	SKIN Encrustation(s)	28 to 54
	SKIN Sparsely haired area(s)	49 to 73
	DEAD Killed scheduled	92

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

3% diet Sex: Female	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
21	DEAD Killed scheduled	92
23	DEAD Killed scheduled	92
25	DEAD Killed scheduled	92
27	DEAD Killed scheduled	92
29	DEAD Killed scheduled	92
51	DEAD Killed scheduled	92
53	SKIN Encrustation(s)	0 to 17,28 to 69
	SKIN Sparsely haired area(s)	49 to 92
	DEAD Killed scheduled	92
55	DEAD Killed scheduled	92
57	DEAD Killed scheduled	92
59	SKIN Encrustation(s)	4 to 13,42 to 54,77 to 91
	DEAD Killed scheduled	92
	SKIN Sparsely haired area(s)	92

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

6% diet Sex: Female	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
31	DEAD Killed scheduled	92
33	DEAD Found dead	24
35	SKIN Encrustation(s)	7 to 10
	DEAD Killed scheduled	92
37	DEAD Killed scheduled	92
39	DEAD Killed scheduled	92
61	DEAD Killed scheduled	92
63	DEAD Killed scheduled	92
65	DEAD Killed scheduled	92
67	DEAD Killed scheduled	92
69	DEAD Killed scheduled	92

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 1: Clinical observations

10% diet Sex: Female	Observation Type: All Types	From Day 0 (Start Date) to 92 (Start Date)
1	SKIN Encrustation(s)	7 to 24
	DEAD Killed scheduled	92
3	SKIN Encrustation(s)	7 to 13,18 to 24,28 to 40
	SKIN Wound(s)	14 to 17
	DEAD Killed scheduled	92
5	SKIN Encrustation(s)	0 to 13
	SKIN Sparsely haired area(s)	44 to 92
	DEAD Killed scheduled	92
7	DEAD Killed scheduled	92
9	DEAD Killed scheduled	92
71	DEAD Killed scheduled	92
73	SKIN Encrustation(s)	28 to 32
	DEAD Killed scheduled	92
75	DEAD Killed scheduled	92
	SKIN Sparsely haired area(s)	92
77	DEAD Killed scheduled	92
79	DEAD Killed scheduled	92

Values=Clin Obs Range

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 2: Ophthalmoscopic observations

0% diet Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
32	No abnormalities	X	.	.	X
34	No abnormalities	X	.	.	X
36	No abnormalities	X	.	.	X
38	No abnormalities	X	.	.	X
40	Persistent pupillary membrane, Bilateral	X	.	.	X
62	No abnormalities	X	.	.	X
64	No abnormalities	X	.	.	X
66	No abnormalities	X	.	.	X
68	No abnormalities	X	.	.	X
70	No abnormalities	X	.	.	X

3% diet Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
2	No abnormalities	X	.	.	.
4	No abnormalities	X	.	.	.
6	No abnormalities	X	.	.	.
8	No abnormalities	X	.	.	.
10	No abnormalities	X	.	.	.
72	No abnormalities	X	.	.	.
74	No abnormalities	X	.	.	.
76	No abnormalities	X	.	.	.
78	No abnormalities	X	.	.	.
80	No abnormalities	X	.	.	.

X=Present; . =Animal was not examined at this stage

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 2: Ophthalmoscopic observations

6% diet Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
12	No abnormalities	X	.	.	.
14	Persistent pupillary membrane, Unilateral	X	.	.	.
16	Persistent pupillary membrane, Unilateral	X	.	.	.
18	No abnormalities	X	.	.	.
20	No abnormalities	X	.	.	.
42	No abnormalities	X	.	.	.
44	No abnormalities	X	.	.	.
46	No abnormalities	X	.	.	.
48	No abnormalities	X	.	.	.
50	No abnormalities	X	.	.	.

10% diet Sex: Male	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
22	No abnormalities	X	.	.	X
24	No abnormalities	X	.	.	X
26	No abnormalities	X	.	.	X
28	No abnormalities	X	.	.	X
30	No abnormalities	X	.	.	X
52	No abnormalities	X	.	.	X
54	No abnormalities	X	.	.	X
56	No abnormalities	X	.	.	X
58	No abnormalities	X	.	.	X
60	No abnormalities	X	.	.	X

X=Present; . =Animal was not examined at this stage

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 2: Ophthalmoscopic observations

0% diet Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
11	No abnormalities	.	X	X	.
13	No abnormalities	.	X	X	.
15	No abnormalities	.	X	X	.
17	No abnormalities	.	X	X	.
19	No abnormalities	.	X	X	.
41	No abnormalities	.	X	X	.
43	No abnormalities	.	X	X	.
45	No abnormalities	.	X	X	.
47	Persistent pupillary membrane, Unilateral	.	X	X	.
49	No abnormalities	.	X	X	.

3% diet Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
21	No abnormalities	.	X	.	.
23	No abnormalities	.	X	.	.
25	No abnormalities	.	X	.	.
27	No abnormalities	.	X	.	.
29	Persistent pupillary membrane, Unilateral	.	X	.	.
51	No abnormalities	.	X	.	.
53	No abnormalities	.	X	.	.
55	No abnormalities	.	X	.	.
57	No abnormalities	.	X	.	.
59	Persistent pupillary membrane, Unilateral	.	X	.	.

X=Present; . =Animal was not examined at this stage

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 2: Ophthalmoscopic observations

6% diet Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
31	No abnormalities	.	X	.	.
33	No abnormalities	.	X	.	.
35	No abnormalities	.	X	.	.
37	No abnormalities	.	X	.	.
39	No abnormalities	.	X	.	.
61	No abnormalities	.	X	.	.
63	No abnormalities	.	X	.	.
65	No abnormalities	.	X	.	.
67	No abnormalities	.	X	.	.
69	Iris malformation, Unilateral	.	X	.	.

10% diet Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date			
		1	2	86	87
1	No abnormalities	.	X	X	.
3	No abnormalities	.	X	X	.
5	No abnormalities	.	X	X	.
7	No abnormalities	.	X	X	.
9	No abnormalities	.	X	X	.
71	No abnormalities	.	X	X	.
73	No abnormalities	.	X	X	.
75	No abnormalities	.	X	X	.
77	No abnormalities	.	X	X	.
79	No abnormalities	.	X	X	.

X=Present; . =Animal was not examined at this stage

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

0% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
32	45.5	66.4	112.6	155.0	195.4	237.1	261.5	276.9
34	50.1	63.8	104.8	148.7	190.9	234.0	263.7	283.1
36	45.9	63.1	103.0	141.3	177.8	214.1	244.2	262.6
38	46.2	62.9	105.1	146.9	184.7	220.5	238.4	259.7
40	50.1	66.0	108.1	151.0	193.8	236.4	280.4	311.9
62	50.6	68.4	115.9	166.9	221.5	275.6	306.0	336.8
64	45.2	62.1	102.7	144.1	179.7	220.9	250.1	272.2
66	44.6	62.7	107.1	151.4	194.1	235.3	269.7	291.4
68	46.3	67.4	113.9	158.2	201.8	246.9	276.9	300.8
70	37.2	53.2	89.7	125.2	158.4	195.4	223.1	245.1
Mean	46.17	63.60	106.29	148.87	189.81	231.62	261.40	284.05
SD	3.87	4.26	7.43	11.08	16.58	21.34	23.77	27.19
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

0% diet							
	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
32	295.2	312.9	326.4	340.6	345.2	360.8	361.7
34	299.7	313.1	327.6	335.3	340.2	352.9	348.6
36	277.8	284.8	291.1	299.1	302.7	317.9	317.3
38	272.3	283.2	295.7	302.8	308.2	322.4	325.6
40	331.4	351.9	364.5	380.8	387.1	404.5	401.0
62	369.4	392.2	413.5	421.6	427.6	446.9	448.3
64	287.6	301.2	312.7	319.3	324.6	333.1	329.1
66	313.5	329.1	339.8	350.6	357.3	365.8	368.0
68	319.2	333.7	347.0	357.3	363.5	380.6	382.9
70	265.6	280.8	291.1	301.3	311.5	329.0	328.8
Mean	303.17	318.29	330.94	340.87	346.79	361.39	361.13
SD	31.40	35.04	38.09	39.06	39.10	40.68	40.99
N	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

3% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
2	49.4	72.3	127.8	178.6	226.4	269.9	301.2	325.2
4	47.7	61.1	98.7	141.6	179.3	218.3	253.9	273.8
6	44.1	60.3	103.0	141.9	182.8	223.3	259.4	282.9
8	45.9	60.4	104.2	144.7	185.9	224.7	251.2	269.4
10	51.1	66.5	112.0	160.1	203.7	252.1	282.5	310.7
72	49.1	68.5	115.4	162.4	206.6	248.8	285.9	315.0
74	49.7	64.5	107.5	145.6	184.1	227.3	257.8	281.5
76	42.7	59.1	98.0	136.6	172.2	203.6	226.0	238.9
78	48.9	69.1	114.8	157.5	193.2	233.2	264.9	287.0
80	42.3	60.9	106.0	150.0	195.2	241.4	276.9	292.3
Mean	47.09	64.27	108.74	151.90	192.94	234.26	265.97	287.67
SD	3.14	4.59	9.03	12.72	15.89	19.17	21.35	25.11
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

3% diet	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
2	349.2	366.6	377.8	390.8	398.5	420.4	422.2
4	291.6	304.7	313.3	323.0	330.7	342.5	344.5
6	304.0	321.4	335.9	342.6	347.4	363.8	363.9
8	287.4	302.3	311.6	314.8	322.7	336.3	338.9
10	329.2	345.8	363.1	379.0	384.7	397.2	400.9
72	337.6	359.7	385.7	394.5	409.4	429.6	430.3
74	297.3	309.9	321.0	327.1	334.4	344.2	341.4
76	252.3	262.4	274.8	283.8	290.1	303.0	305.1
78	301.4	316.1	328.6	336.6	342.5	358.8	364.0
80	308.2	318.8	333.8	346.4	361.9	380.7	384.3
Mean	305.82	320.77	334.56	343.86	352.23	367.65	369.55
SD	27.78	30.54	33.45	35.33	36.80	39.58	39.78
N	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

6% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
12	45.9	65.4	117.3	162.7	209.9	254.3	282.8	305.8
14	50.1	67.5	118.9	163.8	210.1	251.3	280.1	302.5
16	43.0	60.9	101.6	130.4	159.3	194.5	222.4	241.5
18	46.3	60.9	101.2	139.3	175.0	215.0	241.2	262.2
20	52.5	70.6	117.9	165.0	216.4	267.8	307.7	343.9
42	49.7	67.8	112.0	159.3	200.0	243.2	277.2	302.5
44	56.2	72.6	120.0	165.4	209.9	252.5	286.3	304.6
46	41.7	57.3	94.9	136.0	172.6	206.2	228.5	245.0
48	48.2	68.6	115.6	162.8	203.4	245.9	280.6	305.5
50	44.6	62.5	106.8	153.1	197.5	242.4	275.2	293.7
Mean	47.82	65.41	110.62	153.78	195.41	237.31	268.20	290.72
SD	4.45	4.87	8.90	13.44	19.45	23.75	27.75	31.76
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

6% diet	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
12	326.9	345.7	361.3	371.9	378.0	398.2	402.8
14	319.7	328.8	338.8	346.4	354.9	363.9	365.1
16	255.1	267.6	277.4	289.0	291.0	302.9	306.7
18	278.9	293.1	304.5	318.4	323.0	335.9	339.3
20	369.6	389.4	406.0	414.1	423.8	441.3	445.5
42	324.0	338.2	354.8	365.7	371.4	388.2	397.1
44	328.9	334.9	347.5	355.7	358.3	369.6	371.2
46	258.8	267.3	281.5	290.0	297.1	310.4	307.9
48	323.9	332.0	344.1	354.5	364.4	375.7	382.9
50	308.8	315.5	333.1	343.1	352.9	370.9	379.4
Mean	309.46	321.25	334.90	344.88	351.48	365.70	369.79
SD	35.40	37.27	38.72	38.01	39.42	41.25	42.94
N	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

10% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
22	36.9	52.2	87.3	123.1	157.5	190.2	213.3	230.5
24	49.7	66.9	107.7	152.2	192.4	230.6	258.2	270.8
26	45.4	63.4	103.6	142.6	177.5	215.5	246.7	269.3
28	44.8	62.1	103.9	144.0	184.8	222.5	249.8	270.7
30	47.5	65.7	110.8	157.7	204.4	250.6	291.1	321.6
52	49.9	70.8	114.9	156.2	193.9	234.4	261.8	281.1
54	57.6	75.8	121.1	163.5	211.3	258.1	298.3	326.9
56	43.3	58.8	97.4	130.6	161.8	195.8	208.2	220.9
58	48.0	68.1	108.3	151.2	188.9	226.9	247.6	255.8
60	40.1	58.6	100.2	143.0	184.5	227.1	259.4	287.1
Mean	46.32	64.24	105.52	146.41	185.70	225.17	253.44	273.47
SD	5.73	6.77	9.45	12.46	16.88	21.18	28.50	33.94
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Male Day(s) Relative to Start Date

10% diet	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
22	244.2	258.7	268.0	281.6	284.2	298.2	299.1
24	284.2	296.8	309.9	317.2	324.5	338.4	335.7
26	285.9	302.2	311.1	322.8	328.4	343.7	348.8
28	289.9	301.8	311.4	318.5	321.9	333.0	332.8
30	340.7	359.6	377.3	387.8	400.1	413.4	418.4
52	284.6	296.3	315.3	324.1	345.4	359.1	364.4
54	346.6	364.6	381.7	395.8	402.4	418.5	420.2
56	224.8	234.6	244.6	255.1	256.0	271.2	271.6
58	260.7	270.2	284.2	303.4	312.6	326.2	335.6
60	309.1	319.3	333.3	347.8	355.1	370.6	376.3
Mean	287.07	300.41	313.68	325.41	333.06	347.23	350.29
SD	38.50	40.82	43.23	43.23	45.83	46.02	47.08
N	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

0% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
11	47.3	65.8	108.4	134.2	158.0	177.5	187.8	194.1
13	43.2	53.0	86.2	112.7	137.0	152.0	164.6	168.9
15	41.3	56.6	90.3	116.1	135.5	154.4	159.3	177.1
17	48.7	63.9	100.4	123.2	136.5	145.0	161.5	170.0
19	50.6	66.5	101.7	128.8	154.6	171.1	192.2	207.2
41	48.3	63.7	101.6	131.5	152.2	169.7	178.3	197.5
43	49.3	63.5	99.4	122.2	138.9	148.7	168.6	180.0
45	43.7	59.2	91.3	115.1	134.0	152.1	161.4	179.8
47	44.9	60.8	96.8	124.8	141.0	153.9	168.9	175.8
49	38.9	52.6	90.7	115.9	138.4	151.8	161.3	174.8
Mean	45.62	60.56	96.68	122.45	142.61	157.62	170.39	182.52
SD	3.83	5.06	6.86	7.44	8.82	10.96	11.77	12.73
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

0% diet	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
11	212.4	228.8	246.0	237.7	233.1	243.2	240.6
13	183.5	190.5	194.0	194.8	198.9	206.9	197.7
15	189.2	192.6	192.9	204.3	210.9	206.4	214.4
17	194.7	209.9	207.7	205.7	203.6	212.9	217.3
19	218.3	219.9	232.6	237.4	242.0	236.6	251.8
41	203.0	206.9	210.2	217.9	222.7	223.1	225.1
43	191.1	193.7	205.9	210.7	215.6	215.5	217.2
45	190.5	190.6	189.6	201.2	206.0	210.9	216.3
47	186.0	185.6	195.9	199.1	202.4	201.7	210.9
49	184.5	188.7	185.2	196.2	201.0	203.2	205.4
Mean	195.32	200.72	206.00	210.50	213.62	216.04	219.67
SD	12.02	14.81	19.57	15.80	14.68	14.12	16.03
N	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

3% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
21	42.4	58.8	102.1	138.0	158.3	180.6	182.6	202.2
23	46.7	61.3	97.4	120.1	131.9	154.5	168.8	177.0
25	45.8	60.1	92.0	112.3	123.2	143.5	156.3	164.3
27	45.5	60.1	92.2	117.7	134.4	148.0	156.3	170.5
29	50.0	68.2	111.5	142.9	164.7	189.3	202.1	211.4
51	45.9	58.8	94.8	125.6	148.5	169.0	183.3	185.1
53	52.8	66.9	106.0	132.9	156.2	175.9	190.1	193.9
55	42.5	55.0	88.9	117.2	138.4	153.3	164.0	179.7
57	49.9	65.2	104.7	133.1	153.2	169.2	175.7	190.6
59	34.7	48.2	79.5	110.7	127.1	147.0	161.2	169.6
Mean	45.62	60.26	96.91	125.05	143.59	163.03	174.04	184.43
SD	5.05	5.87	9.44	11.16	14.43	15.88	15.38	15.16
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

3% diet	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
21	215.1	219.9	219.9	235.8	234.3	237.3	237.4
23	180.0	193.0	201.8	207.2	204.5	211.0	213.4
25	166.0	177.5	183.6	193.6	195.8	203.0	201.0
27	178.6	183.2	184.9	194.0	200.4	199.5	201.1
29	216.5	229.7	237.4	244.9	239.8	247.8	248.5
51	202.3	207.1	216.3	212.7	224.1	224.8	222.7
53	209.4	213.9	221.0	221.9	234.8	235.3	234.3
55	191.9	194.2	192.1	204.9	209.6	209.4	211.0
57	201.2	207.4	210.6	219.2	222.4	221.9	222.4
59	174.5	185.2	201.2	195.9	200.8	203.9	201.3
Mean	193.55	201.11	206.88	213.01	216.65	219.39	219.31
SD	17.98	17.17	17.34	17.59	16.37	16.64	16.73
N	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

6% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
31	44.2	60.8	97.2	121.3	141.3	159.5	166.3	173.5
33	49.4	63.2	98.0	123.0	138.4	-	-	-
35	43.0	58.8	93.3	116.1	134.1	149.9	159.9	175.4
37	45.0	59.8	93.3	120.6	140.9	148.7	162.1	174.1
39	48.8	64.6	102.8	134.1	154.3	171.1	178.1	184.9
61	45.6	61.0	98.6	126.7	147.5	159.6	176.1	189.5
63	49.3	66.4	101.1	128.1	141.8	163.1	176.5	187.5
65	41.0	55.7	92.4	126.4	134.0	153.2	168.9	176.9
67	46.6	62.8	100.4	129.6	151.7	167.5	172.9	187.3
69	43.2	58.6	97.7	130.8	154.9	166.6	192.2	200.1
Mean	45.61	61.17	97.48	125.67	143.89	159.91	172.56	183.24
SD	2.89	3.16	3.53	5.41	7.80	7.98	9.79	8.95
N	10	10	10	10	10	9	9	9

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

6% diet	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
31	189.7	196.1	201.2	199.9	209.2	217.0	208.3
33	-	-	-	-	-	-	-
35	186.8	192.1	194.1	201.2	200.7	201.3	204.4
37	179.6	178.5	192.4	192.4	195.5	193.2	203.3
39	193.8	204.3	210.8	209.2	210.4	214.1	217.9
61	202.2	193.0	211.1	202.3	213.3	219.3	209.6
63	190.4	204.2	207.9	208.1	215.2	219.6	214.4
65	180.9	195.9	207.6	220.8	212.5	213.6	214.0
67	195.4	204.4	200.9	213.3	214.1	214.4	214.1
69	211.5	204.6	217.4	221.3	224.4	216.9	230.9
Mean	192.26	197.01	204.82	207.61	210.59	212.16	212.99
SD	10.06	8.67	8.28	9.73	8.39	8.95	8.29
N	9	9	9	9	9	9	9

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

10% diet	Bodywt day -x (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	-4	0	7	14	21	28	35	42
1	42.7	58.8	99.5	134.2	152.8	170.7	186.9	200.1
3	48.1	61.7	95.9	120.2	132.9	151.9	163.3	171.4
5	44.0	58.9	88.6	105.6	125.7	137.6	152.4	158.3
7	47.7	61.0	96.6	124.1	141.8	159.4	172.2	176.5
9	49.1	64.1	100.7	130.3	151.0	168.6	179.2	193.3
71	49.1	64.9	100.3	130.8	156.9	174.3	194.5	199.6
73	55.2	71.7	106.6	136.2	157.6	170.2	185.0	196.2
75	41.9	57.8	94.7	116.7	128.8	151.4	166.6	172.6
77	45.3	62.2	98.9	127.9	147.3	165.2	176.6	182.3
79	41.5	56.5	91.1	118.9	137.6	148.0	162.4	172.7
Mean	46.46	61.76	97.29	124.49	143.24	159.73	173.91	182.30
SD	4.24	4.41	5.14	9.33	11.63	12.06	12.97	14.32
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 3: Body weight

Sex: Female Day(s) Relative to Start Date

10% diet	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)	Bodywt (g)
	49	56	63	70	77	84	90
1	198.1	209.5	219.2	221.6	215.5	224.0	225.0
3	171.6	184.6	190.6	195.7	189.2	195.0	195.4
5	173.7	177.5	183.4	179.3	185.3	192.4	195.2
7	191.9	196.7	201.6	197.3	199.1	209.4	207.0
9	203.3	206.6	202.2	215.3	218.1	222.4	223.3
71	207.5	208.9	221.5	223.5	226.4	223.6	234.3
73	205.5	207.8	217.8	221.7	220.1	218.9	224.5
75	172.1	188.2	194.5	200.1	191.4	199.2	206.8
77	195.5	197.5	205.7	203.0	208.8	209.2	209.5
79	179.0	180.6	191.6	191.7	201.6	201.8	203.4
Mean	189.82	195.79	202.81	204.92	205.55	209.59	212.44
SD	14.41	12.35	13.22	14.96	14.33	12.17	13.49
N	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Male Daily Food Cons Per Animal (Gram)

0% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
8	5	10.13	12.43	14.79	16.50	16.83	17.59	17.73	18.85	19.69	19.50	19.27	19.13	19.47
14	5	10.94	13.40	15.99	17.94	18.19	18.52	19.54	20.35	21.19	21.37	21.70	21.61	21.12
	Mean	10.5	12.9	15.4	17.2	17.5	18.1	18.6	19.6	20.4	20.4	20.5	20.4	20.3
	SD	0.6	0.7	0.9	1.0	1.0	0.7	1.3	1.1	1.1	1.3	1.7	1.7	1.2
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Male Daily Food Cons Per Animal (Gram)

0% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
8	5	19.22	19.14	18.79	18.68	18.81	18.96	18.56	19.05	19.33	18.72	18.52	17.11	20.55
14	5	20.93	20.43	21.13	20.27	20.00	19.61	19.83	19.43	20.39	19.81	18.79	17.18	19.73
	Mean	20.1	19.8	20.0	19.5	19.4	19.3	19.2	19.2	19.9	19.3	18.7	17.1	20.1
	SD	1.2	0.9	1.7	1.1	0.8	0.5	0.9	0.3	0.8	0.8	0.2	0.1	0.6
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Male Daily Food Cons Per Animal (Gram)

3% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
2	5	9.92	13.11	16.01	17.40	17.70	18.18	18.80	19.84	20.48	20.71	20.49	20.57	20.57
16	5	11.21	13.31	15.78	17.65	18.16	18.97	19.46	20.81	21.00	20.64	20.78	20.75	20.76
	Mean	10.6	13.2	15.9	17.5	17.9	18.6	19.1	20.3	20.7	20.7	20.6	20.7	20.7
	SD	0.9	0.1	0.2	0.2	0.3	0.6	0.5	0.7	0.4	0.1	0.2	0.1	0.1
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Male Daily Food Cons Per Animal (Gram)

3% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
2	5	20.64	19.88	19.66	19.30	18.94	19.20	19.53	19.89	20.29	19.43	18.76	17.45	18.82
16	5	20.86	20.28	20.67	20.50	20.04	20.15	20.05	20.46	20.91	19.89	19.15	18.48	20.02
	Mean	20.8	20.1	20.2	19.9	19.5	19.7	19.8	20.2	20.6	19.7	19.0	18.0	19.4
	SD	0.2	0.3	0.7	0.8	0.8	0.7	0.4	0.4	0.4	0.3	0.3	0.7	0.8
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Male Daily Food Cons Per Animal (Gram)

6% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
4	5	10.77	13.73	16.14	17.59	17.87	18.80	19.94	20.27	20.63	21.07	21.41	20.49	20.60
10	5	10.72	13.06	16.26	18.25	18.20	18.66	19.26	20.52	20.36	21.23	20.63	19.93	20.33
	Mean	10.7	13.4	16.2	17.9	18.0	18.7	19.6	20.4	20.5	21.2	21.0	20.2	20.5
	SD	0.0	0.5	0.1	0.5	0.2	0.1	0.5	0.2	0.2	0.1	0.6	0.4	0.2
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Male Daily Food Cons Per Animal (Gram)

6% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
4	5	21.09	20.66	19.75	19.41	19.34	19.55	19.41	19.64	20.25	18.93	18.76	18.18	19.03
10	5	20.08	19.25	18.36	18.91	18.61	18.27	18.51	19.07	19.28	18.74	18.19	17.01	18.66
	Mean	20.6	20.0	19.1	19.2	19.0	18.9	19.0	19.4	19.8	18.8	18.5	17.6	18.8
	SD	0.7	1.0	1.0	0.4	0.5	0.9	0.6	0.4	0.7	0.1	0.4	0.8	0.3
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Male Daily Food Cons Per Animal (Gram)

10% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
6	5	9.65	12.21	14.49	16.98	17.16	18.01	18.36	18.93	19.80	19.71	20.38	19.57	19.53
12	5	10.35	12.37	15.08	17.20	17.32	17.05	17.95	19.13	20.11	19.58	19.57	18.89	19.01
	Mean	10.0	12.3	14.8	17.1	17.2	17.5	18.2	19.0	20.0	19.6	20.0	19.2	19.3
	SD	0.5	0.1	0.4	0.2	0.1	0.7	0.3	0.1	0.2	0.1	0.6	0.5	0.4
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Male Daily Food Cons Per Animal (Gram)

10% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
6	5	19.13	18.91	19.62	18.54	18.64	18.43	18.74	18.84	19.38	18.98	17.72	16.70	18.33
12	5	19.05	18.26	18.55	18.67	18.72	18.50	19.69	19.46	19.84	18.52	20.34	17.01	18.17
	Mean	19.1	18.6	19.1	18.6	18.7	18.5	19.2	19.1	19.6	18.7	19.0	16.9	18.3
	SD	0.1	0.5	0.8	0.1	0.1	0.0	0.7	0.4	0.3	0.3	1.9	0.2	0.1
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Female Daily Food Cons Per Animal (Gram)

0% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
3	5	10.04	11.85	13.04	13.36	13.09	13.86	13.76	13.69	13.75	14.15	14.57	14.56	14.86
9	5	10.18	11.72	13.20	13.88	13.35	13.81	13.62	14.18	14.11	14.49	14.74	15.23	15.17
	Mean	10.1	11.8	13.1	13.6	13.2	13.8	13.7	13.9	13.9	14.3	14.7	14.9	15.0
	SD	0.1	0.1	0.1	0.4	0.2	0.0	0.1	0.3	0.3	0.2	0.1	0.5	0.2
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Female Daily Food Cons Per Animal (Gram)

0% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
3	5	15.43	15.49	15.65	14.96	14.97	14.00	15.03	14.54	15.44	13.46	14.58	12.25	15.57
9	5	14.31	14.18	14.32	14.39	14.13	14.47	14.98	14.71	15.31	13.94	14.53	12.61	16.80
	Mean	14.9	14.8	15.0	14.7	14.6	14.2	15.0	14.6	15.4	13.7	14.6	12.4	16.2
	SD	0.8	0.9	0.9	0.4	0.6	0.3	0.0	0.1	0.1	0.3	0.0	0.3	0.9
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Female Daily Food Cons Per Animal (Gram)

3% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
5	5	9.87	12.34	13.54	14.27	13.63	14.10	13.97	15.03	14.62	14.81	14.79	14.88	14.79
11	5	9.20	11.04	12.68	13.39	13.27	13.52	13.41	14.20	14.13	14.26	14.69	15.14	15.32
	Mean	9.5	11.7	13.1	13.8	13.4	13.8	13.7	14.6	14.4	14.5	14.7	15.0	15.1
	SD	0.5	0.9	0.6	0.6	0.3	0.4	0.4	0.6	0.4	0.4	0.1	0.2	0.4
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Female Daily Food Cons Per Animal (Gram)

3% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
5	5	14.29	14.80	15.51	14.46	15.19	14.68	15.22	14.61	15.51	13.79	14.70	12.41	15.08
11	5	14.67	14.76	14.75	14.89	14.44	15.31	15.03	14.25	16.11	13.10	13.45	12.31	14.38
	Mean	14.5	14.8	15.1	14.7	14.8	15.0	15.1	14.4	15.8	13.4	14.1	12.4	14.7
	SD	0.3	0.0	0.5	0.3	0.5	0.4	0.1	0.3	0.4	0.5	0.9	0.1	0.5
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Female Daily Food Cons Per Animal (Gram)

6% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
7	5	9.86	11.82	13.15	14.12	13.30	13.66	12.80	14.13 n=4	14.48 n=4	15.03 n=4	14.98 n=4	15.05 n=4	15.18 n=4
13	5	10.38	11.99	13.84	14.47	13.87	13.73	14.05	14.65	14.50	14.52	14.90	14.60	14.87
	Mean	10.1	11.9	13.5	14.3	13.6	13.7	13.4	14.4	14.5	14.8	14.9	14.8	15.0
	SD	0.4	0.1	0.5	0.2	0.4	0.0	0.9	0.4	0.0	0.4	0.1	0.3	0.2
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Female Daily Food Cons Per Animal (Gram)

6% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
7	5	15.12 n=4	15.41 n=4	15.32 n=4	14.66 n=4	15.43 n=4	14.79 n=4	14.24 n=4	14.64 n=4	15.63 n=4	13.50 n=4	14.11 n=4	13.30 n=4	16.25 n=4
13	5	14.61	14.64	14.84	14.78	14.81	14.79	15.47	15.15	15.46	13.83	13.51	12.43	14.71
	Mean	14.9	15.0	15.1	14.7	15.1	14.8	14.9	14.9	15.5	13.7	13.8	12.9	15.5
	SD	0.4	0.5	0.3	0.1	0.4	0.0	0.9	0.4	0.1	0.2	0.4	0.6	1.1
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

n = Number of Animals in Cage
Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 4: Food consumption

Sex: Female Daily Food Cons Per Animal (Gram)

10% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		0 → 4	4 → 7	7 → 11	11 → 14	14 → 18	18 → 21	21 → 25	25 → 28	28 → 32	32 → 35	35 → 39	39 → 42	42 → 46
1	5	9.19	11.07	12.46	12.99	12.94	13.14	13.34	13.61	13.46	13.49	13.59	14.05	13.55
15	5	9.13	11.33	12.83	13.54	13.00	13.43	13.50	14.29	14.19	13.80	13.68	13.51	13.65
	Mean	9.2	11.2	12.6	13.3	13.0	13.3	13.4	14.0	13.8	13.6	13.6	13.8	13.6
	SD	0.0	0.2	0.3	0.4	0.0	0.2	0.1	0.5	0.5	0.2	0.1	0.4	0.1
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Sex: Female Daily Food Cons Per Animal (Gram)

10% diet	No. in Cage	Day(s) Relative to Animal Start Date												
		46 → 49	49 → 53	53 → 56	56 → 60	60 → 63	63 → 67	67 → 70	70 → 74	74 → 77	77 → 81	81 → 84	84 → 88	88 → 90
1	5	13.97	13.29	13.60	13.51	12.91	13.23	13.61	13.28	14.43	12.23	13.06	10.86	13.15
15	5	13.17	13.01	14.08	13.02	13.75	13.71	13.88	13.80	14.31	12.86	12.89	11.62	12.79
	Mean	13.6	13.2	13.8	13.3	13.3	13.5	13.7	13.5	14.4	12.5	13.0	11.2	13.0
	SD	0.6	0.2	0.3	0.3	0.6	0.3	0.2	0.4	0.1	0.4	0.1	0.5	0.3
	N	2	2	2	2	2	2	2	2	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Male Daily Water Cons Per Animal (Millilitre)

0% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
8	5	13.20	14.18	15.60	15.84	17.18
14	5	12.90	13.86	15.36	16.64	17.12
	Mean	13.1	14.0	15.5	16.2	17.2
	SD	0.2	0.2	0.2	0.6	0.0
	N	2	2	2	2	2

0% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
8	5	23.76	24.64	22.70	24.64	22.28
14	5	24.26	26.84	25.52	26.24	24.64
	Mean	24.0	25.7	24.1	25.4	23.5
	SD	0.4	1.6	2.0	1.1	1.7
	N	2	2	2	2	2

0% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
8	5	24.12	23.04	24.22	25.62	21.06
14	5	21.74	25.46	24.56	28.24	21.10
	Mean	22.9	24.3	24.4	26.9	21.1
	SD	1.7	1.7	0.2	1.9	0.0
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Male Daily Water Cons Per Animal (Millilitre)

3% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
2	5	13.42	14.14	15.56	15.98	17.60
16	5	14.40	15.58	15.92	16.44	17.16
	Mean	13.9	14.9	15.7	16.2	17.4
	SD	0.7	1.0	0.3	0.3	0.3
	N	2	2	2	2	2

3% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
2	5	25.28	25.48	25.50	24.34	23.66
16	5	25.74	26.26	26.20	26.00	26.46
	Mean	25.5	25.9	25.9	25.2	25.1
	SD	0.3	0.6	0.5	1.2	2.0
	N	2	2	2	2	2

3% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
2	5	25.74	25.14	26.72	27.02	22.60
16	5	23.34	26.78	25.28	27.56	23.12
	Mean	24.5	26.0	26.0	27.3	22.9
	SD	1.7	1.2	1.0	0.4	0.4
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Male Daily Water Cons Per Animal (Millilitre)

6% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
4	5	14.92	15.74	16.04	16.22	17.78
10	5	13.08	14.08	15.06	15.18	16.00
	Mean	14.0	14.9	15.6	15.7	16.9
	SD	1.3	1.2	0.7	0.7	1.3
	N	2	2	2	2	2

6% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
4	5	26.20	25.30	24.86	24.36	25.04
10	5	24.90	25.92	23.84	26.04	23.94
	Mean	25.6	25.6	24.4	25.2	24.5
	SD	0.9	0.4	0.7	1.2	0.8
	N	2	2	2	2	2

6% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
4	5	23.92	22.72	25.48	26.16	20.90
10	5	22.54	25.52	25.94	23.46	22.86
	Mean	23.2	24.1	25.7	24.8	21.9
	SD	1.0	2.0	0.3	1.9	1.4
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Male Daily Water Cons Per Animal (Millilitre)

10% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
6	5	13.42	15.26	16.22	17.14	20.32
12	5	13.72	16.06	16.00	18.20	16.74
	Mean	13.6	15.7	16.1	17.7	18.5
	SD	0.2	0.6	0.2	0.7	2.5
	N	2	2	2	2	2

10% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
6	5	27.02	27.22	25.94	26.16	27.26
12	5	26.96	26.12	26.82	25.52	24.58
	Mean	27.0	26.7	26.4	25.8	25.9
	SD	0.0	0.8	0.6	0.5	1.9
	N	2	2	2	2	2

10% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
6	5	27.58	28.08	27.28	28.78	24.98
12	5	23.56	23.58	26.24	28.10	23.54
	Mean	25.6	25.8	26.8	28.4	24.3
	SD	2.8	3.2	0.7	0.5	1.0
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Female Daily Water Cons Per Animal (Millilitre)

0% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
3	5	13.38	13.64	15.58	15.04	16.98
9	5	13.14	15.12	16.18	16.08	17.50
	Mean	13.3	14.4	15.9	15.6	17.2
	SD	0.2	1.0	0.4	0.7	0.4
	N	2	2	2	2	2

0% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
3	5	22.06	24.46	20.30	19.68	19.90
9	5	21.30	23.56	20.70	17.86	20.20
	Mean	21.7	24.0	20.5	18.8	20.1
	SD	0.5	0.6	0.3	1.3	0.2
	N	2	2	2	2	2

0% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
3	5	20.44	21.96	22.76	21.04	20.02
9	5	20.80	19.44	24.10	24.20	21.78
	Mean	20.6	20.7	23.4	22.6	20.9
	SD	0.3	1.8	0.9	2.2	1.2
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Female Daily Water Cons Per Animal (Millilitre)

3% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
5	5	13.72	14.44	14.88	15.56	17.38
11	5	11.96	11.68	13.04	13.44	16.00
	Mean	12.8	13.1	14.0	14.5	16.7
	SD	1.2	2.0	1.3	1.5	1.0
	N	2	2	2	2	2

3% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
5	5	21.18	17.84	21.00	17.64	19.88
11	5	22.34	21.66	18.92	17.70	22.54
	Mean	21.8	19.8	20.0	17.7	21.2
	SD	0.8	2.7	1.5	0.0	1.9
	N	2	2	2	2	2

3% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
5	5	20.06	19.74	23.42	20.18	20.12
11	5	14.74	20.82	23.82	22.58	17.04
	Mean	17.4	20.3	23.6	21.4	18.6
	SD	3.8	0.8	0.3	1.7	2.2
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Female Daily Water Cons Per Animal (Millilitre)

6% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
7	5	12.52	13.42	13.60	14.70	15.60
13	5	13.84	14.10	16.26	15.46	16.96
	Mean	13.2	13.8	14.9	15.1	16.3
	SD	0.9	0.5	1.9	0.5	1.0
	N	2	2	2	2	2

6% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
7	5	18.25 n=4	21.80 n=4	18.78 n=4	20.83 n=4	18.03 n=4
13	5	17.74	23.20	22.98	20.44	18.46
	Mean	18.0	22.5	20.9	20.6	18.2
	SD	0.4	1.0	3.0	0.3	0.3
	N	2	2	2	2	2

6% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
7	5	18.90 n=4	20.55 n=4	21.38 n=4	20.90 n=4	17.13 n=4
13	5	19.30	22.18	22.56	25.36	18.32
	Mean	19.1	21.4	22.0	23.1	17.7
	SD	0.3	1.2	0.8	3.2	0.8
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 5: Water consumption

Sex: Female Daily Water Cons Per Animal (Millilitre)

10% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
1	5	13.66	14.52	14.26	17.10	18.84
15	5	12.52	14.44	15.76	16.04	17.54
	Mean	13.1	14.5	15.0	16.6	18.2
	SD	0.8	0.1	1.1	0.7	0.9
	N	2	2	2	2	2

10% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		35 → 36	36 → 37	37 → 38	38 → 39	39 → 40
1	5	22.18	22.18	20.78	22.10	21.34
15	5	18.94	21.68	22.50	21.26	20.36
	Mean	20.6	21.9	21.6	21.7	20.9
	SD	2.3	0.4	1.2	0.6	0.7
	N	2	2	2	2	2

10% diet	No. in Cage	Day(s) Relative to Animal Start Date				
		77 → 78	78 → 79	79 → 80	80 → 81	81 → 82
1	5	18.78	20.94	23.18	21.48	17.44
15	5	17.92	20.10	19.48	23.08	18.92
	Mean	18.4	20.5	21.3	22.3	18.2
	SD	0.6	0.6	2.6	1.1	1.0
	N	2	2	2	2	2

Consumption was measured per cage over the periods shown and expressed as g/animal/day

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Male Day: 91 Relative to Start Date

0% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
32	9.03	9.8	0.505	55.9	1.09	19.4	2.40	794	19.0
34	8.73	9.5	0.489	56.0	1.09	19.4	1.93	761	19.6
36	9.03	9.1	0.484	53.6	1.01	18.8	2.74	873	18.5
38	8.97	9.6	0.492	54.8	1.07	19.5	2.08	805	18.6
40	9.41	10.2	0.522	55.5	1.08	19.5	1.85	773	18.5
62	8.70	9.9	0.495	56.9	1.14	20.0	2.83	851	17.7
64	9.51	9.8	0.517	54.4	1.03	19.0	2.10	892	20.8
66	8.39	9.5	0.468	55.8	1.13	20.3	2.17	911	18.1
68	8.69	9.5	0.487	56.0	1.09	19.5	2.62	673	18.1
70	9.38	9.6	0.497	53.0	1.02	19.3	2.44	929	18.4
Mean	8.984	9.65	0.4956	55.19	1.075	19.48	2.316	826.2	18.73
SD	0.366	0.30	0.0159	1.22	0.044	0.44	0.341	79.5	0.89
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Male Day: 91 Relative to Start Date

3% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
2	9.17	9.8	0.508	55.4	1.07	19.3	2.37	768	19.0
4	8.58	9.4	0.488	56.9	1.10	19.3	2.14	680	21.2
6	9.17	9.2	0.492	53.7	1.00	18.7	2.16	831	18.8
8	8.63	9.3	0.474	54.9	1.08	19.6	2.06	808	18.5
10	9.10	10.0	0.511	56.2	1.10	19.6	2.36	908	19.5
72	9.10	10.0	0.514	56.5	1.10	19.5	2.52	774	18.7
74	9.22	10.1	0.515	55.9	1.10	19.6	2.11	1029	18.2
76	9.02	10.2	0.518	57.4	1.13	19.7	2.53	889	18.0
78	9.05	9.4	0.495	54.7	1.04	19.0	2.53	727	18.6
80	9.03	9.5	0.495	54.8	1.05	19.2	3.03	1166	18.2
Mean	9.007	9.69	0.5010	55.63	1.076	19.34	2.381	858.0	18.87
SD	0.222	0.37	0.0144	1.15	0.037	0.32	0.292	147.1	0.93
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Male Day: 91 Relative to Start Date

6% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
12	8.66	9.5	0.493	56.9	1.10	19.3	2.70	711	18.8
14	9.22	10.0	0.519	56.3	1.08	19.3	2.38	694	18.0
16	8.53	8.8	0.456	53.5	1.03	19.3	2.55	856	19.6
18	8.61	9.7	0.496	57.6	1.13	19.6	2.17	799	17.1
20	9.35	9.7	0.507	54.2	1.04	19.1	2.19	934	19.1
42	8.46	9.6	0.490	57.9	1.13	19.6	2.94	810	18.4
44	8.54	9.6	0.490	57.4	1.12	19.6	2.39	1127	19.5
46	9.01	9.6	0.489	54.3	1.07	19.6	1.79	881	19.0
48	8.83	9.8	0.499	56.5	1.11	19.6	2.68	604	19.7
50	9.54	9.5	0.498	52.2	1.00	19.1	2.39	1097	18.5
Mean	8.875	9.58	0.4937	55.68	1.081	19.41	2.418	851.3	18.77
SD	0.384	0.31	0.0161	1.98	0.047	0.22	0.325	168.0	0.81
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Male Day: 91 Relative to Start Date

10% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
22	9.12	9.6	0.502	55.0	1.05	19.1	2.16	745	18.0
24	9.15	9.6	0.503	55.0	1.05	19.1	2.22	783	19.5
26	8.22	9.0	0.465	56.6	1.09	19.4	2.47	757	17.4
28	8.80	9.7	0.501	56.9	1.10	19.4	2.27	683	18.8
30	9.23	9.9	0.520	56.3	1.07	19.0	1.88	919	19.2
52	8.64	9.6	0.487	56.4	1.11	19.7	2.44	746	18.5
54	8.98	9.7	0.508	56.6	1.08	19.1	1.67	1016	18.8
56	8.80	9.4	0.478	54.3	1.07	19.7	1.94	783	19.2
58	9.88	10.8	0.567	57.4	1.09	19.0	2.56	828	17.6
60	8.69	9.2	0.475	54.7	1.06	19.4	2.22	785	19.2
Mean	8.951	9.65	0.5006	55.92	1.078	19.29	2.183	804.5	18.62
SD	0.442	0.48	0.0288	1.07	0.022	0.25	0.282	96.4	0.73
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Female Day: 92 Relative to Start Date

0% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
11	9.18	9.9	0.519	56.5	1.08	19.1	2.06	860	19.4
13	7.77	9.2	0.462	59.5	1.18	19.9	2.60	675	19.1
15	8.28	9.2	0.475	57.4	1.11	19.4	1.77	641	20.1
17	8.02	9.1	0.469	58.5	1.13	19.4	2.67	765	18.4
19	8.49	9.7	0.489	57.6	1.14	19.8	2.48	725	18.6
41	8.17	9.5	0.487	59.6	1.16	19.5	2.60	773	18.7
43	8.31	9.4	0.480	57.8	1.13	19.6	3.05	826	18.8
45	8.16	9.5	0.475	58.2	1.16	20.0	2.56	778	18.3
47	8.32	9.9	0.493	59.3	1.19	20.1	2.82	617	19.2
49	8.64	9.2	0.474	54.9	1.06	19.4	2.16	760	17.9
Mean	8.334	9.46	0.4823	57.91	1.136	19.62	2.477	742.0	18.85
SD	0.382	0.30	0.0160	1.46	0.042	0.33	0.379	78.0	0.63
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Female Day: 92 Relative to Start Date

3% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
21	8.31	9.0	0.469	56.4	1.08	19.2	2.38	757	19.2
23	8.02	9.3	0.467	58.2	1.16	19.9	2.68	767	18.6
25	8.60	9.8	0.504	58.6	1.14	19.4	1.75	777	18.7
27	8.12	9.6	0.481	59.2	1.18	20.0	2.60	800	18.1
29	8.57	9.7	0.491	57.3	1.13	19.8	2.35	844	18.6
51	8.38	10.1	0.502	59.9	1.21	20.1	2.00	710	17.9
53	8.57	9.5	0.475	55.4	1.11	20.0	1.94	894	19.0
55	8.26	9.2	0.456	55.2	1.11	20.2	2.21	786	19.8
57	8.41	9.6	0.482	57.3	1.14	19.9	2.19	707	18.4
59	8.36	9.1	0.464	55.5	1.09	19.6	1.72	987	18.7
Mean	8.360	9.49	0.4791	57.32	1.135	19.81	2.182	802.9	18.70
SD	0.193	0.34	0.0161	1.67	0.039	0.31	0.330	85.7	0.54
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Female Day: 92 Relative to Start Date

6% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
31	8.82	9.9	0.512	58.0	1.12	19.3	1.59	763	18.7
35	8.51	9.5	0.481	56.5	1.12	19.8	2.01	803	18.9
37	8.14	9.1	0.461	56.6	1.12	19.7	2.73	746	17.7
39	9.15	10.2	0.517	56.5	1.11	19.7	1.74	776	21.2
61	7.98	9.4	0.469	58.8	1.18	20.0	2.11	940	19.2
63	7.93	9.0	0.456	57.5	1.13	19.7	1.77	829	19.7
65	7.92	9.2	0.445	56.2	1.16	20.7	2.06	777	18.8
67	8.33	9.4	0.487	58.5	1.13	19.3	2.22	704	19.2
69	8.79	9.4	0.489	55.6	1.07	19.2	2.35	950	18.0
Mean	8.397	9.46	0.4797	57.14	1.127	19.73	2.064	809.8	19.04
SD	0.448	0.38	0.0245	1.10	0.031	0.45	0.348	84.2	1.01
N	9	9	9	9	9	9	9	9	9

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 6: Red blood cell and coagulation parameters

Sex: Female Day: 92 Relative to Start Date

10% diet	RBC (10E12/L)	Hb (mmol/L)	PCV (L/L)	MCV (fL)	MCH (fmol)	MCHC (mmol/L)	Reticulocytes (%)	Thrombocytes (10E9/L)	Prothrom Time (s)
1	7.84	8.9	0.448	57.1	1.14	19.9	2.49	868	19.0
3	7.88	9.2	0.460	58.4	1.17	20.0	3.03	680	18.3
5	7.93	9.1	0.469	59.1	1.15	19.4	2.38	755	19.5
7	7.92	9.4	0.470	59.3	1.19	20.0	2.64	862	18.8
9	8.60	10.0	0.500	58.1	1.16	20.0	2.18	884	21.6
71	7.63	9.1	0.446	58.5	1.19	20.4	2.80	908	18.6
73	7.97	9.3	0.470	59.0	1.17	19.8	2.62	812	18.0
75	8.31	9.3	0.456	54.9	1.12	20.4	2.29	956	17.5
77	8.69	9.8	0.495	57.0	1.13	19.8	1.66	813	18.6
79	9.07	9.8	0.499	55.0	1.08	19.6	1.90	1018	16.7
Mean	8.184	9.39	0.4713	57.64	1.149	19.93	2.399	855.6	18.66
SD	0.463	0.36	0.0203	1.62	0.034	0.31	0.412	97.1	1.30
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Male Day: 91 Relative to Start Date

0% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
32	5.4	4.3	0.9	0.03	0.01	0.08	80.5	16.7	0.6	0.1	1.4
34	5.9	4.4	1.3	0.06	0.02	0.09	73.8	22.5	1.1	0.3	1.6
36	3.7	2.7	0.8	0.04	0.01	0.08	73.8	22.3	1.2	0.2	2.2
38	4.0	2.5	1.3	0.09	0.01	0.08	63.3	32.0	2.3	0.2	1.9
40	5.2	4.0	0.9	0.06	0.01	0.17	77.2	17.6	1.1	0.2	3.2
62	5.7	4.2	1.3	0.06	0.01	0.14	73.7	22.1	1.1	0.1	2.4
64	8.3	6.9	1.1	0.07	0.02	0.20	82.6	13.7	0.9	0.2	2.4
66	3.6	2.6	0.9	0.03	0.00	0.07	71.9	24.6	0.9	0.1	2.0
68	5.5	4.2	1.1	0.05	0.00	0.10	76.9	19.8	0.9	0.0	1.9
70	5.6	4.2	1.2	0.07	0.01	0.11	74.4	22.1	1.2	0.1	1.9
Mean	5.29	4.00	1.09	0.058	0.008	0.111	74.81	21.34	1.13	0.15	2.09
SD	1.37	1.26	0.19	0.019	0.006	0.043	5.24	4.99	0.45	0.08	0.50
N	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Male Day: 91 Relative to Start Date

3% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
2	6.0	4.3	1.5	0.08	0.01	0.13	71.4	24.5	1.3	0.1	2.1
4	7.8	5.7	1.8	0.13	0.02	0.16	72.9	22.5	1.7	0.3	2.0
6	5.6	4.5	0.9	0.05	0.01	0.13	79.8	16.6	0.9	0.1	2.3
8	2.6	1.9	0.6	0.03	0.00	0.04	72.9	24.2	1.3	0.1	1.4
10	6.2	4.9	1.0	0.12	0.01	0.12	78.6	16.8	1.9	0.1	2.0
72	8.5	7.0	1.3	0.09	0.02	0.12	82.2	14.8	1.0	0.2	1.4
74	9.1	8.0	0.9	0.06	0.02	0.08	88.2	9.6	0.7	0.2	0.9
76	5.9	4.3	1.4	0.03	0.01	0.15	73.0	23.2	0.5	0.2	2.5
78	5.4	4.0	1.2	0.06	0.01	0.16	73.5	21.3	1.2	0.1	3.0
80	5.7	4.2	1.3	0.05	0.01	0.11	74.4	22.2	0.9	0.1	1.9
Mean	6.28	4.87	1.17	0.071	0.010	0.119	76.69	19.57	1.14	0.15	1.95
SD	1.84	1.70	0.32	0.034	0.007	0.037	5.39	4.90	0.43	0.07	0.60
N	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Male Day: 91 Relative to Start Date

6% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
12	6.0	4.6	1.2	0.08	0.01	0.10	77.0	19.3	1.3	0.1	1.7
14	5.6	4.1	1.3	0.07	0.02	0.15	72.5	22.9	1.2	0.3	2.7
16	3.5	2.6	0.8	0.02	0.00	0.08	74.2	22.4	0.5	0.1	2.4
18	2.7	2.0	0.6	0.02	0.00	0.04	75.9	21.6	0.8	0.0	1.5
20	4.7	3.7	0.8	0.06	0.01	0.09	79.6	16.5	1.3	0.2	2.0
42	6.2	3.4	2.6	0.06	0.01	0.11	55.6	41.3	0.9	0.2	1.8
44	8.1	6.8	1.0	0.10	0.02	0.14	83.7	12.8	1.2	0.2	1.7
46	6.7	5.0	1.5	0.05	0.01	0.11	75.1	22.1	0.7	0.1	1.7
48	5.3	4.2	1.0	0.05	0.01	0.06	79.5	18.2	0.9	0.1	1.2
50	5.2	3.6	1.4	0.07	0.01	0.10	68.8	27.2	1.4	0.2	1.9
Mean	5.40	4.01	1.20	0.057	0.009	0.100	74.19	22.43	1.02	0.15	1.86
SD	1.54	1.31	0.56	0.025	0.005	0.033	7.72	7.71	0.30	0.08	0.43
N	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Male Day: 91 Relative to Start Date

10% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
22	3.5	2.5	0.9	0.01	0.00	0.10	71.3	24.9	0.4	0.1	2.8
24	5.1	3.7	1.2	0.08	0.01	0.06	73.5	23.3	1.6	0.1	1.2
26	5.2	3.8	1.2	0.03	0.01	0.10	73.8	23.1	0.5	0.1	1.9
28	4.1	3.0	0.9	0.04	0.00	0.09	74.3	22.1	1.0	0.1	2.2
30	5.2	4.1	1.0	0.05	0.00	0.08	78.1	19.1	0.9	0.0	1.5
52	6.0	5.0	0.9	0.04	0.01	0.08	82.5	15.2	0.6	0.2	1.3
54	9.8	7.9	1.6	0.06	0.02	0.16	80.7	16.4	0.6	0.2	1.6
56	4.7	3.5	1.0	0.03	0.01	0.07	75.4	22.1	0.6	0.2	1.4
58	7.9	6.1	1.5	0.10	0.02	0.12	77.2	19.6	1.3	0.2	1.5
60	5.1	3.9	1.1	0.08	0.01	0.07	75.5	20.9	1.5	0.1	1.3
Mean	5.66	4.35	1.13	0.051	0.008	0.091	76.23	20.67	0.90	0.13	1.67
SD	1.87	1.59	0.26	0.028	0.006	0.029	3.44	3.10	0.43	0.07	0.50
N	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Female Day: 92 Relative to Start Date

0% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
11	3.4	2.7	0.6	0.03	0.00	0.04	78.9	18.4	1.0	0.0	1.2
13	2.9	2.5	0.3	0.03	0.01	0.04	85.2	11.6	1.2	0.2	1.3
15	3.6	2.8	0.7	0.02	0.00	0.09	78.0	18.3	0.5	0.1	2.4
17	2.0	1.7	0.2	0.01	0.00	0.03	86.0	11.2	0.7	0.2	1.7
19	3.7	2.8	0.8	0.06	0.00	0.09	74.9	20.6	1.6	0.1	2.4
41	4.2	3.6	0.5	0.04	0.01	0.09	85.1	11.2	1.0	0.2	2.1
43	5.4	3.5	1.7	0.05	0.01	0.09	65.5	31.5	0.9	0.1	1.7
45	4.7	3.6	0.8	0.08	0.00	0.12	77.2	18.0	1.7	0.1	2.5
47	5.6	4.5	0.9	0.06	0.01	0.12	79.7	16.5	1.1	0.2	2.1
49	2.9	2.2	0.6	0.03	0.00	0.07	76.4	19.3	1.0	0.1	2.4
Mean	3.84	2.99	0.71	0.042	0.005	0.077	78.69	17.66	1.07	0.13	1.98
SD	1.15	0.81	0.41	0.021	0.003	0.031	6.09	6.01	0.37	0.07	0.48
N	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Female Day: 92 Relative to Start Date

3% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
21	4.1	3.3	0.7	0.05	0.01	0.08	79.4	16.7	1.3	0.2	1.9
23	4.5	3.5	0.8	0.04	0.01	0.12	77.0	18.6	0.9	0.2	2.6
25	4.9	4.0	0.6	0.08	0.02	0.13	82.5	12.1	1.7	0.4	2.6
27	2.5	1.9	0.5	0.05	0.01	0.06	75.5	19.6	2.0	0.3	2.2
29	2.8	2.1	0.6	0.03	0.00	0.08	75.5	20.0	1.1	0.1	2.9
51	4.8	4.0	0.7	0.07	0.01	0.07	82.4	13.7	1.4	0.3	1.4
53	5.6	4.2	1.1	0.09	0.01	0.09	75.4	20.5	1.6	0.2	1.6
55	4.3	3.3	0.7	0.06	0.00	0.14	77.8	16.6	1.4	0.1	3.3
57	3.0	2.4	0.5	0.04	0.00	0.03	80.7	16.7	1.3	0.1	1.0
59	3.4	2.3	0.9	0.10	0.00	0.07	67.8	26.9	2.9	0.0	2.0
Mean	3.99	3.10	0.71	0.061	0.008	0.086	77.40	18.14	1.56	0.19	2.15
SD	1.02	0.86	0.21	0.023	0.006	0.034	4.34	4.09	0.56	0.12	0.71
N	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Female Day: 92 Relative to Start Date

6% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
31	4.4	3.8	0.4	0.04	0.00	0.07	86.5	10.1	1.0	0.1	1.6
35	3.5	2.7	0.6	0.02	0.00	0.13	77.5	17.2	0.7	0.1	3.6
37	2.1	1.6	0.4	0.02	0.00	0.04	77.7	18.7	1.1	0.1	1.9
39	2.3	1.9	0.3	0.03	0.00	0.05	81.5	14.3	1.3	0.2	2.3
61	3.3	2.6	0.6	0.03	0.00	0.07	78.8	17.6	1.0	0.1	2.0
63	4.1	3.4	0.6	0.04	0.00	0.08	82.3	14.0	1.0	0.1	2.0
65	6.9	5.3	1.3	0.07	0.01	0.20	77.0	18.4	1.0	0.2	2.9
67	4.4	3.3	0.9	0.09	0.00	0.13	73.9	20.1	2.0	0.0	2.9
69	3.2	2.1	1.0	0.04	0.00	0.05	65.6	30.8	1.4	0.1	1.7
Mean	3.80	2.96	0.67	0.044	0.004	0.091	77.87	17.91	1.17	0.11	2.32
SD	1.43	1.14	0.31	0.022	0.004	0.051	5.87	5.72	0.37	0.06	0.67
N	9	9	9	9	9	9	9	9	9	9	9

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 7: Total and differential white blood cell counts

Sex: Female Day: 92 Relative to Start Date

10% diet	WBC (10E9/L)	Lympho Absolute (10E9/L)	Neutro Absolute (10E9/L)	Eosino Absolute (10E9/L)	Baso Absolute (10E9/L)	Mono Absolute (10E9/L)	Lympho cytes (%)	Neutro phils (%)	Eosino phils (%)	Baso phils (%)	Mono cytes (%)
1	4.8	3.9	0.7	0.09	0.01	0.07	81.0	14.3	1.9	0.3	1.5
3	3.9	3.1	0.6	0.03	0.01	0.10	80.5	15.6	0.7	0.2	2.6
5	5.1	4.0	0.9	0.07	0.01	0.10	78.4	17.6	1.3	0.1	2.0
7	2.9	2.3	0.5	0.03	0.00	0.06	80.9	15.6	1.1	0.0	2.0
9	3.4	2.6	0.7	0.06	0.01	0.07	75.0	20.7	1.7	0.2	2.0
71	4.4	3.5	0.8	0.04	0.00	0.06	79.4	17.8	1.0	0.1	1.3
73	5.1	4.1	0.7	0.07	0.00	0.15	80.7	14.2	1.4	0.0	3.0
75	3.0	2.0	0.9	0.02	0.01	0.07	66.3	30.0	0.8	0.2	2.4
77	3.8	3.0	0.6	0.06	0.00	0.07	79.9	16.0	1.7	0.1	1.9
79	4.0	3.1	0.8	0.06	0.01	0.06	76.6	19.9	1.5	0.3	1.5
Mean	4.04	3.16	0.72	0.054	0.006	0.082	77.87	18.17	1.31	0.15	2.02
SD	0.80	0.72	0.14	0.022	0.005	0.030	4.53	4.70	0.40	0.11	0.53
N	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

0% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatinine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
32	180	72	55	0.0	1.2	36	68	37	1.19	7.06
34	101	67	45	0.0	1.3	37	65	35	1.17	8.63
36	136	74	43	0.0	0.8	36	62	34	1.21	9.02
38	168	90	55	0.0	1.9	41	63	34	1.17	5.77
40	91	63	43	0.0	1.3	27	62	33	1.14	6.66
62	74	66	41	0.0	1.6	34	65	35	1.17	7.70
64	135	73	57	0.0	1.4	36	60	34	1.31	9.82
66	157	72	53	0.0	1.2	36	63	35	1.25	6.76
68	99	58	39	0.0	1.7	30	61	33	1.18	7.49
70	98	59	38	0.0	1.2	30	65	34	1.10	8.15
Mean	123.9	69.4	46.9	0.00	1.36	34.3	63.4	34.4	1.188	7.706
SD	36.3	9.2	7.3	0.00	0.31	4.1	2.4	1.2	0.059	1.222
N	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

0% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
32	2.13	1.86	1.66	5.9	1.99	2.78	100	5.4	148
34	1.47	1.51	1.22	5.7	2.54	2.83	101	5.9	150
36	2.01	1.80	1.29	5.3	2.28	2.74	100	6.6	148
38	1.64	1.60	1.43	7.5	1.86	2.63	101	6.1	149
40	1.47	1.39	1.13	6.0	3.05	2.72	100	5.4	148
62	2.29	1.85	1.33	5.3	2.74	2.81	100	5.9	147
64	1.69	1.47	0.88	7.1	3.01	2.77	100	6.0	149
66	1.98	1.87	1.23	7.2	2.76	2.76	99	5.9	147
68	1.76	1.54	0.74	6.0	2.49	2.75	100	5.1	149
70	1.94	1.59	0.65	5.6	3.09	2.85	100	5.9	150
Mean	1.838	1.648	1.156	6.16	2.581	2.764	100.1	5.82	148.5
SD	0.276	0.180	0.315	0.81	0.433	0.062	0.6	0.42	1.1
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

3% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatin ine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
2	154	75	51	0.0	1.2	33	68	36	1.13	8.66
4	125	69	48	0.0	1.0	37	64	34	1.13	7.19
6	122	69	45	0.0	0.7	33	64	33	1.06	9.02
8	145	74	37	0.0	1.2	38	61	34	1.26	7.08
10	89	59	47	0.0	1.4	33	61	33	1.18	5.88
72	85	62	37	0.0	1.1	32	70	36	1.06	9.20
74	194	61	48	0.0	1.2	34	61	33	1.18	12.29
76	141	74	44	0.0	1.0	35	64	35	1.21	8.41
78	141	70	40	0.0	1.6	27	61	33	1.18	6.80
80	155	65	38	0.0	1.6	28	65	34	1.10	6.36
Mean	135.1	67.8	43.5	0.00	1.20	33.0	63.9	34.1	1.148	8.089
SD	32.1	5.8	5.1	0.00	0.28	3.5	3.1	1.2	0.064	1.872
N	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

3% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
2	1.74	1.82	1.95	7.2	2.36	2.85	99	5.4	147
4	1.50	1.56	0.81	7.4	2.73	2.78	100	6.1	146
6	2.28	1.94	1.27	7.1	2.38	2.73	100	5.2	148
8	1.39	1.45	1.54	6.3	1.75	2.66	101	6.5	148
10	1.78	1.62	1.03	6.6	2.35	2.63	101	5.3	147
72	1.94	1.63	0.81	6.2	2.86	2.91	99	6.0	148
74	1.68	1.51	0.60	8.0	2.94	2.80	98	6.0	147
76	1.94	1.89	1.57	6.4	2.87	2.85	101	6.4	151
78	1.07	1.27	0.85	6.4	3.18	2.69	99	5.7	148
80	2.32	1.80	0.53	6.3	2.83	2.79	100	5.8	149
Mean	1.764	1.649	1.096	6.79	2.625	2.769	99.8	5.84	147.9
SD	0.385	0.213	0.469	0.60	0.415	0.090	1.0	0.45	1.4
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

6% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatinine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
12	169	68	50	0.0	1.5	39	64	35	1.21	7.03
14	141	57	40	0.0	0.7	35	65	36	1.24	7.79
16	172	74	42	0.0	1.2	38	59	32	1.19	8.32
18	175	70	37	0.0	1.5	31	63	34	1.17	8.67
20	120	69	48	0.0	1.3	35	65	34	1.10	6.95
42	79	67	33	0.0	1.0	32	63	35	1.25	6.35
44	165	72	45	0.0	1.5	34	67	36	1.16	7.95
46	144	71	61	0.0	0.8	38	60	34	1.31	7.35
48	125	59	40	0.0	0.7	34	66	35	1.13	11.29
50	107	67	34	0.0	1.3	31	65	35	1.17	8.26
Mean	139.7	67.4	43.0	0.00	1.15	34.7	63.7	34.6	1.192	7.996
SD	31.9	5.4	8.4	0.00	0.33	2.9	2.5	1.2	0.062	1.361
N	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

6% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
12	1.85	1.69	1.58	7.0	2.71	2.73	100	5.7	148
14	1.39	1.55	1.25	8.3	2.25	2.77	103	5.6	145
16	1.44	1.45	1.04	6.3	2.60	2.74	103	5.9	149
18	1.65	1.69	1.07	7.0	2.81	2.75	104	6.2	143
20	2.01	1.74	1.20	5.9	2.58	2.78	101	5.6	149
42	1.59	1.47	0.82	5.7	2.90	2.78	100	6.1	147
44	2.55	1.86	0.76	6.9	2.86	2.80	97	6.6	146
46	1.58	1.51	1.46	8.2	2.42	2.75	99	5.9	148
48	1.76	1.66	1.10	7.1	2.69	2.87	99	5.7	149
50	1.77	1.57	1.12	7.9	2.42	2.72	100	5.4	148
Mean	1.759	1.619	1.140	7.03	2.624	2.769	100.6	5.87	147.2
SD	0.335	0.131	0.253	0.90	0.212	0.043	2.2	0.35	2.0
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

10% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatinine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
22	143	76	56	0.0	1.2	37	62	34	1.21	5.15
24	109	68	37	0.0	0.9	37	66	35	1.13	7.07
26	177	57	26	0.0	1.2	34	61	33	1.18	8.20
28	152	72	37	0.0	1.1	35	62	34	1.21	8.83
30	133	70	51	0.0	1.2	32	63	34	1.17	8.79
52	66	54	49	0.0	1.0	31	66	35	1.13	9.48
54	155	59	38	0.0	1.3	38	65	35	1.17	9.16
56	137	78	44	0.0	1.6	34	57	32	1.28	4.77
58	124	65	41	0.0	0.9	31	67	36	1.16	9.76
60	98	62	37	0.0	1.1	34	58	31	1.15	5.55
Mean	129.4	66.1	41.6	0.00	1.15	34.3	62.7	33.9	1.179	7.676
SD	31.9	8.1	8.7	0.00	0.21	2.5	3.4	1.5	0.046	1.896
N	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Male Day: 91 Relative to Start Date

10% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
22	1.40	1.48	0.86	7.2	2.50	2.69	104	6.3	144
24	1.51	1.46	0.86	7.4	1.99	2.67	99	5.7	148
26	2.12	1.77	0.62	6.9	2.53	2.66	100	5.4	148
28	1.35	1.57	1.70	7.8	2.63	2.78	101	6.2	149
30	1.65	1.53	1.27	6.5	2.48	2.80	100	5.5	149
52	1.93	1.65	0.93	6.8	3.04	2.90	97	5.3	148
54	1.65	1.36	0.70	7.3	2.84	2.77	99	5.7	147
56	1.57	1.55	1.14	7.5	3.61	2.75	101	6.6	149
58	1.57	1.67	1.08	7.5	2.23	2.87	100	5.2	148
60	1.44	1.33	0.57	6.9	3.26	2.68	102	6.2	149
Mean	1.619	1.537	0.973	7.18	2.711	2.757	100.3	5.81	147.9
SD	0.240	0.137	0.341	0.40	0.486	0.084	1.9	0.48	1.5
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

0% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatinine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
11	50	85	58	0.0	1.1	43	71	39	1.22	6.94
13	53	71	36	0.0	0.0	37	71	40	1.29	5.95
15	50	72	28	0.0	0.7	44	65	36	1.24	5.47
17	53	74	31	0.0	0.0	40	71	39	1.22	4.71
19	79	81	40	0.0	1.6	41	70	39	1.26	6.27
41	32	73	32	0.0	2.1	38	66	37	1.28	6.11
43	90	86	33	0.0	1.8	48	67	37	1.23	6.47
45	57	82	30	0.0	0.5	34	64	36	1.29	4.73
47	89	77	34	0.0	2.2	38	69	39	1.30	5.04
49	60	84	59	0.0	1.9	38	73	38	1.09	4.69
Mean	61.3	78.5	38.1	0.00	1.19	40.1	68.7	38.0	1.241	5.638
SD	18.8	5.8	11.2	0.00	0.85	4.0	3.0	1.4	0.062	0.822
N	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

0% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
11	0.94	1.17	0.71	6.6	1.81	2.88	97	5.4	140
13	1.03	1.28	1.06	7.4	2.20	2.90	98	5.9	141
15	1.66	1.82	0.86	7.0	1.77	2.78	97	5.3	140
17	1.58	2.13	2.79	6.8	1.78	2.79	98	6.0	140
19	2.08	2.37	0.76	7.2	2.00	2.77	97	5.7	141
41	1.66	1.99	0.75	7.5	2.92	2.81	96	6.2	140
43	1.90	1.96	0.74	6.5	1.95	2.69	96	5.2	139
45	1.05	1.30	0.63	5.8	2.52	2.77	97	5.5	141
47	1.86	2.26	0.69	6.9	3.09	2.79	97	5.4	140
49	2.06	2.23	0.81	7.5	2.67	2.90	98	5.9	140
Mean	1.582	1.851	0.980	6.92	2.271	2.808	97.1	5.65	140.2
SD	0.430	0.445	0.647	0.53	0.494	0.067	0.7	0.34	0.6
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

3% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatinine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
21	73	79	39	0.0	1.1	42	72	41	1.32	6.24
23	62	67	30	0.0	0.8	42	70	40	1.33	6.97
25	77	66	35	0.0	0.8	40	68	38	1.27	6.68
27	61	85	37	0.0	0.0	35	70	40	1.33	5.84
29	31	75	33	0.0	0.6	32	67	37	1.23	5.54
51	28	79	34	0.0	0.0	41	66	36	1.20	5.55
53	87	85	49	0.0	1.3	38	69	37	1.16	5.82
55	70	73	34	0.0	0.2	37	65	37	1.32	5.13
57	56	65	30	0.0	1.6	30	66	37	1.28	5.93
59	54	74	31	0.0	1.6	38	69	39	1.30	5.16
Mean	59.9	74.8	35.2	0.00	0.80	37.5	68.2	38.2	1.274	5.886
SD	18.9	7.3	5.7	0.00	0.61	4.1	2.2	1.7	0.061	0.603
N	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

3% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
21	1.34	1.57	0.93	6.1	2.03	2.91	97	5.2	139
23	1.08	1.38	0.95	7.0	1.62	2.83	98	5.2	141
25	1.26	1.59	1.09	7.6	1.73	2.87	100	5.4	143
27	1.45	1.77	1.14	6.2	1.51	2.86	100	6.2	142
29	1.53	1.79	1.51	6.3	2.09	2.80	98	6.0	142
51	1.94	2.11	1.40	7.2	2.71	2.87	96	5.7	141
53	1.47	1.64	0.76	7.2	2.56	2.76	96	5.0	141
55	1.08	1.41	0.74	6.9	2.30	2.80	100	5.9	140
57	1.55	2.04	1.07	5.8	2.76	2.83	96	5.3	142
59	1.15	1.38	0.64	5.8	1.99	2.75	99	5.3	141
Mean	1.385	1.668	1.023	6.61	2.130	2.828	98.0	5.52	141.2
SD	0.264	0.260	0.281	0.65	0.445	0.051	1.7	0.40	1.1
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

6% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatinine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
31	76	90	61	0.0	0.0	40	71	39	1.22	5.87
35	63	74	33	0.0	0.9	35	62	34	1.21	5.12
37	89	78	35	0.0	1.3	39	74	40	1.18	4.84
39	74	73	40	0.0	1.4	34	63	35	1.25	4.99
61	28	68	28	0.0	1.2	40	69	40	1.38	5.80
63	84	77	41	0.0	0.0	39	66	37	1.28	4.85
65	50	65	25	0.0	1.3	40	63	35	1.25	5.67
67	68	81	41	0.0	1.4	37	67	38	1.31	5.65
69	69	77	37	0.0	1.2	34	68	36	1.13	6.48
Mean	66.8	75.9	37.9	0.00	0.97	37.6	67.0	37.1	1.244	5.474
SD	18.5	7.3	10.3	0.00	0.57	2.6	4.0	2.3	0.074	0.559
N	9	9	9	9	9	9	9	9	9	9

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

6% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
31	1.32	1.47	1.08	6.6	2.27	2.88	96	5.9	139
35	1.71	1.65	0.59	5.5	2.06	2.74	99	5.5	141
37	1.96	2.28	1.21	7.9	1.69	2.81	99	5.2	140
39	0.75	1.07	1.05	6.2	3.02	2.73	100	6.3	143
61	1.25	1.44	0.54	6.1	2.36	2.80	98	5.5	142
63	1.61	1.69	1.08	6.8	2.87	2.73	97	6.1	138
65	1.00	1.33	1.07	6.7	2.35	2.77	97	5.7	141
67	1.47	1.85	0.57	8.6	2.13	2.78	98	5.2	142
69	1.71	1.97	0.61	7.0	2.39	2.69	99	5.2	142
Mean	1.420	1.639	0.867	6.82	2.349	2.770	98.1	5.62	140.9
SD	0.381	0.363	0.279	0.94	0.402	0.056	1.3	0.41	1.6
N	9	9	9	9	9	9	9	9	9

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

10% diet	ALP (U/L)	ASAT (U/L)	ALAT (U/L)	GGT (U/L)	Bilirub Total (umol/L)	Creatinine (umol/L)	Total Protein (g/L)	Albumin (g/L)	Albumin/ Globulin	Glucose Plasma (mmol/L)
1	73	73	38	0.0	0.0	36	71	40	1.29	6.58
3	37	75	34	0.0	0.2	38	70	38	1.19	9.63
5	73	69	36	0.0	0.0	40	66	37	1.28	6.57
7	59	71	28	0.0	0.9	38	68	39	1.34	6.43
9	47	104	75	0.0	1.1	35	63	35	1.25	4.83
71	49	72	34	0.0	2.0	40	69	40	1.38	5.41
73	116	88	31	0.0	0.6	48	68	38	1.27	4.40
75	53	69	28	0.0	0.0	37	64	37	1.37	4.95
77	39	70	34	0.0	1.8	33	64	35	1.21	5.98
79	59	63	31	0.1	1.2	27	66	36	1.20	5.39
Mean	60.5	75.4	36.9	0.01	0.78	37.2	66.9	37.5	1.277	6.017
SD	23.1	11.9	13.8	0.03	0.75	5.4	2.7	1.8	0.070	1.482
N	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 8: Clinical chemistry

Sex: Female Day: 92 Relative to Start Date

10% diet	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Urea (mmol/L)	PO4 (mmol/L)	Ca (mmol/L)	Cl (mmol/L)	K (mmol/L)	Na (mmol/L)
1	1.16	1.60	1.42	6.5	1.69	2.86	96	5.5	138
3	1.01	1.41	1.55	7.3	2.21	2.96	95	5.4	140
5	1.36	1.92	2.92	9.1	2.16	2.80	96	5.1	139
7	1.42	1.87	1.91	7.1	1.66	2.89	97	5.4	140
9	1.76	1.92	1.33	7.9	2.32	2.76	98	5.9	140
71	1.27	1.72	0.93	6.6	2.65	2.86	96	5.5	143
73	1.80	1.93	1.19	7.3	2.15	2.76	98	5.7	141
75	1.35	1.79	1.86	6.6	2.63	2.82	98	6.0	141
77	1.49	1.92	0.92	6.4	2.78	2.81	96	5.1	143
79	1.58	1.62	0.41	6.0	2.86	2.68	103	5.7	138
Mean	1.420	1.770	1.444	7.08	2.311	2.820	97.3	5.53	140.3
SD	0.249	0.179	0.688	0.90	0.422	0.078	2.3	0.30	1.8
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Male Day: 86 Relative to Start Date

0% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
32	3.0	1.055
34	5.0	1.037
36	1.0	1.082
38	2.0	1.084
40	4.0	1.051
62	3.0	1.062
64	2.0	1.080
66	2.0	1.088
68	3.0	1.078
70	3.0	1.063
Mean	2.80	1.0680
SD	1.14	0.0169
N	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Male Day: 86 Relative to Start Date

3% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
2	3.0	1.057
4	2.0	1.061
6	2.0	1.060
8	2.0	1.059
10	3.0	1.059
72	1.5	1.080
74	2.0	1.062
76	2.0	1.080
78	3.0	1.052
80	2.0	1.078
Mean	2.25	1.0648
SD	0.54	0.0104
N	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Male Day: 86 Relative to Start Date

6% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
12	4.0	1.045
14	2.0	1.061
16	1.0	1.056
18	3.5	1.040
20	4.0	1.049
42	2.0	1.063
44	3.5	1.041
46	1.0	1.088
48	7.0	1.028
50	5.5	1.040
Mean	3.35	1.0511
SD	1.93	0.0168
N	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Male Day: 86 Relative to Start Date

10% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
22	1.0	1.088
24	4.0	1.042
26	3.0	1.050
28	1.0	1.076
30	3.0	1.056
52	5.0	1.042
54	5.0	1.045
56	1.5	1.084
58	2.5	1.046
60	2.0	1.088
Mean	2.80	1.0617
SD	1.49	0.0199
N	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Female Day: 88 Relative to Start Date

0% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
11	2.5	1.059
13	1.5	1.063
15	0.5	1.090
17	3.0	1.053
19	2.0	1.068
41	2.5	1.055
43	1.0	1.062
45	0.5	1.110
47	3.0	1.032
49	1.0	1.092
Mean	1.75	1.0684
SD	0.98	0.0227
N	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Female Day: 88 Relative to Start Date

3% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
21	1.0	1.100
23	2.0	1.054
25	2.0	1.050
27	0.5	1.106
29	2.5	1.064
51	2.5	1.056
53	2.0	1.060
55	0.5	1.070
57	2.0	1.051
59	1.0	1.090
Mean	1.60	1.0701
SD	0.77	0.0209
N	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Female Day: 88 Relative to Start Date

6% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
31	3.0	1.049
35	1.0	1.060
37	1.0	1.065
39	3.0	1.048
61	NM	NM
63	1.0	1.063
65	1.0	1.078
67	1.0	1.082
69	2.0	1.042
Mean	1.63	1.0609
SD	0.92	0.0143
N	8	8

NM= Not Measured; no sample could be obtained

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 9: Urinalysis: volume and density

Sex: Female Day: 88 Relative to Start Date

10% diet	ConcUrin Volume (mL)	Urinary Spec.Gravity (kg/L)
1	3.0	1.049
3	4.0	1.038
5	2.5	1.049
7	2.0	1.039
9	1.0	1.068
71	6.0	1.023
73	2.5	1.038
75	1.5	1.038
77	3.5	1.042
79	3.0	1.046
Mean	2.90	1.0430
SD	1.41	0.0115
N	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Male Day: 86 Relative to Start Date

0% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
32	0	1	7.0	2	0	1	3.2	0	0
34	0	2	8.5	2	0	2	3.2	0	0
36	0	2	7.0	2	1	1	3.2	1	0
38	0	2	7.0	3	0	1	3.2	1	0
40	0	2	7.5	2	0	2	3.2	1	1
62	0	2	7.0	2	0	1	3.2	1	0
64	0	2	7.0	2	0	1	3.2	1	0
66	0	2	6.0	2	1	2	3.2	1	0
68	0	2	6.5	2	0	1	3.2	0	0
70	0	3	7.0	2	0	1	3.2	1	0
Mean	-	-	7.05	2.1	0.2	1.3	3.20	0.7	0.1
SD	-	-	0.64	0.3	0.4	0.5	0.00	0.5	0.3
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Male Day: 86 Relative to Start Date

3% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
2	0	2	7.0	2	0	1	3.2	1	0
4	0	1	6.0	2	0	1	3.2	1	0
6	0	2	6.5	2	0	2	3.2	1	0
8	0	2	7.5	2	0	2	3.2	1	0
10	0	2	7.0	2	0	1	3.2	1	0
72	0	2	6.5	2	0	1	3.2	1	0
74	0	2	7.0	2	0	1	3.2	1	0
76	0	2	6.0	2	0	1	3.2	1	1
78	0	2	7.0	2	0	0	3.2	0	0
80	0	2	6.0	2	0	0	3.2	1	0
Mean	-	-	6.65	2.0	0.0	1.0	3.20	0.9	0.1
SD	-	-	0.53	0.0	0.0	0.7	0.00	0.3	0.3
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Male Day: 86 Relative to Start Date

6% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
12	0	2	7.5	2	0	1	3.2	0	1
14	0	1	7.0	2	0	2	3.2	1	0
16	0	1	7.0	2	0	1	3.2	1	0
18	0	2	7.5	2	0	1	3.2	0	1
20	0	2	9.0	2	0	1	3.2	1	0
42	0	2	7.0	2	0	1	3.2	1	0
44	0	2	8.5	2	0	2	3.2	0	0
46	0	1	7.0	3	0	1	3.2	1	0
48	0	2	8.5	1	0	1	3.2	0	0
50	0	1	8.5	2	0	1	3.2	0	0
Mean	-	-	7.75	2.0	0.0	1.2	3.20	0.5	0.2
SD	-	-	0.79	0.5	0.0	0.4	0.00	0.5	0.4
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Male Day: 86 Relative to Start Date

10% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
22	0	1	6.0	2	0	1	3.2	1	0
24	0	1	7.0	2	1	1	3.2	0	0
26	0	1	8.5	2	0	2	3.2	1	1
28	0	1	7.0	2	0	2	3.2	1	0
30	0	1	7.0	2	0	2	3.2	1	0
52	0	2	8.5	2	0	1	3.2	0	0
54	0	1	7.5	2	0	1	3.2	0	0
56	0	2	6.5	3	0	2	3.2	1	0
58	0	0	7.5	2	0	1	3.2	1	0
60	0	0	7.0	2	1	2	3.2	1	0
Mean	-	-	7.25	2.1	0.2	1.5	3.20	0.7	0.1
SD	-	-	0.79	0.3	0.4	0.5	0.00	0.5	0.3
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Female Day: 88 Relative to Start Date

0% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
11	0	0	6.5	1	0	1	3.2	1	0
13	0	0	5.5	2	0	1	3.2	1	0
15	0	0	6.0	2	0	0	3.2	1	0
17	0	0	7.0	2	0	0	3.2	0	0
19	0	0	6.5	2	0	1	3.2	1	0
41	0	0	6.5	2	0	0	3.2	0	0
43	0	0	6.5	2	0	0	3.2	1	0
45	0	0	6.0	3	0	0	3.2	1	0
47	0	0	6.5	1	0	0	3.2	0	0
49	0	0	6.0	3	0	1	3.2	1	0
Mean	-	-	6.30	2.0	0.0	0.4	3.20	0.7	0.0
SD	-	-	0.42	0.7	0.0	0.5	0.00	0.5	0.0
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Female Day: 88 Relative to Start Date

3% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
21	0	0	6.0	3	0	1	3.2	1	0
23	0	0	6.0	1	0	0	3.2	0	0
25	0	0	5.5	1	0	0	3.2	0	0
27	0	0	5.5	3	0	0	3.2	2	0
29	0	1	6.5	2	0	1	3.2	1	0
51	0	0	6.5	1	0	0	3.2	0	0
53	0	0	6.0	2	0	0	3.2	1	0
55	0	0	5.5	2	1	0	3.2	1	0
57	0	0	6.0	1	0	0	3.2	0	0
59	0	0	6.0	2	0	1	3.2	1	0
Mean	-	-	5.95	1.8	0.1	0.3	3.20	0.7	0.0
SD	-	-	0.37	0.8	0.3	0.5	0.00	0.7	0.0
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Female Day: 88 Relative to Start Date

6% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
31	0	0	6.0	1	0	0	3.2	0	0
35	0	1	6.0	2	0	1	3.2	1	0
37	0	0	6.0	2	0	1	3.2	1	0
39	0	2	8.5	1	0	1	3.2	0	0
61	NM	NM	NM	NM	NM	NM	NM	NM	NM
63	0	0	6.0	2	0	1	3.2	1	0
65	0	0	6.0	2	0	0	3.2	1	0
67	0	0	5.5	2	0	0	3.2	1	0
69	0	0	6.5	1	0	0	3.2	0	0
Mean	-	-	6.31	1.6	0.0	0.5	3.20	0.6	0.0
SD	-	-	0.92	0.5	0.0	0.5	0.00	0.5	0.0
N	8	8	8	8	8	8	8	8	8

NM= Not Measured; no sample could be obtained

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 10: Urinalysis: semi-quantitative observations

Sex: Female Day: 88 Relative to Start Date

10% diet	Appear-ance ((0-6))	Clarity ((0-4))	pH (strip)	Protein ((0-4))	Glucose ((0-4))	Ketones ((0-4))	Urobili (umol/L)	Bilirubin ((0-3))	Occ bld ((0-3))
1	0	0	6.5	2	0	1	3.2	1	0
3	0	0	6.5	1	0	0	3.2	0	0
5	0	0	6.5	1	0	0	3.2	0	0
7	0	0	9.0	2	0	1	3.2	0	0
9	0	0	6.0	2	0	1	3.2	1	1
71	0	2	8.5	1	0	0	3.2	0	0
73	0	0	6.5	1	0	0	3.2	0	0
75	0	0	6.0	1	0	0	3.2	0	0
77	0	0	6.5	1	0	0	3.2	0	1
79	0	0	6.5	1	0	1	3.2	0	0
Mean	-	-	6.85	1.3	0.0	0.4	3.20	0.2	0.2
SD	-	-	1.03	0.5	0.0	0.5	0.00	0.4	0.4
N	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Male Day: 86 Relative to Start Date

0% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))	Sperms ((0-1))
32	0	0	3	3	4	0	4	0	1
34	0	0	2	1	5	0	3	0	1
36	0	0	0	0	1	0	3	0	1
38	NM [1]	NM [1]	NM [1]	NM [1]	5	NM [1]	NM [1]	NM [1]	NM [1]
40	NM [1]	NM [1]	NM [1]	NM [1]	5	NM [1]	NM [1]	NM [1]	NM [1]
62	0	0	1	1	2	0	3	0	1
64	0	0	1	3	1	0	4	0	1
66	1	0	1	1	0	0	3	0	1 [2]
68	0	0	3	1	0	0	3	0	1
70	0	0	3	4	4	0	4	0	1
Mean	0.1	0.0	1.8	1.8	2.7	0.0	3.4	0.0	1.0
SD	0.4	0.0	1.2	1.4	2.1	0.0	0.5	0.0	0.0
N	8	8	8	8	10	8	8	8	8

[1] Sample was full of crystals and could not be evaluated

[2] Could not be evaluated because sample contained a lot of sperm

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Male Day: 86 Relative to Start Date

3% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))	Sperms ((0-1))
2	1	0	1	2	4	0	2	0	1
4	0	0	0	1	2	0	2	0	1
6	0	1	1	0	4	0	3	0	1
8	0	0	2	1	4	0	2	0	1
10	2	0	1	1	5	0	3	0	1
72	0	0	1	3	4	0	3	0	1
74	0	0	1	2	4	0	3	0	1
76	1	1	1	0	0	0	3	0	1
78	NM [1]	NM [1]	NM [1]	NM [1]	5	NM [1]	NM [1]	NM [1]	NM [1]
80	1	3	2	3	2	0	3	0	1
Mean	0.6	0.6	1.1	1.4	3.4	0.0	2.7	0.0	1.0
SD	0.7	1.0	0.6	1.1	1.6	0.0	0.5	0.0	0.0
N	9	9	9	9	10	9	9	9	9

[1] Sample was full of crystals and could not be evaluated

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Male Day: 86 Relative to Start Date

6% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))	Sperms ((0-1))
12	1	0	2	0	2	0	5	0	1
14	1	1	2	2	3	0	4	0	1
16	0	0	2	2	1	0	4	0	1
18	1	0	1	1	4	0	3	0	1
20	NM [1]	NM [1]	NM [1]	NM [1]	5	NM [1]	NM [1]	NM [1]	NM [1]
42	1	0	1	2	1	0	4	0	1
44	0	0	1	1	4	0	3	0	1
46	0	0	1	1	1	0	4	0	1
48	2	2	4	4	5	0	5	0	1
50	1	2	3	3	5	0	5	0	1
Mean	0.8	0.6	1.9	1.8	3.1	0.0	4.1	0.0	1.0
SD	0.7	0.9	1.1	1.2	1.7	0.0	0.8	0.0	0.0
N	9	9	9	9	10	9	9	9	9

[1] Sample was full of crystals and could not be evaluated

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Male Day: 86 Relative to Start Date

10% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))	Sperms ((0-1))
22	0	0	1	4	5	0	5	0	1
24	1	1	3	2	1	0	4	0	1
26	1	0	1	1	1	0	3	0	1
28	1	0	2	0	3	0	4	0	1
30	0	0	1	1	3	0	2	0	1
52	NM [1]	NM [1]	NM [1]	NM [1]	5	NM [1]	NM [1]	NM [1]	NM [1]
54	0	0	0	1	1	0	4	0	1
56	1	0	1	1	1	0	5	0	1
58	0	1	2	2	3	0	3	0	0
60	0	0	1	3	5	0	5	0	1
Mean	0.4	0.2	1.3	1.7	2.8	0.0	3.9	0.0	0.9
SD	0.5	0.4	0.9	1.2	1.8	0.0	1.1	0.0	0.3
N	9	9	9	9	10	9	9	9	9

[1] Sample was full of crystals and could not be evaluated

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Female Day: 88 Relative to Start Date

0% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))
11	0	0	2	2	1	0	2	0
13	1	0	3	1	0	0	3	0
15	0	0	1	1	0	0	2	0
17	0	0	1	2	3	0	3	0
19	0	0	3	2	3	0	3	0
41	1	0	2	1	3	0	2	0
43	1	0	1	0	0	1 [1]	2	0
45	0	0	2	1	0	0	2	0
47	2	0	2	1	0	0	3	0
49	0	0	2	1	2	0	3	0
Mean	0.5	0.0	1.9	1.2	1.2	0.1	2.5	0.0
SD	0.7	0.0	0.7	0.6	1.4	0.3	0.5	0.0
N	10	10	10	10	10	10	10	10

[1] Hyaline cylinder

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Female Day: 88 Relative to Start Date

3% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))
21	2	0	2	1	1	0	4	0
23	0	0	1	2	0	0	2	0
25	1	0	1	0	0	0	3	0
27	0	0	0	0	3	0	3	0
29	0	0	1	2	2	0	2	0
51	1	0	3	2	0	0	2	0
53	0	0	3	1	0	0	4	0
55	1	0	2	2	3	0	3	0
57	0	1	2	0	0	0	3	0
59	2	0	1	1	2	0	3	0
Mean	0.7	0.1	1.6	1.1	1.1	0.0	2.9	0.0
SD	0.8	0.3	1.0	0.9	1.3	0.0	0.7	0.0
N	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Female Day: 88 Relative to Start Date

6% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))
31	0	0	3	2	0	0	2	0
33	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]
35	1	0	1	1	0	0	3	0
37	0	0	1	1	0	0	2	0
39	0	0	2	2	5	0	3	0
61	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]	NM[1]
63	1	0	3	1	2	0	3	0
65	1	0	2	1	0	0	4	0
67	1	0	2	1	0	1[2]	2	0
69	0	0	3	3	3	0	3	0
Mean	0.5	0.0	2.1	1.5	1.3	0.1	2.8	0.0
SD	0.5	0.0	0.8	0.8	1.9	0.4	0.7	0.0
N	8	8	8	8	8	8	8	8

[1] NM= Not Measured; no sample could be obtained

[2] Hyaline cyllinder

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 11: Urinalysis: microscopic observations

Sex: Female Day: 88 Relative to Start Date

10% diet	Red Bld Cells ((0-5))	WhiteBld Cells ((0-5))	Epithel Cells ((0-5))	Amorph Material ((0-5))	Crystals ((0-5))	Casts ((0-5))	Bacteria ((0-5))	Worm Eggs ((0-1))
1	1	0	1	0	1	0	1	0
3	1	0	2	1	0	0	2	0
5	1	0	1	1	0	0	2	0
7	3	0	1	1	2	0	4	0
9	2	0	1	1	1	0	2	0
71	NM [1]	NM [1]	NM [1]	NM [1]	NM [1]	NM [1]	NM [1]	NM [1]
73	0	0	3	2	1	0	4	0
75	0	0	3	1	0	0	3	0
77	1	0	4	2	2	0	3	0
79	1	0	2	1	0	0	2	0
Mean	1.1	0.0	2.0	1.1	0.8	0.0	2.6	0.0
SD	0.9	0.0	1.1	0.6	0.8	0.0	1.0	0.0
N	9	9	9	9	9	9	9	9

[1] NM = Not Measured; sample was full of amorphous urate crystals

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Male Day(s) Relative to Start Date

0% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Testes (g)	Epididymides (g)	Prostate (g)	Seminal vesicles (g)	Caecum full (g)	Caecum empty (g)
	91	91	91	91	91	91	91	91	91	91	91	91	91	91
32	346.5	2.12	0.93	0.056	1.99	7.92	0.507	0.295	3.69	1.24	1.00	1.01	4.999	0.999
34	332.0	2.12	0.92	0.049	1.92	7.82	0.610	0.278	3.42	1.08	1.02	1.17	4.504	0.901
36	307.6	1.97	0.87	0.046	1.77	7.19	0.570	0.323	3.43	1.12	0.84	1.03	2.730	0.839
38	311.1	1.93	0.88	0.053	1.64	6.93	0.503	0.313	3.29	1.14	0.85	1.01	3.501	1.064
40	379.9	2.31	1.13	0.073	2.17	8.57	0.558	0.340	3.87	1.13	0.90	0.91	4.049	0.895
62	427.6	2.12	1.12	0.061	2.24	10.02	0.673	0.384	3.32	1.20	1.01	0.84	4.940	1.304
64	310.9	1.95	0.84	0.065	1.72	6.48	0.459	0.242	3.13	0.89	0.64	0.75	4.946	1.347
66	353.5	2.05	0.93	0.043	1.85	7.97	0.522	0.364	3.72	1.23	0.83	1.27	3.947	1.078
68	367.5	2.02	0.91	0.061	2.11	9.45	0.707	0.384	3.47	1.14	1.13	1.07	3.781	0.920
70	315.9	2.13	0.94	0.045	1.92	7.30	0.466	0.399	3.44	1.06	0.89	1.06	3.590	0.860
Mean	345.25	2.072	0.947	0.0552	1.933	7.965	0.5575	0.3322	3.478	1.123	0.911	1.012	4.0987	1.0207
SD	38.51	0.113	0.099	0.0098	0.197	1.112	0.0840	0.0514	0.223	0.101	0.136	0.151	0.7466	0.1800
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Male Day(s) Relative to Start Date

3% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Testes (g)	Epididymides (g)	Prostate (g)	Seminal vesicles (g)	Caecum full (g)	Caecum empty (g)
	91	91	91	91	91	91	91	91	91	91	91	91	91	91
2	399.3	2.10	1.03	0.063	2.02	8.97	0.557	0.406	3.71	1.16	0.75	1.14	5.098	1.421
4	332.4	2.07	0.87	0.033	1.97	8.03	0.550	0.262	3.26	1.10	0.86	1.07	6.653	1.283
6	349.9	2.01	1.02	0.047	2.06	8.53	0.679	0.440	3.44	1.27	1.00	0.81	5.338	0.920
8	322.3	2.05	0.89	0.040	1.75	7.23	0.605	0.387	3.04	1.06	0.81	0.92	3.828	1.162
10	379.0	2.27	1.12	0.071	2.14	8.73	0.621	0.448	3.94	1.15	1.13	1.09	5.359	1.391
72	404.7	2.08	1.13	0.055	2.20	9.66	0.642	0.322	3.47	1.19	0.88	1.11	5.914	1.326
74	327.5	2.09	0.82	0.049	1.91	7.64	0.591	0.256	3.48	1.14	0.85	0.82	6.343	1.402
76	289.9	1.96	0.78	0.050	1.59	6.80	0.529	0.277	3.27	1.05	0.69	0.80	3.963	1.161
78	342.3	1.94	0.92	0.062	2.11	8.85	0.664	0.298	3.54	1.25	0.94	1.02	4.850	1.080
80	368.7	2.08	1.16	0.059	2.50	9.40	0.644	0.448	3.24	1.17	1.15	1.30	4.936	0.993
Mean	351.60	2.065	0.974	0.0529	2.025	8.384	0.6082	0.3544	3.439	1.154	0.906	1.008	5.2282	1.2139
SD	36.27	0.091	0.136	0.0114	0.249	0.936	0.0509	0.0796	0.257	0.072	0.151	0.166	0.9177	0.1781
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Male Day(s) Relative to Start Date

6% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Testes (g)	Epididymides (g)	Prostate (g)	Seminal vesicles (g)	Caecum full (g)	Caecum empty (g)
	91	91	91	91	91	91	91	91	91	91	91	91	91	91
12	380.8	2.16	1.17	0.054	1.97	8.44	0.569	0.424	3.96	1.30	0.96	1.04	7.515	1.315
14	351.9	2.05	1.00	0.058	2.05	8.89	0.715	0.347	3.64	1.25	0.87	1.18	7.879	1.212
16	293.0	2.01	0.91	0.045	1.67	6.84	0.604	0.292	3.30	1.06	0.90	1.02	4.170	0.960
18	323.7	2.01	0.87	0.052	1.77	7.71	0.509	0.297	3.25	1.08	0.81	1.08	6.415	2.047
20	423.9	2.22	1.22	0.065	2.30	10.79	0.668	0.426	3.97	1.17	1.00	0.96	8.570	2.065
42	377.7	2.16	0.95	0.038	1.95	8.18	0.647	0.297	3.40	1.18	1.14	0.77	8.612	1.692
44	353.5	2.14	1.15	0.062	1.98	7.47	0.626	0.545	3.75	1.16	0.93	0.97	8.582	1.566
46	295.8	1.93	0.85	0.050	1.63	6.84	0.554	0.242	3.19	1.03	0.79	0.92	5.475	1.186
48	362.3	2.01	0.99	0.064	2.04	9.72	0.653	0.412	3.41	1.18	1.02	1.09	5.704	1.487
50	355.0	1.99	1.00	0.061	2.16	8.72	0.462	0.412	3.17	1.18	0.81	0.97	5.085	1.035
Mean	351.76	2.068	1.011	0.0549	1.952	8.360	0.6007	0.3694	3.504	1.159	0.923	1.000	6.8007	1.4565
SD	39.74	0.095	0.129	0.0088	0.211	1.249	0.0774	0.0906	0.306	0.083	0.111	0.111	1.6408	0.3894
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Male Day(s) Relative to Start Date

10% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Testes (g)	Epididymides (g)	Prostate (g)	Seminal vesicles (g)	Caecum full (g)	Caecum empty (g)
	91	91	91	91	91	91	91	91	91	91	91	91	91	91
22	281.9	1.92	0.79	0.055	1.78	7.38	0.535	0.217	2.82	0.98	0.91	1.23	7.318	1.237
24	321.7	2.05	0.87	0.044	2.25	7.98	0.588	0.263	3.41	1.07	1.03	1.32	8.007	1.499
26	324.0	1.99	1.03	0.065	1.94	7.55	0.649	0.277	3.37	1.23	0.60	0.98	7.354	1.747
28	321.0	1.98	0.90	0.057	1.72	7.65	0.576	0.272	3.43	1.03	0.78	0.88	7.974	1.684
30	393.8	2.13	1.09	0.056	1.98	9.92	0.682	0.358	3.80	1.25	1.07	1.00	9.912	1.553
52	343.3	2.06	0.95	0.051	2.02	9.48	0.655	0.282	3.81	1.07	0.76	0.77	8.289	2.095
54	391.6	2.14	1.14	0.070	2.25	9.57	0.691	0.387	3.65	1.32	1.04	0.90	9.229	1.681
56	259.8	1.90	0.74	0.036	1.55	6.22	0.431	0.213	2.87	0.96	0.82	0.80	6.568	1.413
58	315.1	1.97	0.94	0.046	1.77	8.44	0.562	0.446	3.32	1.14	0.83	1.05	7.456	1.575
60	359.4	2.09	0.94	0.044	2.06	8.35	0.507	0.503	3.46	1.20	1.12	1.02	6.080	1.467
Mean	331.16	2.023	0.939	0.0524	1.932	8.254	0.5876	0.3218	3.394	1.125	0.896	0.995	7.8187	1.5951
SD	42.87	0.084	0.125	0.0103	0.228	1.149	0.0833	0.0978	0.337	0.122	0.166	0.175	1.1468	0.2303
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Female Day(s) Relative to Start Date

0% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Ovaries (g)	Uterus (g)	Caecum full (g)	Caecum empty (g)
	92	92	92	92	92	92	92	92	92	92	92	92
11	226.9	1.99	0.67	0.096	1.48	5.43	0.460	0.301	0.117	1.108	2.206	0.866
13	189.3	1.88	0.64	0.065	1.38	4.71	0.388	0.224	0.100	0.675	2.922	0.736
15	196.9	1.89	0.59	0.064	1.15	4.45	0.395	0.266	0.081	0.409	2.412	0.699
17	207.2	1.87	0.63	0.068	1.36	5.42	0.438	0.350	0.089	1.306	3.199	0.693
19	232.7	2.07	0.78	0.078	1.41	6.19	0.410	0.338	0.089	0.629	2.495	0.904
41	214.6	1.90	0.65	0.053	1.24	5.54	0.401	0.195	0.079	0.459	3.810	0.679
43	207.1	2.00	0.72	0.090	1.42	5.30	0.354	0.278	0.080	2.206 [1]	2.459	0.689
45	202.4	1.95	0.63	0.072	1.28	4.89	0.414	0.247	0.111	0.658	1.545	0.729
47	195.3	1.88	0.71	0.062	1.20	5.45	0.390	0.293	0.099	0.484	3.621	0.586
49	195.6	1.91	0.65	0.062	1.23	5.16	0.275	0.284	0.094	0.280	3.182	0.593
Mean	206.80	1.934	0.667	0.0710	1.315	5.254	0.3925	0.2776	0.0939	0.8214	2.7851	0.7174
SD	14.21	0.067	0.055	0.0134	0.110	0.488	0.0503	0.0477	0.0130	0.5800	0.6912	0.1018
N	10	10	10	10	10	10	10	10	10	10	10	10

[1] Uterus swollen

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Female Day(s) Relative to Start Date

3% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Ovaries (g)	Uterus (g)	Caecum full (g)	Caecum empty (g)
	92	92	92	92	92	92	92	92	92	92	92	92
21	225.6	1.98	0.71	0.090	1.45	5.46	0.396	0.324	0.089	0.609	3.512	0.754
23	200.7	1.94	0.56	0.054	1.36	4.78	0.398	0.279	0.096	1.194	3.042	0.806
25	190.8	1.95	0.69	0.058	1.25	4.64	0.424	0.330	0.086	0.966	3.219	0.759
27	191.0	1.87	0.64	0.075	1.21	4.67	0.379	0.301	0.064	0.528	2.445	0.596
29	236.5	2.01	0.86	0.089	1.59	5.93	0.439	0.304	0.090	1.114	3.318	1.026
51	212.0	1.96	0.61	0.055	1.24	4.73	0.374	0.252	0.083	0.485	4.168	0.788
53	226.7	2.00	0.76	0.077	1.37	5.00	0.399	0.264	0.094	0.517	2.770	0.870
55	198.9	1.87	0.59	0.082	1.21	5.16	0.479	0.206	0.094	0.445	3.207	0.747
57	213.0	1.91	0.68	0.061	1.37	5.37	0.445	0.312	0.076	0.381	4.004	0.906
59	191.4	1.77	0.58	0.056	1.17	4.54	0.296	0.357	0.113	0.313	2.409	0.971
Mean	208.66	1.926	0.668	0.0697	1.322	5.028	0.4029	0.2929	0.0885	0.6552	3.2094	0.8223
SD	16.68	0.073	0.093	0.0145	0.131	0.448	0.0497	0.0438	0.0130	0.3163	0.5869	0.1247
N	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Female Day(s) Relative to Start Date

6% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Ovaries (g)	Uterus (g)	Caecum full (g)	Caecum empty (g)
	92	92	92	92	92	92	92	92	92	92	92	92
31	203.8	1.92	0.66	0.072	1.33	5.10	0.335	0.284	0.116	0.475	4.620	1.262
35	193.9	1.85	0.69	0.075	1.30	4.71	0.496	0.343	0.084	0.412	2.604	0.768
37	189.7	1.88	0.66	0.064	1.32	6.55	0.440	0.309	0.103	1.640 [1]	3.421	0.946
39	205.7	1.91	0.73	0.078	1.32	5.39	0.449	0.443	0.098	1.027	4.186	1.196
61	204.8	1.86	0.61	0.065	1.19	5.22	0.337	0.204	0.076	0.546	3.595	0.912
63	209.1	1.90	0.68	0.063	1.34	4.96	0.367	0.275	0.100	0.594	3.476	0.809
65	202.8	1.81	0.62	0.068	1.25	5.12	0.501	0.196	0.099	0.397	3.498	0.894
67	204.0	1.85	0.71	0.056	1.22	5.23	0.367	0.322	0.074	0.395	4.191	0.852
69	210.2	1.94	0.71	0.074	1.41	5.74	0.331	0.355	0.129	0.396	3.769	0.958
Mean	202.67	1.880	0.674	0.0683	1.298	5.336	0.4026	0.3034	0.0977	0.6536	3.7067	0.9552
SD	6.71	0.041	0.041	0.0070	0.067	0.536	0.0694	0.0764	0.0179	0.4208	0.5819	0.1677
N	9	9	9	9	9	9	9	9	9	9	9	9

[1] Uterus swollen

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 12: Absolute organ weights

Sex: Female Day(s) Relative to Start Date

10% diet	Terminal body wgt (g)	Brain (g)	Heart (g)	Adrenals (g)	Kidneys (g)	Liver (g)	Spleen (g)	Thymus (g)	Ovaries (g)	Uterus (g)	Caecum full (g)	Caecum empty (g)
	92	92	92	92	92	92	92	92	92	92	92	92
1	214.4	1.90	0.69	0.076	1.33	4.83	0.416	0.318	0.099	1.196	4.871	1.029
3	186.1	1.97	0.54	0.055	1.16	4.72	0.454	0.232	0.090	1.121	5.244	1.347
5	184.1	1.88	0.61	0.060	1.22	4.78	0.494	0.307	0.075	0.478	5.135	0.961
7	197.4	1.92	0.64	0.063	1.32	5.45	0.455	0.285	0.077	0.431	4.530	0.965
9	209.8	2.01	0.63	0.064	1.39	5.61	0.442	0.325	0.084	0.375	5.154	1.466
71	218.7	1.83	0.62	0.061	1.38	5.73	0.425	0.224	0.109	0.538	5.731	1.353
73	208.4	1.92	0.71	0.062	1.27	5.19	0.432	0.337	0.092	1.242	4.651	1.444
75	192.5	1.85	0.62	0.070	1.19	5.14	0.445	0.306	0.094	1.023	4.657	1.062
77	200.6	1.88	0.62	0.064	1.36	5.19	0.420	0.271	0.075	0.446	5.398	1.227
79	194.4	1.87	0.63	0.062	1.28	5.69	0.379	0.334	0.117	0.339	4.813	1.234
Mean	200.64	1.903	0.631	0.0637	1.290	5.233	0.4362	0.2939	0.0912	0.7189	5.0184	1.2088
SD	11.83	0.055	0.046	0.0057	0.080	0.378	0.0302	0.0403	0.0143	0.3751	0.3805	0.1935
N	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Male Day(s) Relative to Start Date

0% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Testes rel.wgt (g/kg body wgt)	Epididy rel.wgt (g/kg body wgt)	Prostate rel.wgt (g/kg body wgt)	Sem ves rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	91	91	92	91	91	91	91	91	91	91	91	91	91	91
32	346.5	6.12	2.68	0.162	5.74	22.9	1.46	0.85	10.65	3.58	2.89	2.91	14.4	2.9
34	332.0	6.39	2.77	0.148	5.78	23.6	1.84	0.84	10.30	3.25	3.07	3.52	13.6	2.7
36	307.6	6.40	2.83	0.150	5.75	23.4	1.85	1.05	11.15	3.64	2.73	3.35	8.9	2.7
38	311.1	6.20	2.83	0.170	5.27	22.3	1.62	1.01	10.58	3.66	2.73	3.25	11.3	3.4
40	379.9	6.08	2.97	0.192	5.71	22.6	1.47	0.89	10.19	2.97	2.37	2.40	10.7	2.4
62	427.6	4.96	2.62	0.143	5.24	23.4	1.57	0.90	7.76	2.81	2.36	1.96	11.6	3.0
64	310.9	6.27	2.70	0.209	5.53	20.8	1.48	0.78	10.07	2.86	2.06	2.41	15.9	4.3
66	353.5	5.80	2.63	0.122	5.23	22.5	1.48	1.03	10.52	3.48	2.35	3.59	11.2	3.0
68	367.5	5.50	2.48	0.166	5.74	25.7	1.92	1.04	9.44	3.10	3.07	2.91	10.3	2.5
70	315.9	6.74	2.98	0.142	6.08	23.1	1.48	1.26	10.89	3.36	2.82	3.36	11.4	2.7
Mean	345.25	6.046	2.749	0.1603	5.609	23.03	1.617	0.965	10.155	3.272	2.645	2.967	11.91	2.98
SD	38.51	0.512	0.159	0.0257	0.282	1.23	0.184	0.142	0.963	0.323	0.343	0.550	2.11	0.56
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Male Day(s) Relative to Start Date

3% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Testes rel.wgt (g/kg body wgt)	Epididy rel.wgt (g/kg body wgt)	Prostate rel.wgt (g/kg body wgt)	Sem ves rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	91	91	92	91	91	91	91	91	91	91	91	91	91	91
2	399.3	5.26	2.58	0.158	5.06	22.5	1.39	1.02	9.29	2.91	1.88	2.85	12.8	3.6
4	332.4	6.23	2.62	0.099	5.93	24.2	1.65	0.79	9.81	3.31	2.59	3.22	20.0	3.9
6	349.9	5.74	2.92	0.134	5.89	24.4	1.94	1.26	9.83	3.63	2.86	2.31	15.3	2.6
8	322.3	6.36	2.76	0.124	5.43	22.4	1.88	1.20	9.43	3.29	2.51	2.85	11.9	3.6
10	379.0	5.99	2.96	0.187	5.65	23.0	1.64	1.18	10.40	3.03	2.98	2.88	14.1	3.7
72	404.7	5.14	2.79	0.136	5.44	23.9	1.59	0.80	8.57	2.94	2.17	2.74	14.6	3.3
74	327.5	6.38	2.50	0.150	5.83	23.3	1.80	0.78	10.63	3.48	2.60	2.50	19.4	4.3
76	289.9	6.76	2.69	0.172	5.48	23.5	1.82	0.96	11.28	3.62	2.38	2.76	13.7	4.0
78	342.3	5.67	2.69	0.181	6.16	25.9	1.94	0.87	10.34	3.65	2.75	2.98	14.2	3.2
80	368.7	5.64	3.15	0.160	6.78	25.5	1.75	1.22	8.79	3.17	3.12	3.53	13.4	2.7
Mean	351.60	5.917	2.765	0.1502	5.765	23.85	1.741	1.006	9.837	3.304	2.583	2.863	14.93	3.47
SD	36.27	0.520	0.195	0.0273	0.477	1.16	0.173	0.194	0.845	0.287	0.374	0.339	2.69	0.54
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Male Day(s) Relative to Start Date

6% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Testes rel.wgt (g/kg body wgt)	Epididy rel.wgt (g/kg body wgt)	Prostate rel.wgt (g/kg body wgt)	Sem ves rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	91	91	92	91	91	91	91	91	91	91	91	91	91	91
12	380.8	5.67	3.07	0.142	5.17	22.2	1.49	1.11	10.40	3.41	2.52	2.73	19.7	3.5
14	351.9	5.83	2.84	0.165	5.83	25.3	2.03	0.99	10.34	3.55	2.47	3.35	22.4	3.4
16	293.0	6.86	3.11	0.154	5.70	23.3	2.06	1.00	11.26	3.62	3.07	3.48	14.2	3.3
18	323.7	6.21	2.69	0.161	5.47	23.8	1.57	0.92	10.04	3.34	2.50	3.34	19.8	6.3
20	423.9	5.24	2.88	0.153	5.43	25.5	1.58	1.00	9.37	2.76	2.36	2.26	20.2	4.9
42	377.7	5.72	2.52	0.101	5.16	21.7	1.71	0.79	9.00	3.12	3.02	2.04	22.8	4.5
44	353.5	6.05	3.25	0.175	5.60	21.1	1.77	1.54	10.61	3.28	2.63	2.74	24.3	4.4
46	295.8	6.52	2.87	0.169	5.51	23.1	1.87	0.82	10.78	3.48	2.67	3.11	18.5	4.0
48	362.3	5.55	2.73	0.177	5.63	26.8	1.80	1.14	9.41	3.26	2.82	3.01	15.7	4.1
50	355.0	5.61	2.82	0.172	6.08	24.6	1.30	1.16	8.93	3.32	2.28	2.73	14.3	2.9
Mean	351.76	5.926	2.878	0.1568	5.558	23.73	1.720	1.046	10.015	3.315	2.634	2.880	19.20	4.13
SD	39.74	0.490	0.217	0.0226	0.280	1.81	0.239	0.215	0.799	0.244	0.264	0.473	3.52	0.98
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Male Day(s) Relative to Start Date

10% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Testes rel.wgt (g/kg body wgt)	Epididy rel.wgt (g/kg body wgt)	Prostate rel.wgt (g/kg body wgt)	Sem ves rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	91	91	92	91	91	91	91	91	91	91	91	91	91	91
22	281.9	6.81	2.80	0.195	6.31	26.2	1.90	0.77	10.00	3.48	3.23	4.36	26.0	4.4
24	321.7	6.37	2.70	0.137	6.99	24.8	1.83	0.82	10.60	3.33	3.20	4.10	24.9	4.7
26	324.0	6.14	3.18	0.201	5.99	23.3	2.00	0.85	10.40	3.80	1.85	3.02	22.7	5.4
28	321.0	6.17	2.80	0.178	5.36	23.8	1.79	0.85	10.69	3.21	2.43	2.74	24.8	5.2
30	393.8	5.41	2.77	0.142	5.03	25.2	1.73	0.91	9.65	3.17	2.72	2.54	25.2	3.9
52	343.3	6.00	2.77	0.149	5.88	27.6	1.91	0.82	11.10	3.12	2.21	2.24	24.1	6.1
54	391.6	5.46	2.91	0.179	5.75	24.4	1.76	0.99	9.32	3.37	2.66	2.30	23.6	4.3
56	259.8	7.31	2.85	0.139	5.97	23.9	1.66	0.82	11.05	3.70	3.16	3.08	25.3	5.4
58	315.1	6.25	2.98	0.146	5.62	26.8	1.78	1.42	10.54	3.62	2.63	3.33	23.7	5.0
60	359.4	5.82	2.62	0.122	5.73	23.2	1.41	1.40	9.63	3.34	3.12	2.84	16.9	4.1
Mean	331.16	6.175	2.838	0.1587	5.863	24.93	1.778	0.964	10.297	3.412	2.720	3.056	23.71	4.85
SD	42.87	0.577	0.157	0.0270	0.533	1.50	0.162	0.241	0.617	0.229	0.465	0.710	2.58	0.70
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Female Day(s) Relative to Start Date

0% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Ovaries rel.wgt (g/kg body wgt)	Uterus rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	92	92	92	92	92	92	92	92	92	92	92	92
11	226.9	8.77	2.95	0.423	6.52	23.9	2.03	1.33	0.516	4.88	9.7	3.8
13	189.3	9.93	3.38	0.343	7.29	24.9	2.05	1.18	0.528	3.57	15.4	3.9
15	196.9	9.60	3.00	0.325	5.84	22.6	2.01	1.35	0.411	2.08	12.2	3.6
17	207.2	9.03	3.04	0.328	6.56	26.2	2.11	1.69	0.430	6.30	15.4	3.3
19	232.7	8.90	3.35	0.335	6.06	26.6	1.76	1.45	0.382	2.70	10.7	3.9
41	214.6	8.85	3.03	0.247	5.78	25.8	1.87	0.91	0.368	2.14	17.8	3.2
43	207.1	9.66	3.48	0.435	6.86	25.6	1.71	1.34	0.386	10.65	11.9	3.3
45	202.4	9.63	3.11	0.356	6.32	24.2	2.05	1.22	0.548	3.25	7.6	3.6
47	195.3	9.63	3.64	0.317	6.14	27.9	2.00	1.50	0.507	2.48	18.5	3.0
49	195.6	9.76	3.32	0.317	6.29	26.4	1.41	1.45	0.481	1.43	16.3	3.0
Mean	206.80	9.376	3.230	0.3427	6.367	25.40	1.899	1.343	0.4558	3.948	13.56	3.46
SD	14.21	0.436	0.234	0.0539	0.463	1.54	0.218	0.210	0.0677	2.765	3.64	0.34
N	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Female Day(s) Relative to Start Date

3% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Ovaries rel.wgt (g/kg body wgt)	Uterus rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	92	92	92	92	92	92	92	92	92	92	92	92
21	225.6	8.78	3.15	0.399	6.43	24.2	1.76	1.44	0.395	2.70	15.6	3.3
23	200.7	9.67	2.79	0.269	6.78	23.8	1.98	1.39	0.478	5.95	15.2	4.0
25	190.8	10.22	3.62	0.304	6.55	24.3	2.22	1.73	0.451	5.06	16.9	4.0
27	191.0	9.79	3.35	0.393	6.34	24.5	1.98	1.58	0.335	2.76	12.8	3.1
29	236.5	8.50	3.64	0.376	6.72	25.1	1.86	1.29	0.381	4.71	14.0	4.3
51	212.0	9.25	2.88	0.259	5.85	22.3	1.76	1.19	0.392	2.29	19.7	3.7
53	226.7	8.82	3.35	0.340	6.04	22.1	1.76	1.16	0.415	2.28	12.2	3.8
55	198.9	9.40	2.97	0.412	6.08	25.9	2.41	1.04	0.473	2.24	16.1	3.8
57	213.0	8.97	3.19	0.286	6.43	25.2	2.09	1.46	0.357	1.79	18.8	4.3
59	191.4	9.25	3.03	0.293	6.11	23.7	1.55	1.87	0.590	1.64	12.6	5.1
Mean	208.66	9.264	3.196	0.3331	6.333	24.11	1.937	1.414	0.4265	3.142	15.38	3.94
SD	16.68	0.525	0.292	0.0580	0.306	1.22	0.255	0.259	0.0745	1.519	2.56	0.54
N	10	10	10	10	10	10	10	10	10	10	10	10

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Female Day(s) Relative to Start Date

6% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Ovaries rel.wgt (g/kg body wgt)	Uterus rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	92	92	92	92	92	92	92	92	92	92	92	92
31	203.8	9.42	3.24	0.353	6.53	25.0	1.64	1.39	0.569	2.33	22.7	6.2
35	193.9	9.54	3.56	0.387	6.70	24.3	2.56	1.77	0.433	2.12	13.4	4.0
37	189.7	9.91	3.48	0.337	6.96	34.5	2.32	1.63	0.543	8.65	18.0	5.0
39	205.7	9.29	3.55	0.379	6.42	26.2	2.18	2.15	0.476	4.99	20.4	5.8
61	204.8	9.08	2.98	0.317	5.81	25.5	1.65	1.00	0.371	2.67	17.6	4.5
63	209.1	9.09	3.25	0.301	6.41	23.7	1.76	1.32	0.478	2.84	16.6	3.9
65	202.8	8.93	3.06	0.335	6.16	25.2	2.47	0.97	0.488	1.96	17.2	4.4
67	204.0	9.07	3.48	0.275	5.98	25.6	1.80	1.58	0.363	1.94	20.5	4.2
69	210.2	9.23	3.38	0.352	6.71	27.3	1.57	1.69	0.614	1.88	17.9	4.6
Mean	202.67	9.283	3.330	0.3375	6.409	26.38	1.994	1.499	0.4817	3.264	18.26	4.71
SD	6.71	0.303	0.212	0.0359	0.370	3.22	0.388	0.378	0.0849	2.237	2.66	0.81
N	9	9	9	9	9	9	9	9	9	9	9	9

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 13: Relative organ weights

Sex: Female Day(s) Relative to Start Date

10% diet	Terminal body wgt (g)	Brain rel.wgt (g/kg body wgt)	Heart rel.wgt (g/kg body wgt)	Adrenals rel.wgt (g/kg body wgt)	Kidneys rel.wgt (g/kg body wgt)	Liver rel.wgt (g/kg body wgt)	Spleen rel.wgt (g/kg body wgt)	Thymus rel.wgt (g/kg body wgt)	Ovaries rel.wgt (g/kg body wgt)	Uterus rel.wgt (g/kg body wgt)	Caecum-F rel.wgt (g/kg body wgt)	Caecum-E rel.wgt (g/kg body wgt)
	92	92	92	92	92	92	92	92	92	92	92	92
1	214.4	8.86	3.22	0.354	6.20	22.5	1.94	1.48	0.462	5.58	22.7	4.8
3	186.1	10.59	2.90	0.296	6.23	25.4	2.44	1.25	0.484	6.02	28.2	7.2
5	184.1	10.21	3.31	0.326	6.63	26.0	2.68	1.67	0.407	2.60	27.9	5.2
7	197.4	9.73	3.24	0.319	6.69	27.6	2.30	1.44	0.390	2.18	22.9	4.9
9	209.8	9.58	3.00	0.305	6.63	26.7	2.11	1.55	0.400	1.79	24.6	7.0
71	218.7	8.37	2.83	0.279	6.31	26.2	1.94	1.02	0.498	2.46	26.2	6.2
73	208.4	9.21	3.41	0.298	6.09	24.9	2.07	1.62	0.441	5.96	22.3	6.9
75	192.5	9.61	3.22	0.364	6.18	26.7	2.31	1.59	0.488	5.31	24.2	5.5
77	200.6	9.37	3.09	0.319	6.78	25.9	2.09	1.35	0.374	2.22	26.9	6.1
79	194.4	9.62	3.24	0.319	6.58	29.3	1.95	1.72	0.602	1.74	24.8	6.3
Mean	200.64	9.515	3.147	0.3178	6.433	26.12	2.185	1.469	0.4547	3.587	25.07	6.02
SD	11.83	0.629	0.184	0.0260	0.251	1.76	0.246	0.213	0.0680	1.863	2.13	0.89
N	10	10	10	10	10	10	10	10	10	10	10	10

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Appendix 14: Pathology

Animal:	32	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

thymus : microhaemorrhage(s)
patches of peyer : lymphangiectasis; focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual

Histopathology - The following Tissues were Not Examined:

None

Animal:	34	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

thymus : spots; red, unilateral [thymus : microhaemorrhage(s) (H)]

Histopathology Observations [Correlation]:

stomach : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s) [thymus : spots; red, unilateral (G)]

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	36	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

(G) = Gross Pathology, (H) = Histo Pathology

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20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 14: Pathology

Animal:	36 (Continued)	Group:	1 - Control	Sex:	Male

Gross Pathology Observations [Correlation]:

habitus/clinical signs : kink in tail

Histopathology Observations [Correlation]:

kidneys : inflammation; mononuclear, multifocal, minimal
liver : inflammation; mononuclear, focal, minimal
lymph node, axillary : cyst(s)
pancreas : inflammation; mononuclear, focal, minimal
prostate gland : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s)
thymus : starry sky appearance
trachea/bronchi : inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; lungs; lymph node, mesenteric; skeletal muscle; nerve, peripheral; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	38	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

lungs : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	40	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	40 (Continued)	Group:	1 - Control	Sex:	Male
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

liver : inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thymus; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	62	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

habitus/clinical signs : kink in tail

Histopathology Observations [Correlation]:

liver : inflammation; mononuclear, multifocal, minimal
spleen : erythropoiesis; extramedullary, minimal
thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	64	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	64 (Continued)	Group:	1 - Control	Sex:	Male

Histopathology Observations [Correlation] (Continued):

epididymides : inflammation; mononuclear, focal, minimal
heart : inflammation; mononuclear, focal, minimal
stomach : inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; esophagus; eyes; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; testes; thymus; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	66	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

lungs : inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thymus; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	68	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

kidneys : basophilic tubules; minimal
liver : inflammation; mononuclear, multifocal, minimal
thymus : microhaemorrhage(s)

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	68 (Continued)	Group:	1 - Control	Sex:	Male

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	70	Group:	1 - Control	Sex:	Male
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

thymus : spots; red [thymus : microhaemorrhage(s) (H)]

Histopathology Observations [Correlation]:

liver : vasculitis; chronic, single, mild
thymus : microhaemorrhage(s) [thymus : spots; red (G)]
trachea/bronchi : inflammation; mononuclear, focal, minimal
patches of peyer : lymphangiectasis; focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual

Histopathology - The following Tissues were Not Examined:

None

Animal:	11	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

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Appendix 14: Pathology

Animal:	11 (Continued)	Group:	1 - Control	Sex:	Female

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	13	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Interim		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

trachea/bronchi : carina; inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	15	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

liver : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	15 (Continued)	Group:	1 - Control	Sex:	Female

None

Animal:	17	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

thymus : microhaemorrhage(s)
trachea/bronchi : carina; inflammation; mononuclear, focal, minimal
uterus : lumen; dilatation; mild [uterus : swollen (G)]
salivary gland(s), parotis : inflammation; mixed, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thyroid gland; urinary bladder; vagina; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	19	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

liver : inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	41	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal: 41 (Continued)	Group: 1 - Control		Sex: Female
	Removal Reason: Killed Terminal		
Necropsy Date: 07/Mar/2017	Study Day (Week) of Death: 92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

ovaries : mineralization; focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal: 43	Group: 1 - Control		Sex: Female
Species: Rat			
	Dose: 0% diet		
	Removal Reason: Killed Terminal		
Necropsy Date: 07/Mar/2017	Study Day (Week) of Death: 92 (13)		

Gross Pathology Observations [Correlation]:

thymus : spots; red [thymus : microhaemorrhage(s) (H)]
uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

lungs : inflammation; mononuclear, focal, minimal
stomach : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s) [thymus : spots; red (G)]
uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; thyroid gland; trachea/bronchi; urinary bladder; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal: 45	Group: 1 - Control		Sex: Female
Species: Rat			
	Dose: 0% diet		
	Removal Reason: Killed Terminal		
Necropsy Date: 07/Mar/2017	Study Day (Week) of Death: 92 (13)		

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	45 (Continued)	Group:	1 - Control	Sex:	Female

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	47	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

intestine, colon - Lost In Processing

Animal:	49	Group:	1 - Control	Sex:	Female
Species:	Rat				
		Dose:	0% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

liver : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s)

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	49 (Continued)	Group:	1 - Control	Sex:	Female

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	2	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	4	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	6	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	6 (Continued)	Group:	2 - Low-dose	Sex:	Male

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	8	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	10	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	72	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	72 (Continued)	Group:	2 - Low-dose	Sex:	Male
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	74	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

thymus : spots; red [thymus : microhaemorrhage(s) (H)]

Histopathology Observations [Correlation]:

thymus : microhaemorrhage(s) [thymus : spots; red (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	76	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	78	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	78 (Continued)	Group:	2 - Low-dose	Sex:	Male
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	80	Group:	2 - Low-dose	Sex:	Male
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	21	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	23	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	23 (Continued)	Group:	2 - Low-dose	Sex:	Female
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	25	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	27	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	29	Group:	2 - Low-dose	Sex:	Female

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	29 (Continued)	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	51	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	53	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

skin/subcutis : sparsely haired [skin/subcutis : acanthosis; focal, mild (H)]

Histopathology Observations [Correlation]:

skin/subcutis : acanthosis; focal, mild [skin/subcutis : sparsely haired (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	55	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	57	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	59	Group:	2 - Low-dose	Sex:	Female
Species:	Rat				
		Dose:	3% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

skin/subcutis : sparsely haired [skin/subcutis : encrustation (H)]

Histopathology Observations [Correlation]:

skin/subcutis : acanthosis; focal, mild
skin/subcutis : encrustation [skin/subcutis : sparsely haired (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	59 (Continued)	Group:	2 - Low-dose	Sex:	Female

None

Animal:	12	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	14	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	16	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

diaphragm : hernia diaphragmatica

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	16 (Continued)	Group:	3 - Mid-dose	Sex:	Male

Histopathology - The following Tissues were Not Examined:

None

Animal:	18	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	20	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

stomach : deposition; yellow [stomach : gross finding not confirmed (H)]

Histopathology Observations [Correlation]:

stomach : gross finding not confirmed [stomach : deposition; yellow (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	42	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

stomach : deposition; yellow

Histopathology Observations [Correlation]:

stomach : inflammation; mononuclear, focal, minimal
stomach : gross finding not confirmed

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	42 (Continued)	Group:	3 - Mid-dose	Sex:	Male

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	44	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	46	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	48	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	48 (Continued)	Group:	3 - Mid-dose	Sex:	Male

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	50	Group:	3 - Mid-dose	Sex:	Male
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	31	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	33	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Found Dead		
Necropsy Date:	29/Dec/2016	Study Day (Week) of Death:	24 (3)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	33 (Continued)	Group:	3 - Mid-dose	Sex:	Female

Histopathology Observations [Correlation]:

eyes : dystrophy; lenticular, moderate
kidneys : mineralization; medullary, minimal
liver : inflammation; mixed, multifocal, minimal
thymus : microhaemorrhage(s)
trachea/bronchi : inflammation; mononuclear, focal, mild

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thyroid gland; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

mammary glands - Lost At Necropsy

Animal:	35	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	37	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	37 (Continued)	Group:	3 - Mid-dose	Sex:	Female

None

Animal:	39	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	61	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	63	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	63 (Continued)	Group:	3 - Mid-dose	Sex:	Female

Histopathology - The following Tissues were Not Examined:

None

Animal:	65	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	67	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	69	Group:	3 - Mid-dose	Sex:	Female
Species:	Rat				
		Dose:	6% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	69 (Continued)	Group:	3 - Mid-dose	Sex:	Female

None

Histopathology - The following Tissues were Not Examined:

None

Animal:	22	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

habitus/clinical signs : kink in tail

Histopathology Observations [Correlation]:

kidneys : inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thymus; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	24	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

kidneys : inflammation; mononuclear, focal, minimal
lungs : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; liver; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	26	Group:	4 - High-dose	Sex:	Male

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	26 (Continued)	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

pancreas : degeneration; focal, minimal
thymus : microhaemorrhage(s)
thymus : starry sky appearance
patches of peyer : lymphangiectasis; focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual

Histopathology - The following Tissues were Not Examined:

None

Animal:	28	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

liver : inflammation; mononuclear, multifocal, minimal
pituitary gland : cyst(s)
thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	30	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	30 (Continued)	Group:	4 - High-dose	Sex:	Male
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

thymus : discoloration; red [thymus : microhaemorrhage(s) (H)]

Histopathology Observations [Correlation]:

lungs : inflammation; mononuclear, focal, minimal
thymus : microhaemorrhage(s) [thymus : discoloration; red (G)]
trachea/bronchi : inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	52	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

prostate gland : inflammation; mononuclear, focal, minimal
spleen : erythropoiesis; extramedullary, mild

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; stomach; testes; thymus; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	54	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal: 54 (Continued) Group: 4 - High-dose Sex: Male

Gross Pathology Observations [Correlation] (Continued):

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

parathyroid glands - Lost In Processing

Animal: 56 Group: 4 - High-dose Sex: Male
Species: Rat
Dose: 10% diet
Removal Reason: Killed Terminal
Necropsy Date: 06/Mar/2017 Study Day (Week) of Death: 91 (13)

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

thymus : microhaemorrhage(s)

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal: 58 Group: 4 - High-dose Sex: Male
Species: Rat
Dose: 10% diet
Removal Reason: Killed Terminal
Necropsy Date: 06/Mar/2017 Study Day (Week) of Death: 91 (13)

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

thymus : microhaemorrhage(s)

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	58 (Continued)	Group:	4 - High-dose	Sex:	Male

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; pituitary gland; prostate gland; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thyroid gland; trachea/bronchi; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	60	Group:	4 - High-dose	Sex:	Male
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	06/Mar/2017	Study Day (Week) of Death:	91 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

heart : inflammation; mononuclear, focal, minimal
lungs : inflammation; mixed, focal, minimal
pituitary gland : remnant(s) rathkes pouch
prostate gland : inflammation; mononuclear, focal, minimal
trachea/bronchi : inflammation; mononuclear, focal, mild

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; coagulating glands; epididymides; esophagus; eyes; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lymph node, axillary; lymph node, mesenteric; skeletal muscle; nerve, peripheral; pancreas; parathyroid glands; salivary gland(s), submaxillary/mandibular; seminal vesicles; skin/subcutis; spinal cord; spleen; stomach; testes; thymus; thyroid gland; urinary bladder; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	1	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

liver : medial lobe; nodule [liver : gross finding not confirmed (H)]
uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

liver : gross finding not confirmed [liver : medial lobe; nodule (G)]
pancreas : inflammation; mononuclear, focal, minimal

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	1 (Continued)	Group:	4 - High-dose	Sex:	Female

Histopathology Observations [Correlation] (Continued):

spleen : haematopoiesis; extramedullary, minimal
stomach : inflammation; mononuclear, focal, mild
thymus : microhaemorrhage(s)
thyroid gland : ectopic thymus
uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; trachea/bronchi; urinary bladder; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	3	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

kidneys : mineralization; medullary, minimal
kidneys : basophilic tubules; minimal
uterus : lumen; dilatation; mild [uterus : swollen (G)]
uterus : inflammation; mixed, focal, mild

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	5	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

skin/subcutis : sparsely haired [skin/subcutis : gross finding not confirmed (H)]

(G) = Gross Pathology, (H) = Histo Pathology

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Appendix 14: Pathology

Animal:	5 (Continued)	Group:	4 - High-dose	Sex:	Female

Histopathology Observations [Correlation]:

skin/subcutis : gross finding not confirmed [skin/subcutis : sparsely haired (G)]

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	7	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	9	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

ovaries : mineralization; focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

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Appendix 14: Pathology

Animal:	9 (Continued)	Group:	4 - High-dose	Sex:	Female

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	71	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

salivary gland(s), parotis : degeneration; multifocal, mild

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

parathyroid glands - Lost In Processing

Animal:	73	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

(G) = Gross Pathology, (H) = Histo Pathology

25/Jul/2017 10:11:23

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 14: Pathology

Animal:	75	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

skin/subcutis : sparsely haired [skin/subcutis : gross finding not confirmed (H)]
uterus : swollen [uterus : lumen; dilatation; mild (H)]

Histopathology Observations [Correlation]:

skin/subcutis : gross finding not confirmed [skin/subcutis : sparsely haired (G)]
skin/subcutis : encrustation; focal, minimal
uterus : lumen; dilatation; mild [uterus : swollen (G)]

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	77	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

No observations found

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; trachea/bronchi; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

Animal:	79	Group:	4 - High-dose	Sex:	Female
Species:	Rat				
		Dose:	10% diet		
		Removal Reason:	Killed Terminal		
Necropsy Date:	07/Mar/2017	Study Day (Week) of Death:	92 (13)		

(G) = Gross Pathology, (H) = Histo Pathology

25/Jul/2017 10:11:23

20880/02 - Sub-chronic (13-week) oral toxicity study with 2'-Fucosyllactose in rats

Appendix 14: Pathology

Animal: 79 (Continued) Group: 4 - High-dose Sex: Female

Gross Pathology Observations [Correlation]:

all organs/tissues : no visible lesions

Histopathology Observations [Correlation]:

trachea/bronchi : carina; inflammation; mononuclear, focal, minimal

Histopathology - The following Tissues were Within Normal Limits:

adrenal glands; aorta; bone marrow, sternum; brain; esophagus; eyes; heart; intestine, cecum; intestine, colon; intestine, duodenum; intestine, ileum; intestine, jejunum; intestine, rectum; kidneys; liver; lungs; lymph node, axillary; lymph node, mesenteric; mammary glands; skeletal muscle; nerve, peripheral; ovaries; oviducts; pancreas; parathyroid glands; pituitary gland; salivary gland(s), submaxillary/mandibular; skin/subcutis; spinal cord; spleen; stomach; thymus; thyroid gland; urinary bladder; uterus; vagina; salivary gland(s), parotis; salivary gland(s) sublingual; patches of peyer

Histopathology - The following Tissues were Not Examined:

None

From: Katrina Emmel
To: Morissette, Rachel
Cc: Steven Overgaard; Richard Kraska
Subject: Re: clarification on GRAS notice for 2"-fucosyllactose
Date: Thursday, October 19, 2017 1:39:45 PM

Hello Dr. Morissette,

The ingredient is intended for use in non-exempt infant formula and follow-on formula.

Please let me know if you have any further questions.

Thank you,

Katrina

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

emmel@gras-associates.com

On Oct 19, 2017, at 10:16 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

Hi Katrina,
Sorry, one more question. Can you please clarify the type of infant formula that you are intending to add you ingredient to? Is this a milk-based non-exempt infant formula for term infants or another category of formula? The term conventional formula doesn't have regulatory meaning so we need to clarify the intended use.

Thanks,

Rachel

Rachel Morissette, Ph.D.
Consumer Safety Officer

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
U.S. Food and Drug Administration
rachel.morissette@fda.hhs.gov

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

From: Morissette, Rachel
Sent: Thursday, October 19, 2017 11:58 AM
To: Katrina Emmel <emmel@gras-associates.com>
Cc: Steven Overgaard <smovergaard@gras-associates.com>; Richard Kraska

<kraska@gras-associates.com>
Subject: RE: clarification on GRAS notice for 2'-fucosyllactose

Thank you for clarifying.

Best regards,

Rachel

Rachel Morissette, Ph.D.
Consumer Safety Officer

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
U.S. Food and Drug Administration
rachel.morissette@fda.hhs.gov

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

From: Katrina Emmel [mailto:emmel@gras-associates.com]
Sent: Thursday, October 19, 2017 11:57 AM
To: Morissette, Rachel <Rachel.Morissette@fda.hhs.gov>
Cc: Steven Overgaard <smovergaard@gras-associates.com>; Richard Kraska <kraska@gras-associates.com>
Subject: Re: clarification on GRAS notice for 2'-fucosyllactose

Hello Dr. Morisette,

I apologize for the confusion. On Form 3667, there is only space to enter the information for one notifier, so I wasn't able to include both companies. Both Glycosyn, LLC and FrieslandCampina Domo B.V. are the joint notifiers of this GRAS dossier.

Please let me know if you have any further questions. I look forward to receipt of the acknowledgment letter.

Thank you,

Katrina

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

emmel@gras-associates.com

On Oct 19, 2017, at 8:43 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:

Dear Dr. Emmel,

My name is Dr. Rachel Morissette and I am the Consumer Safety Officer assigned to your recent GRAS notice for 2'-fucosyllactose. Before I can issue your filing letter, I need to clarify which company/companies is/are the notifier on this notice. Form 3667 listed Glycosyn, LLC as the notifier in Section B, but in Section F Glycosyn, LLC and FrieslandCampina Domo B.V. are both listed as the undersigned. Can you please confirm which company or if both are to be listed as the notifier in this GRAS notice?

Thank you for your attention in this matter.

Regards,

Rachel Morissette, Ph.D.
Consumer Safety Officer

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
U.S. Food and Drug Administration
rachel.morissette@fda.hhs.gov

From: Katrina Emmel
To: Morissette, Rachel
Cc: Richard Kraska
Subject: Re: GRN 000735 questions to address
Date: Wednesday, December 20, 2017 1:49:21 PM

Dear Dr. Morissette,

I am confirming receipt of the questions that were raised by your review team regarding GRN 735. Our team will provide a response within 10 business days.

Please note that I will be traveling for the holidays and will have limited avialability, so my colleague Dr. Richard Kraska--with GRAS Associates-- will be coordinating our response in my absence. I have copied him on this email so you have his contact information should any other questions arise. I would greatly appreciate it if you would copy both of us on future emails to ensure nothing inadvertently falls through the cracks.

Thank you,

Katrina

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

emmel@gras-associates.com

> On Dec 20, 2017, at 6:20 AM, Morissette, Rachel <Rachel.Morissette@fda.hhs.gov> wrote:
>
> Dear Dr. Emmel,
> Please see attached a list of questions raised by our review team to be addressed for GRN 000735. We ask that you respond to these questions within 10 business days. Please provide responses in email format or in a separate document; do not send a revised notice.
>
> Best regards,
>
> **Rachel Morissette, Ph.D.**
> *Consumer Safety Officer*
>
> **Center for Food Safety and Applied Nutrition**
> **Office of Food Additive Safety**
> **U.S. Food and Drug Administration**
> rachel.morissette@fda.hhs.gov
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>
> <12-20-17 GRN735 Questions for Notifier.pdf>

From: Richard Kraska
To: Morissette, Rachel
Subject: Response on GRN 737
Date: Friday, January 05, 2018 10:57:05 AM
Attachments: Response Ltr to FDA GRN 735.pdf
Emmel CV.pdf
Lonnerdal CV .pdf
Kraska CV.pdf
Archer CV.pdf
Expert Panel Qualifications.pdf
U.S. Intakes Report 2"-FL NHANES.pdf
2"-FL Table 10 Updated_.pdf

Hi Rachel

Attached please find our letter responding to your questions. Please confirm your receipt of this message.

In response to FDA comments, we have added Dr. Bo Lönnerdal to the expert panel. Dr. Lönnerdal is a recognized expert in pediatric nutrition.

Other attachments included are:

- CVs for all four members of the expert panel
- A short statement of qualification for the members of the expert panel
- A correction of Table 10 in the dossier
- A corrected, non-confidential report for the dietary intake estimate to be used to correct Appendix 8

Thank you for your help and we hope these responses are useful in the review.

Regards
Rich

Richard Kraska, Ph.D., DABT
Chief Scientific Officer and Executive Vice President
Co-Founder
GRAS Associates, LLC
27499 Riverview Center Parkway
Bonita Springs, FL 34134
T: 239-444-1724 | C: 216-470-7280 | F: 239-444-1723| E: kraska@gras-associates.com

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January 5, 2018

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. Rachel Morissette
Re: GRN 735 –2'-fucosyllactose (2'-FL) –Response to Questions Posed in an Email Dated 12/20/17

Dear Dr. Morissette:

Per your request, GRAS Associates, LLC, acting as the agent for Glycosyn and Friesland Campina, is providing a response to complete FDA's request for additional information as denoted in the attachment to your email dated December 20, 2017, as follows:

1) *Substitution of Corrected Version of Appendix 8*

We have attached a correction of the report that constitutes Appendix 8. It removes unintended confidential markings and corrects Table 3-1 in response to FDA questions 4 and 5.

2) *Questions on composition of Expert Panel*

We appreciate FDA's questions in light of the publication FDA's recent draft guidance on convening a GRAS Panel. We can assure you that Dr. Emmel and Dr. Kraska are sensitive to questions of bias and have the highest regard for scientific integrity and conflict of interest. We are providing a short statement of the qualifications of all the panelists and a current curriculum vitae for each member. We did not include a panel member with expertise in infant nutrition or a medical background in pediatrics because Friesland Campina experts in these area provided technical support in construction of the notice. We also noted that in previous GRAS notices for 2'-FL, there was favorable review by these experts. We felt that the main needs of expertise for the panel were chemistry—to link the composition of a new source of 2'-FL to the test materials used in previous published studies, microbiology --- to review the safety questions that might arise from the new organism and toxicology—to review the new unpublished studies provided with the notice. However, in view of FDA's comments we have contracted with Dr. Bo Lönnerdal from the University of California at Davis to review the dossier and the panel report and join the expert panel. We are including a letter from Dr. Lönnerdal indicating his agreement with the panel findings.

3) *Please clarify if 2'-FL is intended for milk-based infant formulas only or also for soy-based infant formulas*

The intended use of 2'-FL in infant formula is for all types of non-exempt infant formula.

4) *Table 10 indicates a proposed use of 2'-FL in "infant meal replacement products such as Pediasure." PediaSure and similar products are for children older than 12 months of age, not for infants. Please clarify that these are meal replacement products for children older than 12 months of age.*

We confirm these meal replacement products are for children older than 12 months of age. A corrected version of Table 10 is included to reflect that.

5) In Table 10, it is unclear what the intended use level of 2'-FL is going to be infant formula –2.4 g/L or 0.40 g/kcal. Please provide the conversion used between these two use levels.

We have corrected Table 10 to indicate that these levels are equivalent and included a footnote showing the conversion.

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

We look forward to your feedback.

Sincerely,

(b) (6)

Richard Kraska, Ph.D., DABT
Chief Scientific Officer
GRAS Associates, LLC
27499 Riverview Center Blvd., Suite 212
Bonita Springs, FL 34134
kraska@gras-associates.com

87 pages of Curriculum Vitae removed in accordance with the Privacy Act of 1974.

ESTIMATED DAILY INTAKE OF 2'-FL BY THE U.S. POPULATION FROM PROPOSED FOOD-USES (2013-2014 NHANES)

PREPARED FOR:
Glycosyn LLC
6H Gill Street
Woborn, MA
01801
United States

DATE:
21 September 2017

Estimated Daily Intake of 2'-FL by the U.S. Population from Proposed Food-Uses (2013-2014 NHANES)

TABLE OF CONTENTS

List of Tables

Estimated Daily Intake of 2'-FL by the U.S. Population from Proposed Food-Uses (2013-2014 NHANES)

1.0 INTRODUCTION

Glycosyn LLC proposes to use 2'-fucosyllactose (2'-FL) as an ingredient in foods marketed in the United States (U.S.). Such foods include products falling under the following food categories: beverages and beverage bases, breakfast cereals, dairy product analogs, frozen dairy desserts and mixes, gelatins, puddings, and fillings, grain products and pastas, commercial jams and jellies, whole and skim milk, milk products, processed fruits and fruit juices, sweet sauces, toppings, and syrups, non-exempt infant and follow-on formula, and baby foods.

Estimates for the intake of 2'-FL from foods were based on the proposed food-uses and use levels for 2'-FL in conjunction with food consumption data included in the U.S. National Center for Health Statistics' (NCHS) National Health and Nutrition Examination Surveys (NHANES) 2013-2014 (CDC, 2015, 2016; USDA, 2016). Calculations for the mean and 90th percentile *per capita* and consumer-only intakes were performed for all proposed food-uses of 2'-FL and the percentage of consumers were determined. Similar calculations were used to estimate the intake of 2'-FL resulting from each individual proposed food-use, including the calculations of percent consumers. In both cases, the per person and per kilogram body weight intakes were reported for the following population groups:

Infants, ages 0 to 5 months;
Infants, ages 6 to 11 months;
Toddlers, ages 12 to 35 months;
Children, ages 3 to 11 years;
Female teenagers, ages 12 to 19 years;
Male teenagers, ages 12 to 19 years;
Women of child-bearing age, ages 16 to 45 years;
Female adults, ages 20 years and up;
Male adults, ages 20 years and up;
Elderly, ages 65 years and up; and
Total population (all age and gender groups combined).

In addition to the NHANES-based assessment of exposures from proposed food uses, exposure estimates of 2'-FL from proposed uses in medical foods were considered independently, based on the intended dosages for target populations for which these products were intended.

2.0 FOOD CONSUMPTION SURVEY DATA

2.1 Survey Description

NHANES for the years 2013-2014 are available for public use (CDC, 2015). NHANES are conducted as continuous, annual surveys, and are released in 2-year cycles. During each year of the ongoing NHANES program, individuals from the United States are sampled from up to 30 different study locations in a complex multi-stage probability design intended to ensure the data are a nationally representative sample of the U.S. population.

NHANES 2013-2014 dietary survey data were collected from individuals and households *via* 24-hour dietary recalls administered on 2 non-consecutive days (Day 1 and Day 2) throughout all 4 seasons of the year. Day 1 data were collected in-person, and Day 2 data were collected by telephone in the following 3 to 10 days, on different days of the week, to achieve the desired degree of statistical independence. The data were collected by first selecting Primary Sampling Units (PSUs), which were counties throughout the U.S., of which 30 PSUs are visited per year. Smaller contiguous counties were combined to attain a minimum population size. These PSUs were segmented and households were chosen within each segment. One or more participants within a household were interviewed. For NHANES 2013-2014, 14,332 individuals were selected for the sample, 10,175 were interviewed (71.0%) and 9,813 were examined (68.5%).

In addition to collecting information on the types and quantities of foods being consumed, NHANES 2013-2014 collected socio-economic, physiological and demographic information from individual participants in the survey, such as sex, age, body weight, and other variables (such as height and race-ethnicity) that may be useful in characterizing consumption. The inclusion of this information allows for further assessment of food intake based on consumption by specific population groups of interest within the total population. The primary sample design for NHANES 2013-2014 includes an oversample of Non-Hispanic Asian persons, Hispanic persons, non-Hispanic black persons, older adults, and "low income whites/others", however sample weights were incorporated to allow estimates from these subgroups to be combined to obtain national estimates that reflect the relative proportions of these groups in the population as a whole (CDC, 2015).

2.2 Statistical Methods

For the intake assessment, consumption data from individual dietary records, detailing food items ingested by each survey participant, were collated by computer and used to generate estimates for the intake of 2'-FL by the U.S. population[1]. Estimates for the daily intake of 2'-FL represent projected 2-day averages for each individual from Day 1 and Day 2 of NHANES 2013-2014; these average amounts comprised the distribution from which mean and percentile intake estimates were determined. Mean and percentile estimates were generated incorporating survey weights in order to provide representative intakes for the entire U.S. population. "*Per capita*" intake refers to the estimated intake of 2'-FL averaged over all individuals surveyed, regardless of whether they consumed food products in which 2'-FL is proposed for use, and therefore includes individuals with "zero" intakes (*i.e*. those who reported no intake of food products containing 2'-FL during the 2 survey days). "Consumer-only" intake refers to the estimated intake of 2'-FL by those individuals who reported consuming food products in which the use of 2'-FL is currently under consideration. Individuals were considered "consumers" if they reported consumption of 1 or more food products in which 2'-FL is proposed for use on either Day 1 or Day 2 of the survey.

Mean and 90th percentile intake estimates based on sample sizes of less than 30 and 80, respectively, may not be considered statistically reliable due to the limited sampling size (CDC, 2013). As such, the reliability of estimates for the intake of 2'-FL based on consumption estimates derived from individual population groups of a limited sample size should be interpreted with caution. These values are marked with an asterisk in the relevant data tables.

[1] Statistical analysis and data management were conducted in DaDiet Software (Dazult Ltd., 2017). DaDiet Software is a web-based software tool that allows accurate estimate of exposure to nutrients and to substances added to foods, including contaminants, food additives and novel ingredients. The main input components are concentration (use level) data and food consumption data. Data sets are combined in the software to provide accurate and efficient exposure assessments.

3.0 FOOD USAGE DATA

The individual proposed food-uses and use-levels for 2'-FL employed in the current intake analysis are summarized in Table 3-1. Food codes representative of each proposed food-use were chosen from the NHANES 2013-2014 (CDC, 2016). Food codes were grouped in food-use categories according to Title 21, Section §170.3 of the Code of Federal Regulations (CFR, 2017a). If necessary, adjustment factors were developed for composite foods/mixtures based on data provided in the Food and Nutrition Database for Dietary Studies (FNDDS) (USDA, 2016). All food codes included in the current intake assessment are listed in Appendix C.

Table 3-1 Summary of the Individual Proposed Food-Uses and Use-Levels for 2'-FL in the U.S.

Food Category (21 CFR 170.3)	Food-Uses	Maximum 2'-FL Level (g/serving)	RACC[a] (g or mL)	Maximum 2'-FL Use-Levels (g/100 g)
Beverages and Beverage Bases	Energy drinks	0.28	360	0.08
	Fitness water and third quenchers, sports and isotonic drinks	0.28	360	0.08
Breakfast Cereals	Ready-to-eat breakfast cereals for adults and children	1.2	15 (puffed) 40 (high-fiber) 60 (biscuit-types)	8.0 3.0 2.0
	Hot cereals for adults and children	1.2	40 (dry) ~ 250 (prepared)	0.48 (as consumed)
Dairy Product Analogs	Milk substitutes such as soy milk and imitation milks	0.28	240	0.12
Frozen Dairy Desserts and Mixes	Frozen desserts including ice creams* and frozen yogurts, frozen novelties	1.2	~ 70	1.7
Gelatins, puddings, and fillings	Dairy-based puddings, custards, and mousses	1.2	~ 70	1.7
	Fruit pie filling	1.2	85	1.41
	"Fruit prep" such as fruit filling in bars, cookies, yogurt, cakes	1.2	~ 40	3.0
Grain Products and Pastas	Bars, including snack bars, meal-replacement bars, breakfast bars	0.48	40	1.20
Jams and Jellies, Commercial	Jellies and jams, fruit preserves*, fruit butters	1.2	~ 20	6.0
Milk, Whole and Skim	All *acidophilus* or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder*	0.28	240	0.12
Milk Products	Flavored milks, including chocolate milk, coffee drinks, cocoa, smoothies (dairy and fruit-based), other fruit and dairy combinations, yogurt drinks fermented milk drinks including kefir**	0.28	240	0.12
	Milk-based meal replacement beverages or diet beverages**	0.28	240	0.12
	Yogurt*, **	1.2	225	0.53
	Formula intended for pregnant women ("mum" formulas; -9 to 0 months)	1.2	200[b]	0.6
Processed Fruits and Fruit Juices	Fruit drinks, including vitamin and mineral-fortified products	0.28	240	0.12
	Fruit juices*	0.28	240	0.12

Table 3-1 Summary of the Individual Proposed Food-Uses and Use-Levels for 2'-FL in the U.S.

Food Category (21 CFR 170.3)	Food-Uses	Maximum 2'-FL Level (g/serving)	RACC[a] (g or mL)	Maximum 2'-FL Use-Levels (g/100 g)
Sweet Sauces, Toppings, and Syrups	Syrups used to flavor milk beverages	0.28	40	0.70
Other Categories				
Non-Exempt Infant and Follow-On Formula	Infant Formula (0 to 6 months), including ready-to-drink formula or formula prepared from powder	0.24	100[b]	0.24 (0.40 g/100 kcal)[c]
	Follow-On Formula (6 to 12 months), including ready-to-drink formula or formula prepared from powder	0.24	100[b]	0.24 (0.40 g/100 kcal)[c]
Baby Foods	Meal replacement products such as Pediasure	0.24	120[b]	0.2
	Growing-Up (Toddler) Milks (12 to 36 months)	0.24	120[b]	0.2
	Ready-to-eat, ready-to-serve, hot cereals	1.2	15 (dry) 110 (ready-to-serve)	1.09 (as consumed)
	Yogurt and juice beverages identified as "baby" drinks	1.2	120	1.0
	Desserts including fruit desserts, cobblers, yogurt / fruit combinations ("junior type" desserts)	1.2	110	1.09
	Baby crackers, pretzels, cookies, and snack items	0.4	7	5.7
Medical Foods	Oral nutritional supplements and enteral tube feeding (11 years and older)	4.0	200[b]	2.0

2'-FL = 2'-fucosyllactose; CFR = Code of Federal Regulations; RACC = Reference Amounts Customarily Consumed per Eating Occasion; U.S. = United States.

[a] RACC based on values established in 21 CFR §101.12 (U.S. FDA, 2016, CFR, 2017b). When a range of values is reported for a proposed food-use, particular foods within that food-use may differ with respect to their RACC.

[b] No RACC value exists; therefore, approximate serving sizes are provided according to the food manufacturer instructions.

[C] The intended use level in infant formula and baby meal replacement products is 2.4 g per L (0.24 g per 100 mL), or 0.40 g per 100 kcal. For a 100 mL formula that contains 60 kcal, the conversion is as follows:

$$\frac{100\ mL}{60\ kcal} \times \frac{0.24\ g}{100\ mL} = 0.004 \frac{g}{kcal}\ or\ 0.40 \frac{g}{100 kcal}$$

* 2'-FL is intended for use in unstandardized products when standards of identity do not permit its addition.

** Includes ready-to-drink and powder forms.

It is further noted that 2'-FL is intended for use in medical foods (oral nutritional supplements and enteral tube feeding) at maximum dosages of 4.0 g per product. The dietary exposures from these intended uses are considered separately from the NHANES-based assessment, as the conventional food consumption database would not adequately capture these target uses.

4.0 FOOD SURVEY RESULTS

Estimates for the total daily intakes of 2'-FL from proposed food-uses are provided in Tables 4.1-1 and 4.1-2. Estimates for the daily intake of 2'-FL from individual proposed food-uses in the U.S. are summarized in Tables A-1 to A-10 and B-1 to B-10 of Appendices A and B, respectively. Tables A-1 to A-10 provide estimates for the daily intake of 2'-FL on an absolute basis (g/person/day), whereas Tables B-1 to B-10 provide estimates for the daily intake of 2'-FL on a per kilogram body weight basis (mg/kg body weight/day).

4.1 Estimated Daily Intake of 2'-FL from All Proposed Food-Uses in the U.S.

Table 4.1-1 summarizes the estimated total intake of 2'-FL (g/person/day) from all proposed food-uses in the U.S. population group. Table 4.1-2 presents this data on a per kilogram body weight basis (mg/kg body weight/day). The percentage of consumers was high among all age groups evaluated in the current intake assessment; greater than 57.5% of the infant population and greater than 86.8% of the other population groups consisted of consumers of food products in which 2'-FL is currently proposed for use (Table 4.1-1). Owing to the proposed uses of 2'-FL in milks, juices, cereals, yogurts which are popular food items among toddlers, 100% of individuals aged 12 to 35 months simulated to consume foods in which 2'-FL is proposed for use. The consumer-only estimates are more relevant to risk assessments as they represent exposures in the target population; consequently, only the consumer-only intake results are discussed in detail herein.

Among the total population (all ages), the mean and 90th percentile consumer-only intakes of 2'-FL were determined to be 1.70 and 3.54 g/person/day, respectively. Of the individual population groups, older infants aged 6 to 11 months were determined to have the greatest mean consumer-only intakes of 2'-FL on an absolute basis, at 2.28 g/person/day, whereas male teenagers were estimated to have the highest 90th percentile intake of 2'-FL at 4.29 g/day. Females of childbearing age (16 to 45 years old) had the lowest estimated mean and 90th percentile consumer-only intakes of 1.36 and 2.87 g/person/day, respectively (Table 4.1-1).

Table 4.1-1 Summary of the Estimated Daily Intake of 2'-FL from Proposed Food-Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants	0 to 5 (months)	1.10	2.75	57.5	107	1.91	3.00
Infants	6 to 11 (months)	2.14	3.86	94.1	160	2.28	3.86
Toddlers	12 to 35 (months)	1.83	2.97	100.0	348	1.83	2.97
Children	3 to 11	1.96	3.53	99.7	1,277	1.97	3.53
Female Teenagers	12 to 19	1.47	2.95	94.7	544	1.55	2.95
Male Teenagers	12 to 19	1.85	4.16	92.5	526	2.00	4.29
Women of Child-Bearing Age	16 to 45	1.22	2.82	89.9	1,219	1.36	2.87
Female Adults	20 and up	1.32	2.96	91.9	2,169	1.44	3.05
Male Adults	20 and up	1.59	3.81	86.8	1,842	1.84	3.97
Elderly	65 and up	1.76	3.74	92.8	939	1.90	3.91
Total Population	All Ages	1.55	3.41	91.2	6,973	1.70	3.54

2'-FL = 2'-fucosyllactose; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

On a body weight basis, the total population (all ages) mean and 90th percentile consumer-only intakes of 2'-FL were determined to be 36 and 80 mg/kg body weight/day, respectively. Among the individual population groups, younger infants aged 0 to 5 months were identified as having the highest mean and 90th percentile consumer-only intakes of any population group, of 315 and 532 mg/kg body weight/day, respectively. Female adults and females of childbearing age were predicted to have the lowest mean and 90th percentile intakes at 20 and 43 mg/kg body weight/day, respectively (Table 4.1-2).

Table 4.1-2 Summary of the Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Proposed Food-Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants	0 to 5 (months)	181	477	57.5	107	315	532
Infants	6 to 11 (months)	244	441	94.1	160	259	447
Toddlers	12 to 35 (months)	148	243	100.0	346	148	243
Children	3 to 11	75	147	99.7	1,268	76	147
Female Teenagers	12 to 19	24	52	94.7	536	26	52
Male Teenagers	12 to 19	29	67	92.5	524	31	67
Women of Child-Bearing Age	16 to 45	18	42	89.9	1,209	20	43
Female Adults	20 and up	19	42	91.9	2,156	20	43
Male Adults	20 and up	19	46	86.7	1,833	22	48
Elderly	65 and up	24	53	92.6	928	26	54
Total Population	All Ages	32	76	91.1	6,930	36	80

2'-FL = 2'-fucosyllactose; bw = body weight; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

4.2 Estimated Daily Intake of 2'-FL from Specific Food Categories

4.2.1 Intake of 2'-FL from Infant and Follow-On Formula Among Non-Breastfeeding Infants and Toddlers

In order to consider the intake of 2'-FL from formula products, an additional assessment was undertaken in which the subpopulation of breastfed infants/toddlers were removed, and the intakes were examined by the remaining non-breastfed infants and toddlers to investigate whether 2'-FL intake was greater among this group. This reflected the intake models included under GRN 546 and GRN 571 (Glycom A/S, 2014; Environ International Corp., 2015). The anticipated intake of 2'-FL from (non-exempt) infant formula products among infants and toddlers who are not breastfed are presented in the table below on an absolute (g/day) and per kilogram body weight basis (mg/kg body weight/day). Mean intakes decreased with age from 2.14 to 0.39 g/day, or 354 to 40 mg/kg body weight/day, which is anticipated as children move on to a more varied diet over 6 months of age. Due to the low sample size, the 90th percentile results are only statistically reliable for infants aged 6 to 11 months, at 2.56 g/day or 311 mg/kg body weight/day.

Table 4.2.1-1 Estimated Daily Intake of 2'-FL from Non-Exempt Infant Formula Among Non-Breastfed Infants (2013-2014 NHANES Data)

Population Group	Age Group (Months)	Consumer-Only Intake of 2'-FL¥					
		%	n	g/day		mg/kg body weight/day	
				Mean	90th Percentile	Mean	90th Percentile
Infants	0 to 5	43.0	79	2.14	2.88*	354	498*
Infants	6 to 11	56.6	100	1.67	2.56	192	311
Toddlers	12 to 35	11.7	39	0.39	1.14*	40	101*

2'-FL = 2'-fucosyllactose; NHANES = National Health and Nutrition Examination Survey.

¥ Infants and toddlers recording a breastmilk consumption event in NHANES were removed from these analyses. The results represent intake of 2'-FL from non-exempt infant and follow-on formula among consumers of formula, by age group.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

4.2.2 Intake of 2'-FL from Other Food Categories

Estimates for the mean and 90th percentile daily intakes of 2'-FL from each individual food category are summarized in Tables A-1 to A-10 and B-1 to B-10 on a g/day and mg/kg body weight/day basis, respectively. Among the non-infant population, individuals were identified as being significant consumers of milk products (46.2 to 89.1% consumers among the individual demographics), fruit juices (25.3 to 64.0% consumers), and ready-to-eat breakfast cereals (28.5 to 61.1% consumers).

In terms of contribution to total mean intake of 2'-FL among the non-infant population, ready-to-eat breakfast cereal accounted for 18.5 to 32.3% of total intakes, which were followed by frozen desserts (contributed 5.7 to 29.0% to total intakes) and milks (contributed 8.1 to 26.2% to total mean intakes). The other food categories accounted for less than 8.8% of the total 2'-FL intake (see Tables A-1 to A-10 and/or B-1 to B-10 for further details).

4.2.3 Intake of 2'-FL from Proposed Uses in Medical Foods

As noted in the introduction, 2'-FL is proposed for use in medical foods at maximum dosage levels of 4 g/serving, intended to be consumed by patients aged 11 years and older at no more than 3 servings per day. Medical foods containing 2'-FL will be used under the supervision of a physician for the dietary management of a disease or condition and therefore will not be combined with a diet containing 2'-FL from its conventional food uses described under Table 3-1. Therefore, the anticipated daily intake of 2'-FL from its proposed uses in medical foods is expected to be at a maximum of 12 g/person/day[2] among the target population. Using default body weight values for adolescents and adults as established in the U.S. Environmental Protection Agency's Exposure Factors Handbook (U.S. EPA, 2011), dosages are equivalent to 211 mg/kg body weight/day in a 56.8 kg adolescent and 150 mg/kg body weight/day in an 80.0 kg adult.

5.0 SUMMARY AND CONCLUSIONS

Consumption data and information pertaining to the individual proposed food-uses of 2'-FL were used to estimate the *per capita* and consumer-only intakes of 2'-FL for specific demographic groups and for the total U.S. population. There were a number of assumptions included in the assessment which render exposure estimates that may be considered suitably conservative. For example, it has been assumed in both exposure assessments that all food products within a food category contain 2'-FL at the maximum specified level of use. In reality, the levels added to specific foods will vary depending on the nature of the food product and it is unlikely that 2'-FL will have 100% market penetration in all identified food categories.

In summary, on consumer-only basis, the resulting mean and 90th percentile intakes of 2'-FL by the total (all ages) U.S. population from all proposed food-uses, were estimated to be 1.70 g/person/day (36 mg/kg body weight/day) and 3.54 g/person/day (80 mg/kg body weight/day), respectively. Among the individual population groups, older infants aged 6 to 11 months were determined to have the greatest mean consumer-only intakes of 2'-FL on an absolute basis, at 2.28 g/person/day (259 mg/kg body weight/day), whereas male teenagers were estimated to have the highest 90th percentile intake of 2'-FL at 4.29 g/day (67 mg/kg body weight/day). When intakes were expressed on a body weight basis, younger infants aged 0 to 5 months were identified as having the highest mean and 90th percentile consumer-only intakes of any population group, of 315 and 532 mg/kg body weight/day, respectively. When considering predicted intake of 2'-FL from formula products among non-breastfed infants, estimates of mean consumer-only intake

[2] Calculated as 4.0 g/serving x 3 servings/day = 12 g/day.

ranged from 0.39 g/day (40 mg/kg body weight/day) among toddlers, up to 2.14 g/day (354 mg/kg body weight/day) among young infants aged 0 to 5 months.

Uses of 2'-FL in medical foods at a dosage of 4 g/serving are expected to result in a maximum daily intake of 12 g/day of 2'-FL among its intended target patient population of individuals aged 11 years and older (equivalent to approximately 211 mg/kg body weight/day in adolescents and 150 mg/kg body weight/day in adults).

6.0 REFERENCES

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Appendix A
Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Different Population Groups Within the U.S. (2013-2014 NHANES DATA)

Table A-1 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Infants Aged 0 to 5 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
All	***100***	***1.10***	***2.75***	***57.5***	***107***	***1.91***	***3.00***
Beverages and Beverage Bases							
Energy drinks	0	na	na	0	0	na	na
Fitness water and third quenchers, sports and isotonic drinks	0	na	na	0	0	na	na
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	<0.1	<0.01*	na	0.2	1	0.01*	0.01*
Hot cereals for adults and children	0.1	<0.01*	na	0.9	1	0.15*	0.15*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0	na	na	0	0	na	na
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	0.3	<0.01*	na	0.9	1	0.32*	0.32*
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	0	na	na	0	0	na	na
Fruit pie filling	0	na	na	0	0	na	na
"Fruit prep"	0	na	na	0	0	na	na
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	0	na	na	0	0	na	na
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	0	na	na	0	0	na	na
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	<0.1	<0.01*	na	0.2	1	0.10*	0.09*
Milk Products							
Flavored milks	0	na	na	0	0	na	na
Milk-based meal replacement beverages or diet beverages	0	na	na	0	0	na	na
Yogurt	0	na	na	0	0	na	na
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	0	na	na	0	0	na	na
Fruit juices	0.3	<0.01*	na	2.1	5	0.16*	0.26*
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0	na	na	0	0	na	na
Other							

Table A-1 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Infants Aged 0 to 5 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant formula	92.3	1.02	2.63	52.4	102	1.94	2.78
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0.8	0.01*	na	2.4	4	0.37*	0.66*
Yogurt and juice beverages identified as "baby" drinks	3.0	0.03*	na	4.5	8	0.74*	1.79*
"Junior type" desserts	1.2	0.01*	na	6.5	6	0.20*	0.33*
Baby crackers, pretzels, cookies, and snack items	2.1	0.02*	na	2.6	6	0.86*	1.61*

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-2 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Older Infants Aged 6 to 11 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***2.14***	***3.86***	***94.1***	***160***	***2.28***	***3.86***
Beverages and Beverage Bases							
Energy drinks	0	na	na	0	0	na	na
Fitness water and third quenchers, sports and isotonic drinks	0.1	<0.01*	na	2.7	6	0.11*	0.10*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	1.4	0.03*	0.12	15.9	22	0.19*	0.33*
Hot cereals for adults and children	1.5	0.03*	0.06	11.3	13	0.29*	0.48*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.1	<0.01*	na	1.6	2	0.17*	0.17*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	0.2	<0.01*	na	4.3	8	0.10*	0.25*
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	0.6	0.01*	na	2.9	4	0.45*	0.56*
Fruit pie filling	0.2	0.01*	na	1.7	1	0.31*	0.31*
"Fruit prep"	0	na	na	0	0	na	na
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	0.5	0.01*	na	1.7	1	0.68*	0.68*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	0	na	na	0	0	na	na
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	3.2	0.07	0.29*	15.9	33	0.43	0.73*
Milk Products							
Flavored milks	0.1	<0.01*	na	2.0	4	0.12*	0.19*
Milk-based meal replacement beverages or diet beverages	0	na	na	0	0	na	na
Yogurt	1.8	0.04*	0.02	10.6	18	0.37*	0.65*
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	0.1	<0.01*	na	2.1	5	0.08*	0.10*
Fruit juices	0.8	0.02*	0.06	14.0	29	0.12*	0.19*
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages		na	na	0	0	na	na
Other							

Table A-2 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Older Infants Aged 6 to 11 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	46.6	1.00	2.38	63.0	107	1.58	2.56
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-Up (Toddler) Milks	3.0	0.06*	na	6.5	7	0.98*	1.43*
Ready-to-eat, ready-to-serve, hot cereals for babies	1.7	0.04*	na	5.0	9	0.74*	0.92*
Yogurt and juice beverages identified as "baby" drinks	18.6	0.40	1.24*	40.5	59	0.98	2.17*
"Junior Type" Desserts	11.2	0.24	0.62*	36.3	55	0.66	1.29*
Baby crackers, pretzels, cookies, and snack items	8.1	0.17	0.60	46.5	82	0.37	0.82

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-3 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Toddlers Aged 12 to 35 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.83***	***2.97***	***100***	***348***	***1.83***	***2.97***
Beverages and Beverage Bases							
Energy drinks	0	0	na	0	0	na	na
Fitness water and third quenchers, sports and isotonic drinks	0.8	0.01*	na	7.0	20	0.21*	0.40*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	18.5	0.34	0.90	61.1	203	0.55	1.07
Hot cereals for adults and children	5.2	0.09	0.40*	17.7	66	0.53	0.87*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	1.4	0.03*	na	7.5	22	0.35*	0.91*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	5.7	0.10	0.49*	17.1	69	0.61	1.21*
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	2.0	0.04*	na	5.6	24	0.64*	1.02*
Fruit pie filling	<0.1	<0.01*	na	0.5	1	0.16*	0.16*
"Fruit prep"	0.5	0.01*	na	5.6	14	0.17*	0.33*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	1.5	0.03*	na	7.7	25	0.35*	0.58*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	5.4	0.10	0.38*	19.9	51	0.50	0.90*
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	26.2	0.48	0.99	89.1	305	0.54	1.04
Milk Products							
Flavored milks	1.5	0.03	0.10*	15.9	59	0.17	0.34*
Milk-based meal replacement beverages or diet beverages	0.9	0.02*	na	4.6	7	0.37*	0.68*
Yogurt	6.9	0.13	0.41	29.3	95	0.43	0.90
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	3.7	0.07	0.22	30.1	128	0.23	0.43
Fruit juices	7.0	0.13	0.34	64.0	213	0.20	0.41
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.2	<0.01*	na	3.2	8	0.09*	0.12*
Other							

Table A-3 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Toddlers Aged 12 to 35 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant formula	1.6	0.03*	na	4.0	13	0.75*	1.21*
Follow-on formula	<0.1	<0.01*	na	<0.1	1	0.58*	0.58*
Meal replacement products	0.9	0.02*	na	2.9	6	0.55*	1.22*
Growing-up (toddler) milks	0.5	0.01*	na	1.1	3	0.79*	0.92*
Ready-to-eat, ready-to-serve, hot cereals for babies	0.7	0.01*	na	1.9	5	0.69*	0.93*
Yogurt and juice beverages identified as "baby" drinks	3.6	0.07*	na	6.0	20	1.11*	2.02*
"Junior type" desserts	1.3	0.02*	na	4.1	12	0.58*	1.20*
Baby crackers, pretzels, cookies, and snack items	4.0	0.07	0.02*	11.5	31	0.65	1.63*

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-4 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Children Aged 3 to 11 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.96***	***3.53***	***99.7***	***1,277***	***1.97***	***3.53***
Beverages and Beverage Bases							
Energy drinks	<0.1	<0.01*	na	0.1	1	0.15*	0.15*
Fitness water and third quenchers, sports and isotonic drinks	1.4	0.03	0.07	12.2	128	0.22	0.43
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	27.1	0.53	1.47	59.0	777	0.90	1.74
Hot cereals for adults and children	2.4	0.05	na	8.3	117	0.57	1.19
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.2	<0.01	na	2.5	33	0.18	0.33*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	21.9	0.43	1.29	35.2	388	1.22	2.41
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	3.9	0.08	na	5.0	67	1.53	3.09*
Fruit pie filling	0.2	<0.01*	na	1.0	15	0.31*	0.42*
"Fruit prep"	0.2	<0.01	na	3.4	46	0.14	0.38*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	1.5	0.03	0.13	11.9	128	0.24	0.45
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.9	0.10	0.38	17.2	224	0.56	1.13
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	13.2	0.26	0.57	80.7	1,041	0.32	0.63
Milk Products							
Flavored milks	3.8	0.08	0.26	35.1	473	0.22	0.44
Milk-based meal replacement beverages or diet beverages	0.1	<0.01*	na	1.4	10	0.21*	0.29*
Yogurt	5.6	0.11	0.45	23.3	260	0.47	0.90
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	6.2	0.12	0.34	50.6	665	0.24	0.44
Fruit juices	6.7	0.13	0.34	56.9	759	0.23	0.45
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.4	0.01	na	4.9	55	0.15	0.30*
Other							

Table A-4 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Children Aged 3 to 11 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	<0.1	<0.01*	na	<0.1	1	0.44*	0.44*
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	0.1	<0.01*	na	0.4	11	0.42*	0.99*
Growing-Up (Toddler) Milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0.1	<0.01*	na	0.3	3	0.77*	0.90*
"Junior Type" Desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	0.1	<0.01*	na	0.2	2	0.82*	0.98*

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-5 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.47***	***2.95***	***94.7***	***544***	***1.55***	***2.95***
Beverages and Beverage Bases							
Energy drinks	0.3	<0.01*	na	1.9	7	0.25*	0.38*
Fitness water and third quenchers, sports and isotonic drinks	1.6	0.02	na	9.2	55	0.26	0.47*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	32.3	0.47	1.49	43.0	230	1.10	1.99
Hot cereals for adults and children	2.3	0.03	na	4.9	38	0.69	1.22*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.3	<0.01*	na	2.0	22	0.18*	0.40*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	21.3	0.31	1.21	24.3	125	1.29	2.04
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	3.9	0.06*	na	4.1	20	1.39*	1.85*
Fruit pie filling	0.3	<0.01*	na	0.7	10	0.60*	1.02*
"Fruit prep"	0.5	0.01*	na	3.0	23	0.24*	0.49*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	3.7	0.05	0.26*	17.0	68	0.32	0.50*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.2	0.06	na	9.7	44	0.63	0.84*
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	10.6	0.16	0.41	59.6	320	0.26	0.50
Milk Products							
Flavored milks	2.8	0.04	0.19	18.9	107	0.22	0.38
Milk-based meal replacement beverages or diet beverages	0.1	<0.01*	na	0.5	6	0.23*	0.29*
Yogurt	4.8	0.07	0.24*	12.8	53	0.54	1.01*
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	7.5	0.11	0.34	37.1	235	0.30	0.70
Fruit juices	3.6	0.05	0.20	25.3	189	0.21	0.42
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.2	<0.01*	na	1.9	6	0.13*	0.15*
Other							

Table A-5 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	0	na	na	0	0	na	na
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	<0.1	<0.01*	na	<0.1	1	1.51*	1.51*
Growing-Up (Toddler) Milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior Type" Desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	<0.1	<0.01*	na	<0.1	1	1.14*	1.14*

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-6 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.85***	***4.16***	***92.5***	***526***	***2.00***	***4.29***
Beverages and Beverage Bases							
Energy drinks	0.7	0.01*	na	4.0	8	0.31*	0.41*
Fitness water and third quenchers, sports and isotonic drinks	6.0	0.11	0.30	19.9	93	0.56	0.79
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	31.4	0.58	1.61	45.5	252	1.27	2.80
Hot cereals for adults and children	1.8	0.03*	na	3.9	28	0.86*	1.92*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.1	<0.01*	na	0.9	11	0.25*	0.55*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	19.4	0.36	1.34	19.8	109	1.82	3.22
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	1.7	0.03*	na	2.5	12	1.26*	2.22*
Fruit pie filling	0.4	0.01*	na	2.2	6	0.34*	0.41*
"Fruit prep"	0.6	0.01*	na	2.0	14	0.52*	0.98*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.1	0.04	0.14*	12.3	52	0.32	0.82*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.4	0.08	na	6.8	50	1.21	2.25*
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	14.4	0.27	0.71	65.3	360	0.41	0.85
Milk Products							
Flavored milks	3.2	0.06	0.21	23.9	140	0.24	0.53
Milk-based meal replacement beverages or diet beverages	0.8	0.02*	na	1.8	9	0.84*	1.19*
Yogurt	1.3	0.02*	na	4.4	27	0.55*	0.92*
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	5.6	0.10	0.29	30.2	209	0.34	0.75
Fruit juices	5.8	0.11	0.30	40.6	224	0.27	0.54
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.3	0.01*	na	1.4	4	0.40*	0.48*
Other							

Table A-6 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	0	na	na	0	0	na	na
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-Up (Toddler) Milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior Type" Desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-7 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Women of Childbearing Age, 16 to 45 Years, Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.22***	***2.82***	***89.9***	***1,219***	***1.36***	***2.87***
Beverages and Beverage Bases							
Energy drinks	0.5	0.01	na	2.5	31	0.22	0.41*
Fitness water and third quenchers, sports and isotonic drinks	1.3	0.02	na	5.8	72	0.27	0.50*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	25.8	0.32	1.09	31.0	410	1.02	2.10
Hot cereals for adults and children	5.1	0.06	na	9.1	141	0.69	1.23
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.7	0.01	na	6.2	86	0.15	0.29
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	23.0	0.28	0.96	21.8	261	1.28	2.94
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	2.9	0.04	na	3.6	54	1.00	1.68*
Fruit pie filling	0.7	0.01	na	2.0	31	0.42	0.65*
"Fruit prep"	1.1	0.01	na	4.2	62	0.32	1.10*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	3.7	0.05	0.21	14.1	154	0.32	0.54
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	3.5	0.04	na	7.8	93	0.54	1.13
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	8.7	0.11	0.35	46.2	644	0.23	0.50
Milk Products							
Flavored milks	2.9	0.04	0.15	12.1	172	0.29	0.57
Milk-based meal replacement beverages or diet beverages	0.6	0.01*	na	2.4	27	0.32*	0.44*
Yogurt	7.2	0.09	0.38	15.1	178	0.58	1.05
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	7.0	0.09	0.30	27.4	395	0.31	0.65
Fruit juices	5.1	0.06	0.22	27.8	409	0.22	0.39
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.2	<0.01*	na	1.0	7	0.20*	0.25*
Other							

Table A-7 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Women of Childbearing Age, 16 to 45 Years, Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	0	na	na	0	0	na	na
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-Up (Toddler) Milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior Type" Desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	<0.1	<0.01*	na	<0.1	1	1.14*	1.14*

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-8 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Female Adults Aged 20 and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.32***	***2.96***	***91.9***	***2,169***	***1.44***	***3.05***
Beverages and Beverage Bases							
Energy drinks	0.2	<0.01	na	1.4	32	0.21	0.40*
Fitness water and third quenchers, sports and isotonic drinks	0.9	0.01	na	3.7	78	0.31	0.50*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	22.3	0.30	1.03	31.0	711	0.95	1.85
Hot cereals for adults and children	7.3	0.10	0.42	13.6	394	0.71	1.20
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	1.1	0.01	na	7.5	176	0.20	0.48
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	22.7	0.30	1.21	24.9	547	1.20	2.56
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	5.2	0.07	na	5.5	133	1.26	2.26
Fruit pie filling	2.0	0.03	na	5.1	101	0.51	1.17
"Fruit prep"	1.3	0.02	na	6.3	150	0.28	0.56
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.7	0.04	0.14	10.7	211	0.34	0.60
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.4	0.06	0.09	10.7	243	0.55	1.13
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	8.1	0.11	0.35	48.9	1,179	0.22	0.47
Milk Products							
Flavored milks	1.9	0.03	na	9.3	243	0.28	0.52
Milk-based meal replacement beverages or diet beverages	1.1	0.01	na	4.2	77	0.34	0.60*
Yogurt	8.8	0.12	0.45	19.1	379	0.61	1.05
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	5.4	0.07	0.24	22.3	558	0.32	0.63
Fruit juices	4.5	0.06	0.21	28.4	727	0.21	0.39
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	<0.1	<0.01*	na	0.6	12	0.25*	0.36*
Other							

Table A-8 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Female Adults Aged 20 and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	0	na	na	0	0	na	na
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-Up (Toddler) Milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior Type" Desserts	<0.1	<0.01*	na	<0.1	1	1.85*	1.85*
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-9 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Male Adults Aged 20 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.59***	***3.81***	***86.8***	***1,842***	***1.84***	***3.97***
Beverages and Beverage Bases							
Energy drinks	0.7	0.01	na	4.2	90	0.28	0.40
Fitness water and third quenchers, sports and isotonic drinks	2.0	0.03	na	8.1	163	0.40	0.77
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	25.0	0.40	1.29	28.5	574	1.40	2.55
Hot cereals for adults and children	6.3	0.10	0.28	10.4	292	0.97	1.94
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.6	0.01	na	4.2	95	0.22	0.44
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	24.0	0.38	1.57	24.5	448	1.56	2.96
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	4.9	0.08	na	4.7	97	1.64	3.06
Fruit pie filling	1.4	0.02	na	4.5	86	0.51	0.97
"Fruit prep"	1.3	0.02	na	7.0	134	0.29	0.53
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.5	0.04	0.14	12.3	186	0.32	0.67
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	5.9	0.09	0.38	12.2	253	0.77	1.26
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	9.6	0.15	0.44	48.3	1,019	0.32	0.67
Milk Products							
Flavored milks	1.6	0.03	na	8.6	177	0.30	0.54
Milk-based meal replacement beverages or diet beverages	1.1	0.02	na	3.6	65	0.50	1.16*
Yogurt	4.4	0.07	0.28	11.0	201	0.65	1.30
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	4.3	0.07	0.26	18.9	448	0.36	0.67
Fruit juices	4.4	0.07	0.27	26.1	615	0.27	0.48
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	<0.1	<0.01*	na	0.6	9	0.12*	0.17*
Other							

Table A-9 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by Male Adults Aged 20 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	0	na	na	0	0	na	na
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-Up (Toddler) Milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior Type" Desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-10 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by the Elderly Aged 65 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.76***	***3.74***	***92.8***	***939***	***1.90***	***3.91***
Beverages and Beverage Bases							
Energy drinks	<0.1	<0.01*	na	0.1	3	0.18*	0.19*
Fitness water and third quenchers, sports and isotonic drinks	0.3	0.01*	na	2.1	21	0.27*	0.39*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	22.5	0.40	1.28	39.7	359	1.00	1.81
Hot cereals for adults and children	8.1	0.14	0.58	17.1	224	0.83	1.69
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.7	0.01	na	5.8	63	0.21	0.49*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	29.0	0.51	1.65	35.5	306	1.44	2.70
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	5.9	0.10	na	8.0	78	1.30	2.07*
Fruit pie filling	2.9	0.05	na	7.9	68	0.64	1.17*
"Fruit prep"	1.8	0.03	0.05	11.3	88	0.28	0.67
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	1.0	0.02	na	7.0	51	0.24	0.32*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.9	0.09	0.30	13.8	138	0.62	1.20
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	8.6	0.15	0.45	59.7	574	0.25	0.55
Milk Products							
Flavored milks	1.0	0.02	na	6.4	74	0.27	0.49*
Milk-based meal replacement beverages or diet beverages	1.4	0.02	na	6.1	45	0.40	0.68*
Yogurt	4.9	0.09	0.45	15.9	136	0.55	0.90
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	2.9	0.05	0.20	19.2	198	0.27	0.55
Fruit juices	4.1	0.07	0.25	34.1	360	0.21	0.39
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.1	<0.01*	na	0.7	7	0.26*	0.42*
Other							

Table A-10 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by the Elderly Aged 65 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	0	na	na	0	0	na	na
Follow-On Formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-Up (Toddler) Milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior Type" Desserts	0.1	<0.01*	na	0.1	1	1.85*	1.85*
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table A-11 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by the Total U.S. Population (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***1.55***	***3.41***	***91.2***	***6,973***	***1.70***	***3.54***
Beverages and Beverage Bases							
Energy drinks	0.4	0.01	na	2.4	138	0.26	0.41
Fitness water and third quenchers, sports and isotonic drinks	1.7	0.03	na	7.5	543	0.36	0.62
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	24.6	0.38	1.21	35.2	2,770	1.08	2.08
Hot cereals for adults and children	5.5	0.08	0.25	10.9	949	0.78	1.36
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.7	0.01	na	5.0	361	0.21	0.44
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	21.9	0.34	1.26	25.1	1,695	1.35	2.75
Gelatins, puddings, and fillings							
Dairy-based puddings, custards, and mousses	4.4	0.07	na	4.9	357	1.41	2.83
Fruit pie filling	1.2	0.02	na	3.9	220	0.50	0.99
"Fruit prep"	1.0	0.02	na	5.7	381	0.27	0.53
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.4	0.04	0.14	11.6	671	0.32	0.60
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	5.0	0.08	0.19	11.8	865	0.65	1.20
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	10.4	0.16	0.46	54.3	4,258	0.30	0.61
Milk Products							
Flavored milks	2.2	0.03	0.15	13.4	1,203	0.25	0.47
Milk-based meal replacement beverages or diet beverages	0.9	0.01	na	3.3	174	0.41	0.87
Yogurt	5.9	0.09	0.41	15.6	1,033	0.58	1.05
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	5.1	0.08	0.28	25.5	2,248	0.31	0.61
Fruit juices	4.8	0.07	0.26	32.0	2,761	0.23	0.45
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.1	0.00	na	1.3	94	0.17	0.42
Other							

Table A-11 Estimated Daily Intake of 2'-FL from Individual Proposed Food-Uses by the Total U.S. Population (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant Formula	1.0	0.02	na	0.9	223	1.62	2.64
Follow-On Formula	<0.1	<0.01*	na	<0.1	1	0.58*	0.58*
Meal replacement products	<0.1	<0.01*	na	0.1	18	0.52*	1.41*
Growing-Up (Toddler) Milks	<0.1	<0.01*	na	0.1	10	0.91*	1.04*
Ready-to-eat, ready-to-serve, hot cereals for babies	<0.1	<0.01*	na	0.1	18	0.66*	0.93*
Yogurt and juice beverages identified as "baby" drinks	0.3	0.01	na	0.5	90	0.99	2.07
"Junior Type" Desserts	0.2	<0.01	na	0.4	74	0.63	1.25*
Baby crackers, pretzels, cookies, and snack items	0.2	<0.01	na	0.7	122	0.52	1.62

2'-FL = 2'-fucosyllactose; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Appendix B
Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Different Population Groups Within the U.S. (2013-2014 NHANES Data)

Table B-1 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Infants Aged 0 to 5 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***181***	***477***	***57.5***	***107***	***315***	***532***
Beverages and Beverage Bases							
Energy drinks	0	na	na	0	0	na	na
Fitness water and third quenchers, sports and isotonic drinks	0	na	na	0	0	na	na
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	<0.1	<1*	na	0.2	1	<1*	1*
Hot cereals for adults and children	0.1	<1*	na	0.9	1	25*	25*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0	na	na	0	0	na	na
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	0.3	<1*	na	0.9	1	54*	54*
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	0	na	na	0	0	na	na
Fruit pie filling	0	na	na	0	0	na	na
"Fruit prep"	0	na	na	0	0	na	na
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	0	na	na	0	0	na	na
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	0	na	na	0	0	na	na
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	<0.1	<1*	na	0.2	1	12*	10*
Milk Products							
Flavored milks	0	na	na	0	0	na	na
Milk-based meal replacement beverages or diet beverages	0	na	na	0	0	na	na
Yogurt	0	na	na	0	0	na	na
Processed Fruits and Fruit Juices						na	
Fruit drinks, including vitamin and mineral-fortified products	0	na	na	0	0	na	na
Fruit juices	0.3	<1*	na	2.1	5	22*	37*
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0	na	na	0	0	na	na
Other							

Table B-1 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Infants Aged 0 to 5 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant formula	92.3	167	441	52.4	102	319	482
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0.6	1*	na	2.4	4	45*	76*
Yogurt and juice beverages identified as "baby" drinks	3.5	6*	na	4.5	8	141*	315*
"Junior type" desserts	0.9	2*	na	6.5	6	26*	40*
Baby crackers, pretzels, cookies, and snack items	2.0	4*	na	2.6	6	138*	263*

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-2 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Older Infants Aged 6 to 11 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***244***	***441***	***94.1***	***160***	***259***	***447***
Beverages and Beverage Bases							
Energy drinks	0	na	na	0	0	na	na
Fitness water and third quenchers, sports and isotonic drinks	0.1	<1*	na	2.7	6	11*	11*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	1.4	3*	14*	15.9	22	21*	47*
Hot cereals for adults and children	1.5	4*	8*	11.3	13	33*	54*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.1	<1*	na	1.6	2	22*	22*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	0.2	<1*	na	4.3	8	11*	30*
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	0.6	2*	na	2.9	4	53*	73*
Fruit pie filling	0.3	<1*	na	1.7	1	40*	40*
"Fruit prep"	0	na	na	0	0	na	na
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	0.6	1*	na	1.7	1	87*	87*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	0	na	na	0	0	na	na
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	3.1	7	30*	15.9	33	47	85*
Milk Products							
Flavored milks	0.1	<1*	na	2.0	4	14*	23*
Milk-based meal replacement beverages or diet beverages	0	na	na	0	0	na	na
Yogurt	1.9	5*	2*	10.6	18	43*	81*
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	0.1	<1*	na	2.1	5	9*	11*
Fruit juices	0.8	2*	6*	14	29	13*	19*
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0	na	na	0	0	na	na

Table B-2 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Older Infants Aged 6 to 11 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Other							
Infant formula	47.1	115	284	63	107	183	307
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	3.0	7*	na	6.5	7	113*	163*
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	1.8	4*	na	5.0	9	87*	116*
Yogurt and juice beverages identified as "baby" drinks	18.7	46	141*	40.5	59	113	240*
"Junior type" desserts	10.9	27	76*	36.3	55	73	152*
Baby crackers, pretzels, cookies, and snack items	7.7	19	64	46.5	82	41	91

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-3 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Toddlers Aged 12 to 35 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***148***	***243***	***100***	***346***	***148***	***243***
Beverages and Beverage Bases							
Energy drinks	0	na	na	0	0	na	na
Fitness water and third quenchers, sports and isotonic drinks	0.8	1*	na	7.0	20	17*	31*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	18.2	27	69	60.7	201	44	88
Hot cereals for adults and children	5.3	8	33*	17.9	66	44	75*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	1.5	2*	na	7.6	22	30*	81*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	4.7	7	28*	16.6	68	42	92*
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	2.0	3*	na	5.6	24	52*	83*
Fruit pie filling	<0.1	<1*	na	0.5	1	15*	15*
"Fruit prep"	0.5	1*	na	5.7	14	14*	32*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	1.4	2*	na	7.8	25	27*	49*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.5	7	22*	19.4	50	34	63*
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	26.7	40	83	89.0	303	44	85
Milk Products							
Flavored milks	1.4	2	7*	15.9	58	13	23*
Milk-based meal replacement beverages or diet beverages	0.9	1*	na	4.7	7	30*	52*
Yogurt	7.1	11	32	29.5	95	35	78
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	3.8	6	16	30.4	128	19	34
Fruit juices	6.8	10	26	63.7	211	16	34
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.2	<1*	na	3.2	8	8*	9*
Other							

Table B-3 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Toddlers Aged 12 to 35 Months Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant formula	1.9	3*	na	4.0	13	71*	111*
Follow-on formula	<0.1	<1*	na	<0.1	1	48*	48*
Meal replacement products	1.3	2*	na	3.0	6	64*	203*
Growing-up (toddler) milks	0.6	1*	na	1.1	3	85*	102*
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	1.0	1*	na	1.9	5	77*	122*
Yogurt and juice beverages identified as "baby" drinks	3.9	6*	na	6.1	20	96*	195*
"Junior type" desserts	1.4	2*	na	4.2	12	50*	104*
Baby crackers, pretzels, cookies, and snack items	4.3	6	2*	11.4	30	56	112*

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-4 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Children Aged 3 to 11 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***75***	***147***	***99.7***	***1,268***	***76***	***147***
Beverages and Beverage Bases							
Energy drinks	<0.1	<1*	na	0.1	1	4*	4*
Fitness water and third quenchers, sports and isotonic drinks	1.2	1	3	12.4	128	8	16
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	27.7	21	59	59.0	771	36	73
Hot cereals for adults and children	2.9	2	na	8.4	117	27	59
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.3	<1	na	2.6	33	8	15*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	19.9	15	48	35.3	386	42	90
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	4.2	3	na	5.1	67	63	127*
Fruit pie filling	0.2	<1*	na	1.0	15	12*	17*
"Fruit prep"	0.2	<1	na	3.4	45	5	12*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	1.4	1	4	12.1	128	9	14
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.9	4	14	16.9	221	22	49
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	13.5	10	23	80.6	1,034	13	25
Milk Products							
Flavored milks	3.8	3	10	35.5	472	8	16
Milk-based meal replacement beverages or diet beverages	0.1	<1*	na	1.4	10	6*	8*
Yogurt	6.2	5	18	23.6	258	20	46
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	5.8	4	13	50.4	660	9	17
Fruit juices	6.8	5	14	56.8	753	9	18
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.5	<1	na	4.9	54	7	14*
Other							

Table B-4 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Children Aged 3 to 11 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant formula	<0.1	<1*	na	<0.1	1	22*	22*
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0.1	<1*	na	0.4	11	21*	60*
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0.1	<1*	na	0.3	3	36*	44*
"Junior type" desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	0.1	<1*	na	0.2	2	50*	69*

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-5 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***24***	***52***	***94.7***	***536***	***26***	***52***
Beverages and Beverage Bases							
Energy drinks	0.3	<1*	na	1.9	7	4*	7*
Fitness water and third quenchers, sports and isotonic drinks	1.4	<1	na	9.0	53	4	6*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	32.4	8*	24	43.3	228	18*	30*
Hot cereals for adults and children	2.4	1	na	5.0	38	12	21*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.3	<1*	na	2.1	22	3*	6*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	21.1	5	19	24.3	122	21	40
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	4.0	1*	na	4.1	20	24*	32*
Fruit pie filling	0.3	<1*	na	0.7	10	12*	20*
"Fruit prep"	0.5	<1*	na	3.0	23	4*	10*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	3.7	1	4*	17.2	68	5	9*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.3	1	na	9.7	42	11	21*
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	10.8	3	7	59.4	315	4	8
Milk Products							
Flavored milks	2.6	1	3	18.9	106	3	6
Milk-based meal replacement beverages or diet beverages	0.1	<1*	na	0.5	6	4*	6*
Yogurt	4.7	1	4*	12.8	52	9	18*
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	7.6	2	5	37.0	231	5	13
Fruit juices	3.4	1	3	25.3	188	3	6
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.2	<1*	na	1.7	5	2*	3*

Table B-5 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Other							
Infant formula	0	na	na	0	0	na	na
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior type" desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	<0.1	<1*	na	<0.1	1	15*	15*

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-6 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***29***	***67***	***92.5***	***524***	***31***	***67***
Beverages and Beverage Bases							
Energy drinks	0.4	<1*	na	4.0	8	3*	4*
Fitness water and third quenchers, sports and isotonic drinks	5.2	1	3	20.1	93	7	14
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	32.2	9	27	45.9	252	20	42
Hot cereals for adults and children	2.0	1*	na	3.9	28	15*	36*
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.1	<1*	na	0.9	11	3*	7*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	18.4	5	22	19.1	107	28	48
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	2.3	1*	na	2.5	12	26*	56*
Fruit pie filling	0.3	<1*	na	2.3	6	4*	9*
"Fruit prep"	0.6	<1*	na	2.0	14	9*	20*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.1	1	2*	12.4	52	5	9*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.1	1	na	6.9	50	17	32*
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	14.8	4	11	65.8	359	6	14
Milk Products							
Flavored milks	3.3	1	4	24.1	140	4	7
Milk-based meal replacement beverages or diet beverages	0.7	<1*	na	1.8	9	11*	15*
Yogurt	1.6	<1*	na	4.5	27	10*	20*
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	5.6	2	5	30.4	208	5	11
Fruit juices	5.8	2	5	40.9	223	4	9
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.3	<1*	na	1.4	4	6*	7*

Table B-6 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Other							
Infant formula	0	na	na	0	0	na	na
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior type" desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-7 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Women of Childbearing Age, 16 to 45 Years, Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***18***	***42***	***89.9***	***1,209***	***20***	***43***
Beverages and Beverage Bases							
Energy drinks	0.5	<1	na	2.6	31	4	7*
Fitness water and third quenchers, sports and isotonic drinks	1.2	<1	na	5.8	70	4	7*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	26.1	5	16	31.1	407	15	30
Hot cereals for adults and children	5.0	1	na	9.0	140	10	19
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.8	<1	na	6.2	86	2	5
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	23.2	4	13	21.9	258	19	40
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	2.9	1	na	3.5	53	15	30*
Fruit pie filling	0.7	<1	na	2.0	30	6	12*
"Fruit prep"	1.0	<1	na	4.1	61	4	16*
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	3.9	1	3	14.2	153	5	9
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	3.3	1	na	7.8	91	8	12
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	8.9	2	5	46.1	637	3	7
Milk Products							
Flavored milks	2.9	1	2	12.2	172	4	9
Milk-based meal replacement beverages or diet beverages	0.6	<1*	na	2.4	27	5*	8*
Yogurt	7.0	1	5	15.1	177	8	18
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	6.8	1	4	27.4	392	4	9
Fruit juices	5.1	1	3	27.8	407	3	6
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.2	<1*	na	1.1	7	4*	5*

Table B-7 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Women of Childbearing Age, 16 to 45 Years, Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Other							
Infant formula	0	na	na	0	0	na	na
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior type" desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	<0.1	<1*	na	<0.1	1	15*	15*

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-8 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Female Adults Aged 20 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***19***	***42***	***91.9***	***2,156***	***20***	***43***
Beverages and Beverage Bases							
Energy drinks	0.2	<1	na	1.4	32	3	6*
Fitness water and third quenchers, sports and isotonic drinks	0.9	<1	na	3.8	78	4	7*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	22.2	4	14	31.0	707	13	25
Hot cereals for adults and children	7.2	1	5	13.4	389	10	19
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	1.2	<1	na	7.5	175	3	7
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	22.9	4	14	24.9	544	17	38
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	5.0	1	na	5.4	132	17	32
Fruit pie filling	2.1	<1	na	5.1	99	8	17
"Fruit prep"	1.3	<1	na	6.3	149	4	9
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.8	1	2	10.7	209	5	10
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.5	1	1	10.7	242	8	14
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	8.3	2	5	48.8	1,172	3	7
Milk Products							
Flavored milks	1.9	<1	na	9.3	243	4	8
Milk-based meal replacement beverages or diet beverages	1.1	<1	na	4.2	77	5	11*
Yogurt	8.5	2	7	19.1	378	8	15
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	5.0	1	3	22.3	556	4	8
Fruit juices	4.5	1	3	28.4	724	3	6
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.1	<1*	na	0.6	12	4*	5*

Table B-8 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Female Adults Aged 20 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Other							
Infant formula	0	na	na	0	0	na	na
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior type" desserts	<0.1	<1*	na	<0.1	1	51*	51*
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-9 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Male Adults Aged 20 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***19***	***46***	***86.7***	***1,833***	***22***	***48***
Beverages and Beverage Bases							
Energy drinks	0.7	<1	na	4.3	90	3	5
Fitness water and third quenchers, sports and isotonic drinks	2.0	<1	na	8.0	161	5	9
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	25.2	5	16	28.6	569	17	30
Hot cereals for adults and children	6.8	1	3	10.5	291	12	28
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.6	<1	0	4.3	95	3	6
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	23.3	4	17	24.1	443	18	33
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	5.0	1	na	4.8	97	20	38
Fruit pie filling	1.4	<1	na	4.4	85	6	10
"Fruit prep"	1.3	<1	na	7.1	133	3	7
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.5	<1	2	12.4	186	4	7
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	5.6	1	4	12.3	253	9	15
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	9.8	2	5	48.6	1,015	4	8
Milk Products							
Flavored milks	1.6	<1	na	8.7	176	3	6
Milk-based meal replacement beverages or diet beverages	1.0	<1	na	3.2	64	6	15*
Yogurt	4.6	1	3	11.1	201	8	15
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	4.1	1	3	19.1	448	4	8
Fruit juices	4.3	1	3	25.7	611	3	7
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	<0.1	<1*	na	0.6	9	1*	2*

Table B-9 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by Male Adults Aged 20 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Other							
Infant formula	0	na	na	0	0	na	na
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior type" desserts	0	na	na	0	0	na	na
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-10 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by the Elderly Aged 65 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***24***	***53***	***92.6***	***928***	***26***	***54***
Beverages and Beverage Bases							
Energy drinks	<0.1	<1*	na	0.1	3	3*	3*
Fitness water and third quenchers, sports and isotonic drinks	0.3	<1*	na	1.7	19	4*	6*
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	22.4	5	18	40.3	356	14	23
Hot cereals for adults and children	8.3	2	8	17.2	220	12	25
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.7	<1	na	5.9	62	3	7*
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	28.9	7	22	35.0	304	20	38
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	6.0	1	na	8.2	78	18	33*
Fruit pie filling	2.9	1	na	7.6	66	9	17*
"Fruit prep"	1.7	<1	1	11.4	87	4	10
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	1.0	<1	na	7.1	50	3	5*
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.9	1	4	14.1	138	9	16
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	8.9	2	6	60.6	570	4	8
Milk Products							
Flavored milks	0.9	<1	na	6.5	73	4	7*
Milk-based meal replacement beverages or diet beverages	1.1	<1	na	5.0	44	5	14*
Yogurt	5.0	1	6	16.1	135	8	13
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	2.7	1	3	19.5	196	3	7
Fruit juices	4.0	1	3	33.4	355	3	6
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.1	<1*	na	0.7	7	4*	5*

Table B-10 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by the Elderly Aged 65 Years and Over Within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Other							
Infant formula	0	na	na	0	0	na	na
Follow-on formula	0	na	na	0	0	na	na
Meal replacement products	0	na	na	0	0	na	na
Growing-up (toddler) milks	0	na	na	0	0	na	na
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0	na	na	0	0	na	na
Yogurt and juice beverages identified as "baby" drinks	0	na	na	0	0	na	na
"Junior type" desserts	<0.1	<1*	na	0.1	1	51*	51*
Baby crackers, pretzels, cookies, and snack items	0	na	na	0	0	na	na

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Table B-11 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by the Total U.S. Population (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***32***	***76***	***91.1***	***6,930***	***36***	***80***
Beverages and Beverage Bases							
Energy drinks	0.2	<1	na	2.4	138	3	6
Fitness water and third quenchers, sports and isotonic drinks	1.3	<1	na	7.5	539	6	12
Breakfast Cereals							
Ready-to-eat breakfast cereals for adults and children	22.7	7	23	35.3	2,751	21	45
Hot cereals for adults and children	4.7	2	3	10.9	943	14	30
Dairy Product Analogs							
Milk substitutes such as soy milk and imitation milks	0.7	<1	na	5.1	360	4	8
Frozen Dairy Desserts and Mixes							
Frozen desserts including ice creams and frozen yogurts, frozen novelties	17.5	6	20	24.9	1,679	23	47
Gelatins, Puddings, and Fillings							
Dairy-based puddings, custards, and mousses	3.8	1	na	4.9	356	25	57
Fruit pie filling	0.8	<1	na	3.8	217	7	15
"Fruit prep"	0.7	<1	na	5.7	378	4	10
Grain Products and Pastas							
Snack, breakfast, and meal replacement bars	2.0	1	2	11.7	669	5	11
Jams and Jellies, Commercial							
Jellies and jams, fruit preserves, fruit butters	4.4	1	3	11.8	858	12	26
Milk, Whole and Skim							
All acidophilus or fortified milks, non-fat and low-fat fluid milks, including fluid milk and reconstituted milk powder	12.1	4	9	54.3	4,232	7	15
Milk Products							
Flavored milks	2.2	1	2	13.4	1,199	5	10
Milk-based meal replacement beverages or diet beverages	0.6	<1	na	3.2	173	7	15
Yogurt	5.7	2	6	15.7	1,029	12	23
Processed Fruits and Fruit Juices							
Fruit drinks, including vitamin and mineral-fortified products	4.6	1	5	25.5	2,236	6	13
Fruit juices	5.0	2	5	31.9	2,744	5	11
Sweet Sauces, Toppings, and Syrups							
Syrups used to flavor milk beverages	0.2	<1	na	1.3	92	5	9
Other							

Table B-11 Estimated Daily Per Kilogram Body Weight Intake of 2'-FL from Individual Proposed Food-Uses by the Total U.S. Population (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infant formula	6.5	2	na	1.0	223	222	401
Follow-on formula	<0.1	<1*	na	<0.1	1	48*	48*
Meal replacement products	0.2	<1*	na	0.1	17	48*	185*
Growing-up (toddler) milks	0.2	<1*	na	0.1	10	103*	122*
Ready-to-eat, ready-to-serve, hot cereals for babies for babies	0.2	<1*	na	0.1	18	76*	133*
Yogurt and juice beverages identified as "baby" drinks	1.7	1	na	0.5	90	104	204
"Junior type" desserts	0.8	<1	na	0.4	74	62	106*
Baby crackers, pretzels, cookies, and snack items	1.1	<1	na	0.7	121	50	110

2'-FL = 2'-fucosyllactose; bw = body weight; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements.

Appendix C
Representative Food Codes for Proposed Food-Uses of 2'-FL in the U.S. (2013-2014 NHANES Data)

Representative Food Codes for Proposed Food and Beverage-Uses of 2'-FL in the U.S. (U.S. NHANES 2013-2014)

Beverages and Beverage Bases

Energy Drinks
[2'-FL] = 0.08 g/100 g

93301216	Vodka and energy drink
95310200	Full Throttle Energy Drink
95310400	Monster Energy Drink
95310500	Mountain Dew AMP Energy Drink
95310550	No Fear Energy Drink
95310555	No Fear Motherload Energy Drink
95310560	NOS Energy Drink
95310600	Red Bull Energy Drink
95310700	Rockstar Energy Drink
95310750	SoBe Energize Energy Juice Drink
95310800	Vault Energy Drink
95311000	Energy Drink
95312400	Monster Energy Drink, Lo Carb
95312500	Mountain Dew AMP Energy Drink, sugar-free
95312550	No Fear Energy Drink, sugar-free
95312555	NOS Energy Drink, sugar-free
95312560	Ocean Spray Cran-Energy Cranberry Energy Juice Drink
95312600	Red Bull Energy Drink, sugar-free
95312700	Rockstar Energy Drink, sugar-free
95312800	Vault Zero Energy Drink
95312900	XS Energy Drink
95312905	XS Gold Plus Energy Drink
95313200	Energy drink, sugar free

Sports Drinks
[2'-FL] = 0.08 g/100 g

94210100	Propel Water
94220100	Propel Zero Water
94220110	Propel Zero Calcium Water
95320200	Gatorade G sports drink
95320500	Powerade sports drink
95321000	Sports drink, not further specified (NFS)
95322200	Gatorade G2 sports drink, low calorie
95322500	Powerade Zero sports drink, low calorie
95323000	Sports drink, low calorie
95330100	Fluid replacement, electrolyte solution
95330500	Fluid replacement, 5% glucose in water

Not Reconstituted Sports Drinks
(Adjusted for not being reconstituted, 16 g of powder to 240 mL of water)
[2'-FL] = 1.28 g/100 g

92900300	Sports drink, dry concentrate, not reconstituted

Breakfast Cereals

Ready-to-Eat Breakfast Cereals for Adults and Children

[2'-FL] = 2.0 to 8.0 g/100 g

57000000	Cereal, NFS
57000050	Kashi cereal, not specified (NS) as to ready to eat or cooked
57000100	Oat cereal, NFS
57100100	Cereal, ready-to-eat, NFS
57101000	All-Bran
57102000	Alpen
57103000	Alpha-Bits
57103020	Alpha-bits with marshmallows
57103100	Apple Cinnamon Cheerios
57104000	Apple Jacks
57106050	Banana Nut Crunch Cereal (Post)
57106060	Banana Nut Cheerios
57106100	Basic 4
57106250	Berry Berry Kix
57106260	Berry Burst Cheerios
57106530	Blueberry Morning, Post
57107000	Booberry
57110000	All-Bran Bran Buds, Kellogg's (formerly Bran Buds)
57117000	Cap'n Crunch
57117500	Cap'n Crunch's Christmas Crunch
57119000	Cap'n Crunch's Crunch Berries
57120000	Cap'n Crunch's Peanut Butter Crunch
57123000	Cheerios
57124000	Chex cereal, NFS
57124030	Chex Chocolate
57124050	Chex Cinnamon
57124100	Chocolate Cheerios
57124200	Chocolate flavored frosted puffed corn cereal
57124300	Chocolate Lucky Charms
57124900	Cinnabon cereal
57125000	Cinnamon Toast Crunch
57125010	Cinnamon Toast Crunch Reduced Sugar
57125900	Honey Nut Clusters (formerly called Clusters)
57126000	Cocoa Krispies
57127000	Cocoa Pebbles
57128000	Cocoa Puffs
57128005	Cocoa Puffs, reduced sugar
57130000	Cookie-Crisp
57131000	Crunchy Corn Bran, Quaker
57132000	Corn Chex
57134000	Corn flakes, NFS
57135000	Corn flakes, Kellogg's
57137000	Corn Puffs
57139000	Count Chocula
57143000	Cracklin' Oat Bran
57143500	Cranberry Almond Crunch, Post
57144000	Crisp Crunch
57148000	Crispix
57148500	Crispy Brown Rice Cereal
57151000	Crispy Rice
57201900	Dora the Explorer Cereal

57206000	Familia
57206700	Fiber One
57206705	Fiber One Caramel Delight
57206710	Fiber One Honey Clusters
57206715	Fiber One Raisin Bran Clusters
57206800	Fiber 7 Flakes, Health Valley
57207000	Bran Flakes, NFS (formerly 40% Bran Flakes, NFS)
57208000	All-Bran Complete Wheat Flakes, Kellogg's
57209000	Natural Bran Flakes, Post (formerly called 40% Bran Flakes, Post)
57211000	Frankenberry
57213000	Froot Loops
57213010	Froot Loops Marshmallow
57213850	Frosted Cheerios
57214000	Frosted Mini-Wheats
57214100	Frosted Wheat Bites
57215000	Frosty O's
57216000	Frosted rice, NFS
57218000	Frosted Rice Krispies, Kellogg's
57219000	Fruit & Fibre (fiber), NFS
57221000	Fruit & Fibre (fiber) with dates, raisins, and walnuts
57221700	Fruit Rings, NFS
57221800	Fruit Whirls
57221810	Fruity Cheerios
57223000	Fruity Pebbles
57224000	Golden Grahams
57227000	Granola, NFS
57228000	Granola, homemade
57229000	Granola, lowfat, Kellogg's
57229500	Granola with Raisins, lowfat, Kellogg's
57230000	Grape-Nuts
57231000	Grape-Nuts Flakes
57231100	Grape-Nuts Trail Mix Crunch
57231200	Great Grains, Raisin, Date, and Pecan Whole Grain Cereal, Post
57231250	Great Grains Double Pecan Whole Grain Cereal, Post
57237100	Honey Bunches of Oats Honey Roasted Cereal
57237200	Honey Bunches of Oats with Vanilla Clusters, Post
57237300	Honey Bunches of Oats with Almonds, Post
57237310	Honey Bunches of Oats with Pecan Bunches
57237900	Honey Bunches of Oats Just Bunches
57238000	Honeycomb, plain
57239000	Honeycomb, strawberry
57239100	Honey Crunch Corn Flakes, Kellogg's
57240100	Honey Nut Chex
57241000	Honey Nut Cheerios
57241200	Honey Nut Shredded Wheat, Post
57243000	Honey Smacks, Kellogg's (formerly Smacks; Honey Smacks)
57301500	Kashi, Puffed
57301505	Kashi Autumn Wheat
57301510	Kashi GOLEAN
57301511	Kashi GOLEAN Crunch
57301512	Kashi GOLEAN Crunch Honey Almond Flax
57301520	Kashi Good Friends
57301530	Kashi Heart to Heart Honey Toasted Oat
57301535	Kashi Heart to Heart Oat Flakes and Blueberry Clusters

57301540	Kashi Honey Sunshine
57302100	King Vitaman
57303100	Kix
57303105	Honey Kix
57304100	Life (plain and cinnamon)
57305100	Lucky Charms
57305150	Frosted oat cereal with marshmallows
57305160	Malt-O-Meal Blueberry Muffin Tops
57305165	Malt-O-Meal Cinnamon Toasters
57305170	Malt-O-Meal Coco-Roos
57305174	Malt-O-Meal Colossal Crunch
57305175	Malt-O-Meal Cocoa Dyno-Bites
57305180	Malt-O-Meal Corn Bursts
57305200	Malt-O-Meal Crispy Rice
57305210	Malt-O-Meal Frosted Flakes
57305215	Malt-O-Meal Frosted Mini Spooners
57305300	Malt-O-Meal Fruity Dyno-Bites
57305400	Malt-O-Meal Honey Graham Squares
57305500	Malt-O-Meal Honey and Nut Toasty O's
57305600	Malt-O-Meal Marshmallow Mateys
57306100	Malt-O-Meal Puffed Rice
57306120	Malt-O-Meal Puffed Wheat
57306130	Malt-O-Meal Raisin Bran
57306500	Malt-O-Meal Golden Puffs (formerly Sugar Puffs)
57306700	Malt-O-Meal Toasted Oat Cereal
57306800	Malt-O-meal Tootie Fruities
57307010	Maple Pecan Crunch Cereal, Post
57307500	Millet, puffed
57308150	Mueslix cereal, NFS
57308190	Muesli, dried fruit and nuts (formerly Muesli with raisins, dates, and almonds)
57308400	MultiGrain Cheerios
57309100	Nature Valley Granola, with fruit and nuts
57316200	Nutty Nuggets, Ralston Purina
57316300	Oat Bran Flakes, Health Valley
57316380	Oat Cluster Cheerios Crunch
57316450	Oatmeal Crisp with Almonds
57316500	Oatmeal Crisp, Raisin (formerly Oatmeal Raisin Crisp)
57316710	Oh's, Honey Graham
57319000	100% Natural Cereal, plain, Quaker
57320500	100 % Natural Cereal, with oats, honey and raisins, Quaker
57321500	100 % Natural Wholegrain Cereal with raisins, lowfat, Quaker
57321900	Organic Flax Plus, Nature's Path
57321905	Organic Flax Plus, Pumpkin Granola, Nature's Path
57323000	Sweet Crunch, Quaker (formerly called Popeye)
57325000	Product 19
57326000	Puffins Cereal
57327450	Quaker Oat Bran Cereal
57327500	Quaker Oatmeal Squares (formerly Quaker Oat Squares)
57328000	Quisp
57329000	Raisin bran, NFS
57330000	Raisin Bran, Kellogg's
57330010	Raisin Bran Crunch, Kellogg's
57331000	Raisin Bran, Post
57332050	Raisin Bran, Total

57332100	Raisin Nut Bran
57335550	Reese's Peanut Butter Puffs cereal
57336000	Rice Chex
57337000	Rice Flakes, NFS
57339000	Rice Krispies, Kellogg's
57339500	Rice Krispies Treats Cereal, Kellogg's
57340000	Rice, puffed
57341000	Shredded Wheat'N Bran
57341200	Smart Start Strong Heart Antioxidants Cereal, Kellogg's
57344000	Special K
57344001	Special K Blueberry
57344005	Special K Chocolatey Delight
57344007	Special K Low Fat Granola
57344010	Special K Red Berries
57344015	Special K Fruit & Yogurt
57344020	Special K Vanilla Almond
57344025	Special K Cinnamon Pecan, Kellogg's
57346500	Oatmeal Honey Nut Heaven, Quaker (formerly Toasted Oatmeal, Honey Nut)
57347000	Corn Pops
57348000	Frosted corn flakes, NFS
57349000	Frosted Flakes, Kellogg's
57349020	Reduced Sugar Frosted Flakes Cereal, Kellogg's
57355000	Golden Crisp (Formerly called Super Golden Crisp)
57401100	Toasted oat cereal
57406100	Total
57407100	Trix
57407110	Trix, reduced sugar
57408100	Uncle Sam Cereal (formerly Uncle Sam's Hi Fiber Cereal)
57409100	Waffle Crisp, Post
57410000	Weetabix Whole Wheat Cereal
57411000	Wheat Chex
57412000	Wheat germ, plain
57413000	Wheat germ, with sugar and honey
57416000	Wheat, puffed, plain
57416010	Wheat, puffed, presweetened with sugar
57417000	Shredded Wheat, 100%
57418000	Wheaties
57419000	Yogurt Burst Cheerios

Hot Cereals for Adults and Children

[2'-FL] = 0.48 g/100 g

56200300	Cereal, cooked, NFS
56200350	Cereal, cooked, instant, NS as to grain
56200390	Barley, cooked, NS as to fat added in cooking
56200400	Barley, cooked, fat not added in cooking
56200490	Buckwheat groats, cooked, NS as to fat added in cooking
56200500	Buckwheat groats, cooked, fat not added in cooking
56200510	Buckwheat groats, cooked, fat added in cooking
56200990	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, NS as to fat added in cooking
56201000	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, fat not added in cooking
56201010	Grits, cooked, corn or hominy, regular, fat not added in cooking
56201020	Grits, cooked, corn or hominy, regular, fat added in cooking
56201030	Grits, cooked, corn or hominy, regular, NS as to fat added in cooking
56201040	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, fat added in cooking

56201060	Grits, cooked, corn or hominy, with cheese, NS as to regular, quick, or instant, NS as to fat added in cooking
56201061	Grits, cooked, corn or hominy, with cheese, NS as to regular, quick, or instant, fat not added in cooking
56201062	Grits, cooked, corn or hominy, with cheese, NS as to regular, quick, or instant, fat added in cooking
56201070	Grits, cooked, corn or hominy, with cheese, regular, NS as to fat added in cooking
56201071	Grits, cooked, corn or hominy, with cheese, regular, fat not added in cooking
56201072	Grits, cooked, corn or hominy, with cheese, regular, fat added in cooking
56201080	Grits, cooked, corn or hominy, with cheese, quick, NS as to fat added in cooking
56201081	Grits, cooked, corn or hominy, with cheese, quick, fat not added in cooking
56201082	Grits, cooked, corn or hominy, with cheese, quick, fat added in cooking
56201090	Grits, cooked, corn or hominy, with cheese, instant, NS as to fat added in cooking
56201091	Grits, cooked, corn or hominy, with cheese, instant, fat not added in cooking
56201092	Grits, cooked, corn or hominy, with cheese, instant, fat added in cooking
56201110	Grits, cooked, corn or hominy, quick, fat not added in cooking
56201120	Grits, cooked, corn or hominy, quick, fat added in cooking
56201130	Grits, cooked, corn or hominy, quick, NS as to fat added in cooking
56201210	Grits, cooked, corn or hominy, instant, fat not added in cooking
56201220	Grits, cooked, corn or hominy, instant, fat added in cooking
56201230	Grits, cooked, corn or hominy, instant, NS as to fat added in cooking
56201240	Grits, cooked, flavored, corn or hominy, instant, fat not added in cooking
56201250	Grits, cooked, flavored, corn or hominy, instant, fat added in cooking
56201260	Grits, cooked, flavored, corn or hominy, instant, NS as to fat added in cooking
56201296	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, made with milk, fat added in cooking
56201298	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, made with milk, fat not added in cooking
56201300	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, made with milk, NS as to fat added in cooking
56201320	Grits, cooked, corn or hominy, regular, made with milk, fat added in cooking
56201322	Grits, cooked, corn or hominy, regular, made with milk, fat not added in cooking
56201324	Grits, cooked, corn or hominy, regular, made with milk, NS as to fat added in cooking
56201330	Grits, cooked, corn or hominy, quick, made with milk, fat added in cooking
56201332	Grits, cooked, corn or hominy, quick, made with milk, fat not added in cooking
56201334	Grits, cooked, corn or hominy, quick, made with milk, NS as to fat added in cooking
56201340	Grits, cooked, corn or hominy, instant, made with milk, fat added in cooking
56201342	Grits, cooked, corn or hominy, instant, made with milk, fat not added in cooking
56201344	Grits, cooked, corn or hominy, instant, made with milk, NS as to fat added in cooking
56201510	Cornmeal mush, made with water
56201520	Cornmeal mush, fried
56201530	Cornmeal mush, made with milk
56201540	Cornmeal, made with milk and sugar, Puerto Rican Style (Harina de maiz)
56201600	Cornmeal, lime-treated, cooked (Masa harina)
56201700	Cornstarch with milk, eaten as a cereal (2 tbsp cornstarch in 2-1/2 cups milk)
56201990	Millet, cooked, NS as to fat added in cooking
56202000	Millet, cooked, fat not added in cooking
56202100	Millet, cooked, fat added in cooking
56202900	Oatmeal, cooked, from fast food
56202960	Oatmeal, cooked, NS as to regular, quick or instant; NS as to fat added in cooking
56202970	Oatmeal, cooked, quick (1 or 3 minutes), NS as to fat added in cooking
56202980	Oatmeal, cooked, regular, NS as to fat added in cooking
56203000	Oatmeal, cooked, NS as to regular, quick or instant, fat not added in cooking
56203010	Oatmeal, cooked, regular, fat not added in cooking
56203020	Oatmeal, cooked, quick (1 or 3 minutes), fat not added in cooking

56203030	Oatmeal, cooked, instant, fat not added in cooking
56203040	Oatmeal, cooked, NS as to regular, quick, or instant, fat added in cooking
56203050	Oatmeal, cooked, regular, fat added in cooking
56203060	Oatmeal, cooked, quick (1 or 3 minutes), fat added in cooking
56203070	Oatmeal, cooked, instant, fat added in cooking
56203080	Oatmeal, cooked, instant, NS as to fat added in cooking
56203110	Oatmeal with maple flavor, cooked
56203200	Oatmeal with fruit, cooked
56203210	Oatmeal, NS as to regular, quick, or instant, made with milk, fat not added in cooking
56203211	Oatmeal, cooked, regular, made with milk, fat not added in cooking
56203212	Oatmeal, cooked, quick (1 or 3 minutes), made with milk, fat not added in cooking
56203213	Oatmeal, cooked, instant, made with milk, fat not added in cooking
56203220	Oatmeal, NS as to regular, quick, or instant, made with milk, fat added in cooking
56203221	Oatmeal, cooked, regular, made with milk, fat added in cooking
56203222	Oatmeal, cooked, quick (1 or 3 minutes), made with milk, fat added in cooking
56203223	Oatmeal, cooked, instant, made with milk, fat added in cooking
56203230	Oatmeal, NS as to regular, quick, or instant, made with milk, NS as to fat added in cooking
56203231	Oatmeal, cooked, regular, made with milk, NS as to fat added in cooking
56203232	Oatmeal, cooked, quick (1 or 3 minutes), made with milk, NS as to fat added in cooking
56203233	Oatmeal, cooked, instant, made with milk, NS as to fat added in cooking
56203540	Oatmeal, made with milk and sugar, Puerto Rican style
56203600	Oatmeal, multigrain, cooked, NS as to fat added in cooking
56203610	Oatmeal, multigrain, cooked, fat not added in cooking
56203620	Oatmeal, multigrain, cooked, fat added in cooking
56206970	Wheat, cream of, cooked, quick, NS as to fat added in cooking
56206980	Wheat, cream of, cooked, regular, NS as to fat added in cooking
56206990	Wheat, cream of, cooked, NS as to regular, quick, or instant, NS as to fat added in cooking
56207000	Wheat, cream of, cooked, NS as to regular, quick, or instant, fat not added in cooking
56207010	Wheat, cream of, cooked, regular, fat not added in cooking
56207020	Wheat, cream of, cooked, quick, fat not added in cooking
56207030	Wheat, cream of, cooked, instant, fat not added in cooking
56207050	Wheat, cream of, cooked, made with milk and sugar, Puerto Rican style
56207060	Wheat, cream of, cooked, instant, fat added in cooking
56207070	Wheat, cream of, cooked, instant, NS as to fat added in cooking
56207080	Wheat, cream of, cooked, NS as to regular, quick, or instant, fat added in cooking
56207082	Wheat, cream of, cooked, NS as to regular, quick, or instant, made with milk, fat added in cooking
56207083	Wheat, cream of, cooked, NS as to regular, quick, or instant, made with milk, fat not added in cooking
56207084	Wheat, cream of, cooked, NS as to regular, quick, or instant, made with milk, NS as to fat added in cooking
56207086	Wheat, cream of, cooked, regular, made with milk, fat added in cooking
56207087	Wheat, cream of, cooked, regular, made with milk, fat not added in cooking
56207088	Wheat, cream of, cooked, regular, made with milk, NS as to fat added in cooking
56207091	Wheat, cream of, cooked, quick, made with milk, fat added in cooking
56207092	Wheat, cream of, cooked, quick, made with milk, fat not added in cooking
56207093	Wheat, cream of, cooked, quick, made with milk, NS as to fat added in cooking
56207094	Wheat, cream of, cooked, instant, made with milk, fat added in cooking
56207095	Wheat, cream of, cooked, instant, made with milk, fat not added in cooking
56207096	Wheat, cream of, cooked, instant, made with milk, NS as to fat added in cooking
56207100	Wheat, rolled, cooked, fat not added in cooking
56207110	Bulgur, cooked or canned, fat not added in cooking
56207120	Bulgur, cooked or canned, fat added in cooking
56207130	Bulgur, cooked or canned, NS as to fat added in cooking
56207140	Wheat, rolled, cooked, NS as to fat added in cooking
56207190	Whole wheat cereal, cooked, NS as to fat added in cooking

56207200 Whole wheat cereal, cooked, fat not added in cooking
56207210 Whole wheat cereal, cooked, fat added in cooking
56207212 Whole wheat cereal, cooked, made with milk
56207220 Wheat, cream of, cooked, regular, fat added in cooking
56207230 Wheat, cream of, cooked, quick, fat added in cooking
56207300 Whole wheat cereal, wheat and barley, cooked, fat not added in cooking
56207330 Whole wheat cereal, wheat and barley, cooked, fat added in cooking
56207340 Whole wheat cereal, wheat and barley, cooked, NS as to fat added in cooking
56207342 Whole wheat cereal, wheat and barley, cooked, made with milk
56207350 Wheat cereal, chocolate flavored, cooked, made with milk
56207360 Wheat cereal, chocolate flavored, cooked, fat not added in cooking
56207365 Wheat cereal, chocolate flavored, cooked, fat added in cooking
56207370 Wheat cereal, chocolate flavored, cooked, NS as to fat added in cooking
56208500 Oat bran cereal, cooked, fat not added in cooking
56208510 Oat bran cereal, cooked, fat added in cooking
56208520 Oat bran cereal, cooked, NS as to fat added in cooking
56208530 Oat bran cereal, cooked, made with milk, fat not added in cooking
56208540 Oat bran cereal, cooked, made with milk, fat added in cooking
56208550 Oat bran cereal, cooked, made with milk, NS as to fat added in cooking
56209000 Rye, cream of, cooked
56210000 Nestum cereal

Uncooked Hot Cereals
{Adjusted for not being cooked, approximately 15 g uncooked oats or bran into 150 mL of milk)
[2'-FL] = 4.8 g/100 g
57601100 Wheat bran, unprocessed
57602100 Oats, raw
57602500 Oat bran, uncooked

Dairy Product Analogs

Milk Substitutes
[2'-FL] = 0.12 g/100 g
11320000 Soy milk
11320100 Soy milk, light
11320200 Soy milk, nonfat
11321000 Soy milk, chocolate
11321100 Soy milk, light, chocolate
11321200 Soy milk, nonfat, chocolate
11340000 Imitation milk, non-soy, sweetened
11350000 Almond milk, sweetened
11350010 Almond milk, sweetened, chocolate
11350020 Almond milk, unsweetened
11350030 Almond milk, unsweetened, chocolate
11360000 Rice milk
11370000 Coconut milk

Mixtures Containing Milk Substitutes
(Adjusted for a Milk Substitute content ranging from 42.2 to 95.7%)
[2'-FL] = 0.05 to 0.11 g/100 g
11512030 Hot chocolate / Cocoa, ready to drink, made with non-dairy milk
11512120 Hot chocolate / Cocoa, ready to drink, made with non-dairy milk and whipped cream

11513310	Chocolate milk, made from dry mix with non-dairy milk
11513375	Chocolate milk, made from reduced sugar mix with non-dairy milk
11513385	Nesquik, chocolate milk, made from dry mix with non-dairy milk
11513395	Nesquik, chocolate milk, made from no sugar added dry mix with non-dairy milk
11514150	Hot chocolate / Cocoa, made with dry mix and non-dairy milk
11514360	Hot chocolate / Cocoa, made with no sugar added dry mix and non-dairy milk
11519215	Strawberry milk, non-dairy
92101903	Coffee, Latte, with non-dairy milk
92101906	Coffee, Latte, with non-dairy milk, flavored
92101913	Coffee, Latte, decaffeinated, with non-dairy milk
92101919	Coffee, Latte, decaffeinated, with non-dairy milk, flavored
92101923	Frozen coffee drink, with non-dairy milk
92101928	Frozen coffee drink, with non-dairy milk and whipped cream
92101933	Frozen coffee drink, decaffeinated, with non-dairy milk
92101938	Frozen coffee drink, decaffeinated, with non-dairy milk and whipped cream
92101960	Coffee, Cafe Mocha, with non-dairy milk
92101975	Coffee, Cafe Mocha, decaffeinated, with non-dairy milk
92102020	Frozen mocha coffee drink, with non-dairy milk
92102050	Frozen mocha coffee drink, with non-dairy milk and whipped cream
92102080	Frozen mocha coffee drink, decaffeinated, with non-dairy milk
92102110	Frozen mocha coffee drink, decaffeinated, with non-dairy milk and whipped cream
92102502	Coffee, Iced Latte, with non-dairy milk
92102505	Coffee, Iced Latte, with non-dairy milk, flavored
92102512	Coffee, Iced Latte, decaffeinated, with non-dairy milk
92102515	Coffee, Iced Latte, decaffeinated, with non-dairy milk, flavored
92102602	Coffee, Iced CafÃ© Mocha, with non-dairy milk
92102612	Coffee, Iced CafÃ© Mocha, decaffeinated, with non-dairy milk
92161002	Coffee, Cappuccino, with non-dairy milk
92162002	Coffee, Cappuccino, decaffeinated, with non-dairy milk
11513750	Chocolate milk, made from syrup with non-dairy milk
11513805	Chocolate milk, made from light syrup with non-dairy milk
11513855	Chocolate milk, made from sugar free syrup with non-dairy milk

Frozen Dairy Desserts and Mixes

Frozen Desserts

[2'-FL] = 1.7 g/100 g

11459990	Yogurt, frozen, NS as to flavor, NS as to type of milk
11460000	Yogurt, frozen, flavors other than chocolate, NS as to type of milk
11460100	Yogurt, frozen, chocolate, NS as to type of milk
11460150	Yogurt, frozen, NS as to flavor, lowfat milk
11460160	Yogurt, frozen, chocolate, lowfat milk
11460170	Yogurt, frozen, flavors other than chocolate, lowfat milk
11460190	Yogurt, frozen, NS as to flavor, nonfat milk
11460200	Yogurt, frozen, chocolate, nonfat milk
11460250	Yogurt, frozen, flavors other than chocolate, with sorbet or sorbet-coated
11460300	Yogurt, frozen, flavors other than chocolate, nonfat milk
11460400	Yogurt, frozen, chocolate, nonfat milk, with low-calorie sweetener
11460410	Yogurt, frozen, flavors other than chocolate, nonfat milk, with low-calorie sweetener
11460420	Yogurt, frozen, NS as to flavor, whole milk
11460430	Yogurt, frozen, chocolate, whole milk
11460440	Yogurt, frozen, flavors other than chocolate, whole milk

11461000	Yogurt, frozen, chocolate-coated
11461200	Yogurt, frozen, sandwich
11461250	Yogurt, frozen, cone, chocolate
11461260	Yogurt, frozen, cone, flavors other than chocolate
11461270	Yogurt, frozen, cone, flavors other than chocolate, lowfat milk
11461280	Yogurt, frozen, cone, chocolate, lowfat milk
13110000	Ice cream, NFS
13110100	Ice cream, regular, flavors other than chocolate
13110110	Ice cream, regular, chocolate
13110120	Ice cream, rich, flavors other than chocolate
13110130	Ice cream, rich, chocolate
13110140	Ice cream, rich, NS as to flavor
13110200	Ice cream, soft serve, flavors other than chocolate
13110210	Ice cream, soft serve, chocolate
13110220	Ice cream, soft serve, NS as to flavor
13110310	Ice cream, no sugar added, NS as to flavor
13110320	Ice cream, no sugar added, flavors other than chocolate
13110330	Ice cream, no sugar added, chocolate
13120050	Ice cream bar or stick, not chocolate covered or cake covered
13120100	Ice cream bar or stick, chocolate covered
13120110	Ice cream bar or stick, chocolate or caramel covered, with nuts
13120120	Ice cream bar or stick, rich chocolate ice cream, thick chocolate covering
13120121	Ice cream bar or stick, rich ice cream, thick chocolate covering
13120130	Ice cream bar or stick, rich ice cream, chocolate covered, with nuts
13120140	Ice cream bar or stick, chocolate ice cream, chocolate covered
13120300	Ice cream bar, cake covered
13120310	Ice cream bar, stick or nugget, with crunch coating
13120400	Ice cream bar or stick with fruit
13120500	Ice cream sandwich
13120550	Ice cream cookie sandwich
13120700	Ice cream cone with nuts, flavors other than chocolate
13120710	Ice cream cone, chocolate covered, with nuts, flavors other than chocolate
13120720	Ice cream cone, chocolate covered or dipped, flavors other than chocolate
13120730	Ice cream cone, no topping, flavors other than chocolate
13120740	Ice cream cone, no topping, NS as to flavor
13120750	Ice cream cone with nuts, chocolate ice cream
13120760	Ice cream cone, chocolate covered or dipped, chocolate ice cream
13120770	Ice cream cone, no topping, chocolate ice cream
13120780	Ice cream cone, chocolate covered, with nuts, chocolate ice cream
13120790	Ice cream sundae cone
13120800	Ice cream soda, flavors other than chocolate
13120810	Ice cream soda, chocolate
13121000	Ice cream sundae, NS as to topping, with whipped cream
13121100	Ice cream sundae, fruit topping, with whipped cream
13121200	Ice cream sundae, prepackaged type, flavors other than chocolate
13121300	Ice cream sundae, chocolate or fudge topping, with whipped cream
13121400	Ice cream sundae, not fruit or chocolate topping, with whipped cream
13121500	Ice cream sundae, fudge topping, with cake, with whipped cream
13122100	Ice cream pie, no crust
13122500	Ice cream pie, with cookie crust, fudge topping, and whipped cream
13126000	Ice cream, fried
13127000	Dippin' Dots, flash frozen ice cream snacks, flavors other than chocolate
13127010	Dippin' Dots, flash frozen ice cream snacks, chocolate
13130100	Light ice cream, NS as to flavor (formerly ice milk)

13130300	Light ice cream, flavors other than chocolate (formerly ice milk)
13130310	Light ice cream, chocolate (formerly ice milk)
13130320	Light ice cream, no sugar added, NS as to flavor
13130330	Light ice cream, no sugar added, flavors other than chocolate
13130340	Light ice cream, no sugar added, chocolate
13130590	Light ice cream, soft serve, NS as to flavor (formerly ice milk)
13130600	Light ice cream, soft serve, flavors other than chocolate (formerly ice milk)
13130610	Light ice cream, soft serve, chocolate (formerly ice milk)
13130620	Light ice cream, soft serve cone, flavors other than chocolate (formerly ice milk)
13130630	Light ice cream, soft serve cone, chocolate (formerly ice milk)
13130640	Light ice cream, soft serve cone, NS as to flavor (formerly ice milk)
13130700	Light ice cream, soft serve, blended with candy or cookies
13135000	Ice cream sandwich, made with light ice cream, flavors other than chocolate
13135010	Ice cream sandwich, made with light chocolate ice cream
13136000	Ice cream sandwich, made with light, no sugar added ice cream
13140100	Light ice cream, bar or stick, chocolate-coated (formerly ice milk)
13140110	Light ice cream, bar or stick, chocolate covered, with nuts (formerly ice milk)
13140450	Light ice cream, cone, NFS (formerly ice milk)
13140500	Light ice cream, cone, flavors other than chocolate (formerly ice milk)
13140550	Light ice cream, cone, chocolate (formerly ice milk)
13140570	Light ice cream, no sugar added, cone, NS as to flavor
13140575	Light ice cream, no sugar added, cone, flavors other than chocolate
13140580	Light ice cream, no sugar added, cone, chocolate
13140600	Light ice cream, sundae, soft serve, chocolate or fudge topping, with whipped cream (formerly ice milk)
13140630	Light ice cream, sundae, soft serve, fruit topping, with whipped cream (formerly ice milk)
13140650	Light ice cream, sundae, soft serve, not fruit or chocolate topping, with whipped cream (formerly ice milk)
13140660	Light ice cream, sundae, soft serve, chocolate or fudge topping (without whipped cream) (formerly ice milk)
13140670	Light ice cream, sundae, soft serve, fruit topping (without whipped cream) (formerly ice milk)
13140680	Light ice cream, sundae, soft serve, not fruit or chocolate topping (without whipped cream) (formerly ice milk)
13140700	Light ice cream, creamsicle or dreamsicle (formerly ice milk)
13140710	Light ice cream, creamsicle or dreamsicle, no sugar added
13140900	Light ice cream, fudgesicle (formerly ice milk)
13142000	Milk dessert bar or stick, frozen, with coconut
13150000	Sherbet, all flavors
13160150	Fat free ice cream, no sugar added, chocolate
13160160	Fat free ice cream, no sugar added, flavors other than chocolate
13160400	Fat free ice cream, flavors other than chocolate
13160410	Fat free ice cream, chocolate
13160420	Fat free ice cream, NS as to flavor
13161000	Milk dessert bar, frozen, made from lowfat milk
13161500	Milk dessert sandwich bar, frozen, made from lowfat milk
13161520	Milk dessert sandwich bar, frozen, with low-calorie sweetener, made from lowfat milk
13161600	Milk dessert bar, frozen, made from lowfat milk and low calorie sweetener
13161630	Light ice cream, bar or stick, with low-calorie sweetener, chocolate-coated (formerly ice milk)
13170000	Baked Alaska
91611050	Ice pop filled with ice cream, all flavor varieties

Gelatins, Puddings, and Fillings

Dairy-Based Puddings, Custards, and Mousses

[2'-FL] = 1.7 g/100 g

13200110	Pudding, NFS
13210110	Pudding, bread
13210150	Puerto Rican bread pudding made with evaporated milk
13210160	Diplomat pudding, Puerto Rican style (Budin Diplomatico)
13210180	Pudding, Mexican bread (Capirotada)
13210190	Pudding, Mexican bread (Capirotada), lower fat
13210220	Pudding, chocolate, NS as to from dry mix or ready-to-eat
13210250	Pudding, chocolate, low calorie, containing artificial sweetener, NS as to from dry mix or ready-to-eat
13210260	Rice flour cream, Puerto Rican style (manjar blanco)
13210270	Custard, Puerto Rican style (Maicena, Natilla)
13210280	Pudding, flavors other than chocolate, NS as to from dry mix or ready-to-eat
13210290	Pudding, flavors other than chocolate, low calorie, containing artificial sweetener, NS as to from dry mix or ready-to-eat
13210300	Custard
13210350	Flan
13210410	Pudding, rice
13210450	Pudding, rice flour, with nuts (Indian dessert)
13210520	Pudding, tapioca, made from dry mix, made with milk
13210530	Pudding, tapioca, chocolate, made with milk
13210610	Pudding, coconut
13210710	Pudding, Indian (milk, molasses and cornmeal-based pudding)
13210750	Pudding, pumpkin
13210810	Puerto Rican pumpkin pudding (Flan de calabaza)
13210820	Fresh corn custard, Puerto Rican style (Mazamorra, Mundo Nuevo)
13220110	Pudding, flavors other than chocolate, prepared from dry mix, milk added
13220120	Pudding, chocolate, prepared from dry mix, milk added
13220210	Pudding, flavors other than chocolate, prepared from dry mix, low calorie, containing artificial sweetener, milk added
13220220	Pudding, chocolate, prepared from dry mix, low calorie, containing artificial sweetener, milk added
13220230	Pudding, ready-to-eat, chocolate, reduced fat
13220235	Pudding, ready-to-eat, chocolate, fat free
13220240	Pudding, ready-to-eat, flavors other than chocolate, reduced fat
13220245	Pudding, ready-to-eat, flavors other than chocolate, fat free
13230110	Pudding, ready-to-eat, flavors other than chocolate
13230120	Pudding, ready-to-eat, low calorie, containing artificial sweetener, flavors other than chocolate
13230130	Pudding, ready-to-eat, chocolate
13230140	Pudding, ready-to-eat, low calorie, containing artificial sweetener, chocolate
13230200	Pudding, ready-to-eat, chocolate and non-chocolate flavors combined
13230500	Pudding, ready-to-eat, tapioca
13230510	Pudding, ready-to-eat, tapioca, fat free
13241000	Pudding, with fruit and vanilla wafers
13250000	Mousse, chocolate
13250100	Mousse, not chocolate
13250200	Mousse, chocolate, lowfat, reduced calorie, prepared from dry mix, water added
13252100	Coconut custard, Puerto Rican style (Flan de coco)
13252200	Milk dessert or milk candy, Puerto Rican style (Dulce de leche)
13252500	Barfi or Burfi, Indian dessert, made from milk and/or cream and/or Ricotta cheese
13252600	Tiramisu
91501010	Gelatin dessert
91501015	Gelatin snacks
91501020	Gelatin dessert with fruit

91501030 Gelatin dessert with whipped cream
91501040 Gelatin dessert with fruit and whipped cream
91501050 Gelatin dessert with cream cheese
91501060 Gelatin dessert with sour cream
91501070 Gelatin dessert with fruit and sour cream
91501080 Gelatin dessert with fruit and cream cheese
91501090 Gelatin dessert with fruit, vegetable, and nuts
91501100 Gelatin salad with vegetables
91501110 Gelatin dessert with fruit and whipped topping
91501120 Gelatin dessert with fruit and vegetables
91511010 Gelatin dessert, dietetic, sweetened with low calorie sweetener
91511020 Gelatin dessert, dietetic, with fruit, sweetened with low calorie sweetener
91511030 Gelatin dessert, dietetic, with whipped topping, sweetened with low calorie sweetener
91511050 Gelatin dessert, dietetic, with cream cheese, sweetened with low calorie sweetener
91511060 Gelatin dessert, dietetic, with sour cream, sweetened with low calorie sweetener
91511070 Gelatin dessert, dietetic, with fruit and sour cream, sweetened with low calorie sweetener
91511080 Gelatin dessert, dietetic, with fruit and cream cheese, sweetened with low calorie sweetener
91511090 Gelatin dessert, dietetic, with fruit and vegetable(s), sweetened with low calorie sweetener
91511100 Gelatin salad, dietetic, with vegetables, sweetened with low calorie sweetener
91511110 Gelatin dessert, dietetic, with fruit and whipped topping, sweetened with low calorie sweetener
91512010 Danish dessert pudding
91520100 Yookan (Yokan), a Japanese dessert made with bean paste and sugar
91550100 Coconut cream cake, Puerto Rican style (Bien me sabe, "Tastes good to me")
91550300 Pineapple custard, Puerto Rican style (Flan de pina)
91560100 Haupia (coconut pudding)
91580000 Gelatin, frozen, whipped, on a stick

Mixtures Containing Dairy-Based Puddings, Custards, and Mousses
(Adjusted for a Gelatin Dessert Content of 9.5 to 42.9%)
[2'-FL] = 0.16 to 0.73 g/100 g
14610200 Cheese, cottage cheese, with gelatin dessert
14610210 Cheese, cottage cheese, with gelatin dessert and fruit
14610250 Cheese, cottage cheese, with gelatin dessert and vegetables

<u>Fruit Pie Filling</u>
[2'-FL] = 1.4 g/100 g
61113500 Lemon pie filling
63113030 Cherry pie filling
63113050 Cherry pie filling, low calorie
63203700 Blueberry pie filling

Mixtures Containing Fruit Pie Filling
(Adjusted for a Pie Filling Content of 35.7% to 61.2%)
[2'-FL] = 0.50 to 0.86 g/100 g
53300100 Pie, NFS
53300170 Pie, individual size or tart, NFS
53300180 Pie, fried, NFS
53301000 Pie, apple, two crust
53301070 Pie, apple, individual size or tart
53301080 Pie, apple, fried pie
53301500 Pie, apple, one crust
53301750 Pie, apple, diet
53302000 Pie, apricot, two crust
53302070 Pie, apricot, individual size or tart

53302080	Pie, apricot, fried pie
53303000	Pie, blackberry, two crust
53303070	Pie, blackberry, individual size or tart
53303500	Pie, berry, not blackberry, blueberry, boysenberry, huckleberry, raspberry, or strawberry; two crust
53303510	Pie, berry, not blackberry, blueberry, boysenberry, huckleberry, raspberry, or strawberry; one crust
53303570	Pie, berry, not blackberry, blueberry, boysenberry, huckleberry, raspberry, or strawberry, individual size or tart
53304000	Pie, blueberry, two crust
53304050	Pie, blueberry, one crust
53304070	Pie, blueberry, individual size or tart
53305000	Pie, cherry, two crust
53305010	Pie, cherry, one crust
53305070	Pie, cherry, individual size or tart
53305080	Pie, cherry, fried pie
53305700	Pie, lemon (not cream or meringue)
53305720	Pie, lemon (not cream or meringue), individual size or tart
53305750	Pie, lemon, fried pie
53306000	Pie, mince, two crust
53306070	Pie, mince, individual size or tart
53307000	Pie, peach, two crust
53307050	Pie, peach, one crust
53307070	Pie, peach, individual size or tart
53307080	Pie, peach, fried pie
53307500	Pie, pear, two crust
53307570	Pie, pear, individual size or tart
53308000	Pie, pineapple, two crust
53308070	Pie, pineapple, individual size or tart
53308300	Pie, plum, two crust
53308500	Pie, prune, one crust
53309000	Pie, raisin, two crust
53309070	Pie, raisin, individual size or tart
53310000	Pie, raspberry, one crust
53310050	Pie, raspberry, two crust
53311000	Pie, rhubarb, two crust
53311050	Pie, rhubarb, one crust
53311070	Pie, rhubarb, individual size or tart
53312000	Pie, strawberry, one crust
53313000	Pie, strawberry-rhubarb, two crust
53314000	Pie, strawberry, individual size or tart
53340000	Pie, apple-sour cream
53340500	Pie, cherry, made with cream cheese and sour cream
53341000	Pie, banana cream
53341070	Pie, banana cream, individual size or tart
53345000	Pie, lemon cream
53345070	Pie, lemon cream, individual size or tart
53346500	Pie, pineapple cream
53347000	Pie, pumpkin
53347070	Pie, pumpkin, individual size or tart
53347100	Pie, raspberry cream
53348000	Pie, strawberry cream
53348070	Pie, strawberry cream, individual size or tart
53381000	Pie, lemon meringue
53381070	Pie, lemon meringue, individual size or tart
53410100	Cobbler, apple

53410200 Cobbler, apricot
53410300 Cobbler, berry
53410500 Cobbler, cherry
53410800 Cobbler, peach
53410850 Cobbler, pear
53410860 Cobbler, pineapple
53410880 Cobbler, plum
53410900 Cobbler, rhubarb

"Fruit Prep"
(Adjusted for a Fruit Prep Content of 40% to 67.3%)
[2'-FL] = 1.2 to 2.0 g/100 g
53415100 Crisp, apple, apple dessert
53415200 Fritter, banana
53415220 Fritter, berry
53415300 Crisp, blueberry
53415400 Crisp, cherry
53415500 Crisp, peach
53415600 Crisp, rhubarb
53440000 Strudel, apple
53440300 Strudel, berry
53440500 Strudel, cherry
53440700 Strudel, peach
53440750 Strudel, pineapple
53440800 Strudel, cheese and fruit
53450000 Turnover or dumpling, apple
53450300 Turnover or dumpling, berry
53450500 Turnover or dumpling, cherry
53450800 Turnover or dumpling, lemon
53451000 Turnover or dumpling, peach
53451500 Turnover, guava
53451750 Turnover, pumpkin
53452100 Pastry, fruit-filled
63402010 Banana whip
63402030 Prune whip

(Adjusted for a Fruit Prep Content of <1% to 38.6%)
[2'-FL] = 0.01 to 1.16 g/100 g
53101250 Cake, angel food, with fruit and icing or filling
53102100 Cake or cupcake, applesauce, without icing or filling
53102200 Cake or cupcake, applesauce, with icing or filling
53102600 Cake or cupcake, banana, without icing or filling
53102700 Cake or cupcake, banana, with icing or filling
53104550 Cheesecake with fruit
53113000 Cake, jelly roll
53118500 Cake, torte
53122070 Cake, shortcake, biscuit type, with whipped cream and fruit
53122080 Cake, shortcake, biscuit type, with fruit
53123070 Cake, shortcake, sponge type, with whipped cream and fruit
53123080 Cake, shortcake, sponge type, with fruit
53123500 Cake, shortcake, with whipped topping and fruit, diet
53220000 Cookie, fruit-filled bar
53220010 Cookie, fruit-filled bar, fat free
53220030 Cookie, fig bar

53220040	Cookie, fig bar, fat free
53224250	Cookie, lemon bar
53233010	Cookie, oatmeal, with raisins
53233080	Cookie, oatmeal sandwich, with peanut butter and jelly filling
53237000	Cookie, raisin
53237010	Cookie, raisin sandwich, cream-filled
53241600	Cookie, butter or sugar, with fruit and/or nuts
53415120	Fritter, apple
53430200	Crepe, dessert type, fruit-filled
53453150	Empanada, Mexican turnover, fruit-filled
53453170	Empanada, Mexican turnover, pumpkin
53510100	Danish pastry, with fruit
53521140	Doughnut, jelly
53610170	Coffee cake, crumb or quick-bread type, with fruit
55801010	Funnel cake with sugar and fruit

Grain Products and Pastas

Bars, Including Snack Bars, Meal-Replacement Bars, Breakfast Bars

[2'-FL] = 1.20 g/100 g

53710400	Fiber One Chewy Bar
53710500	Kellogg's Nutri-Grain Cereal Bar
53710502	Kellogg's Nutri-Grain Yogurt Bar
53710504	Kellogg's Nutri-Grain Fruit and Nut Bar
53710600	Milk 'n Cereal bar
53710700	Kellogg's Special K bar
53710800	Kashi GOLEAN Chewy Bars
53710802	Kashi TLC Chewy Granola Bar
53710804	Kashi GOLEAN Crunchy Bars
53710806	Kashi TLC Crunchy Granola Bar
53710900	Nature Valley Chewy Trail Mix Granola Bar
53710902	Nature Valley Chewy Granola Bar with Yogurt Coating
53710904	Nature Valley Sweet and Salty Granola Bar
53710906	Nature Valley Crunchy Granola Bar
53711000	Quaker Chewy Granola Bar
53711002	Quaker Chewy 90 Calorie Granola Bar
53711004	Quaker Chewy 25% Less Sugar Granola Bar
53711006	Quaker Chewy Dipps Granola Bar
53711100	Quaker Granola Bites
53712000	Snack bar, oatmeal
53712100	Granola bar, NFS
53712200	Granola bar, lowfat, NFS
53712210	Granola bar, nonfat
53713000	Granola bar, reduced sugar, NFS
53713100	Granola bar, peanuts, oats, sugar, wheat germ
53714200	Granola bar, chocolate-coated, NFS
53714210	Granola bar, with coconut, chocolate-coated
53714220	Granola bar with nuts, chocolate-coated
53714230	Granola bar, oats, nuts, coated with non-chocolate coating
53714250	Granola bar, coated with non-chocolate coating
53714300	Granola bar, high fiber, coated with non-chocolate yogurt coating
53714400	Granola bar, with rice cereal

53714500	Breakfast bar, NFS
53720100	Balance Original Bar
53720200	Clif Bar
53720210	Clif Kids Organic Zbar
53720300	PowerBar
53720400	Slim Fast Original Meal Bar
53720500	Snickers Marathon Protein bar
53720600	South Beach Living Meal Bar
53720610	South Beach Living High Protein Bar
53720700	Tiger's Milk bar
53720800	Zone Perfect Classic Crunch nutrition bar
53729000	Nutrition bar or meal replacement bar, NFS
53714510	Breakfast bar, date, with yogurt coating
53714520	Breakfast bar, cereal crust with fruit filling, lowfat

Jams and Jellies, Commercial

Jellies and Jams, Fruit Preserves, Fruit Butters

[2'-FL] = 6.0 g/100 g

63307010	Cranberry-orange relish, uncooked
63307100	Cranberry-raspberry sauce
91401000	Jelly, all flavors
91402000	Jam, preserves, all flavors
91403000	Fruit butter, all flavors
91404000	Marmalade, all flavors
91405000	Jelly, dietetic, all flavors, sweetened with artificial sweetener
91405500	Jelly, reduced sugar, all flavors
91406000	Jams, preserves, marmalades, dietetic, all flavors, sweetened with artificial sweetener
91406500	Jams, preserves, marmalades, sweetened with fruit juice concentrates, all flavors
91406600	Jams, preserves, marmalades, low sugar (all flavors)
91407100	Guava paste
91407120	Sweet potato paste
91407150	Bean paste, sweetened

Milk, Whole and Skim

Acidophilus or Fortified Milks, Fluid Milks, Reconstituted Milk Powders

[2'-FL] = 0.12 g/100 g

11100000	Milk, NFS
11111000	Milk, whole
11111100	Milk, low sodium, whole
11111150	Milk, calcium fortified, whole
11111160	Milk, calcium fortified, low fat (1%)
11111170	Milk, calcium fortified, fat free (skim)
11112110	Milk, reduced fat (2%)
11112120	Milk, acidophilus, low fat (1%)
11112130	Milk, acidophilus, reduced fat (2%)
11112210	Milk, low fat (1%)
11113000	Milk, fat free (skim)
11114300	Milk, lactose free, low fat (1%)
11114320	Milk, lactose free, fat free (skim)

11114330 Milk, lactose free, reduced fat (2%)
11114350 Milk, lactose free, whole
11120000 Milk, dry, reconstituted, NS as to fat content
11121100 Milk, dry, reconstituted, whole
11121210 Milk, dry, reconstituted, low fat (1%)
11121300 Milk, dry, reconstituted, fat free (skim)

Dry Milks
(Adjusted for being reconstituted at 24 g powder to 240 mL water)
[2'-FL] = 1.32 g/100 g
11810000 Milk, dry, not reconstituted, NS as to fat content
11811000 Milk, dry, not reconstituted, whole
11812000 Milk, dry, not reconstituted, low fat (1%)
11813000 Milk, dry, not reconstituted, fat free (skim)

Mixtures Containing Milk
(Adjusted for a Milk Content of 50.3% to 87.5%)
[2'-FL] = 0.06 to 0.11 g/100 g
11513400 Chocolate milk, made from syrup, NS as to type of milk
11513500 Chocolate milk, made from syrup with whole milk
11513550 Chocolate milk, made from syrup with reduced fat milk (2%)
11513600 Chocolate milk, made from syrup with low fat milk (1%)
11513700 Chocolate milk, made from syrup with fat free milk (skim)
11513800 Chocolate milk, made from light syrup, NS as to type of milk
11513801 Chocolate milk, made from light syrup with whole milk
11513802 Chocolate milk, made from light syrup with reduced fat milk (2%)
11513803 Chocolate milk, made from light syrup with low fat milk (1%)
11513804 Chocolate milk, made from light syrup with fat free milk (skim)
11513850 Chocolate milk, made from sugar free syrup, NS as to type of milk
11513851 Chocolate milk, made from sugar free syrup with whole milk
11513852 Chocolate milk, made from sugar free syrup with reduced fat milk (2%)
11513853 Chocolate milk, made from sugar free syrup with low fat milk (1%)
11513854 Chocolate milk, made from sugar free syrup with fat free milk (skim)
92101900 Coffee, Latte
92101901 Coffee, Latte, nonfat
92101904 Coffee, Latte, flavored
92101905 Coffee, Latte, nonfat, flavored
92101910 Coffee, Latte, decaffeinated
92101911 Coffee, Latte, decaffeinated, nonfat
92101917 Coffee, Latte, decaffeinated, flavored
92101918 Coffee, Latte, decaffeinated, nonfat, flavored
92101950 Coffee, Cafe Mocha
92101955 Coffee, Cafe Mocha, nonfat
92101965 Coffee, Cafe Mocha, decaffeinated
92101970 Coffee, Cafe Mocha, decaffeinated, nonfat
92102500 Coffee, Iced Latte
92102501 Coffee, Iced Latte, nonfat
92102510 Coffee, Iced Latte, decaffeinated
92102511 Coffee, Iced Latte, decaffeinated, nonfat
92161000 Coffee, Cappuccino
92161001 Coffee, Cappuccino, nonfat
92162000 Coffee, Cappuccino, decaffeinated
92162001 Coffee, Cappuccino, decaffeinated, nonfat

Mixtures Containing Milk
(Adjusted for a Milk Content of 16.1 to 49.9%)
[2'-FL] = 0.02 to 0.06 g/100 g

92101810	Coffee, macchiato
92101820	Coffee, macchiato, sweetened
92101850	Coffee, cafe con leche
92101851	Coffee, cafe con leche, decaffeinated
92101920	Frozen coffee drink
92101921	Frozen coffee drink, nonfat
92101925	Frozen coffee drink, with whipped cream
92101926	Frozen coffee drink, nonfat, with whipped cream
92101930	Frozen coffee drink, decaffeinated
92101931	Frozen coffee drink, decaffeinated, nonfat
92101935	Frozen coffee drink, decaffeinated, with whipped cream
92101936	Frozen coffee drink, decaffeinated, nonfat, with whipped cream
92102000	Frozen mocha coffee drink
92102010	Frozen mocha coffee drink, nonfat
92102030	Frozen mocha coffee drink, with whipped cream
92102040	Frozen mocha coffee drink, nonfat, with whipped cream
92102060	Frozen mocha coffee drink, decaffeinated
92102070	Frozen mocha coffee drink, decaffeinated, nonfat
92102090	Frozen mocha coffee drink, decaffeinated, with whipped cream
92102100	Frozen mocha coffee drink, decaffeinated, nonfat, with whipped cream
92102503	Coffee, Iced Latte, flavored
92102504	Coffee, Iced Latte, nonfat, flavored
92102513	Coffee, Iced Latte, decaffeinated, flavored
92102514	Coffee, Iced Latte, decaffeinated, nonfat, flavored
92102600	Coffee, Iced Cafe Mocha
92102601	Coffee, Iced Cafe Mocha, nonfat
92102610	Coffee, Iced Cafe Mocha, decaffeinated
92102611	Coffee, Iced Cafe Mocha, decaffeinated, nonfat
92306800	Tea, hot, chai, with milk
92610030	Horchata beverage, made with milk
92611100	Atole de avena (oatmeal beverage with milk)
92613010	Atole (corn meal beverage)
92613510	Atole de chocolate / Champurrado (cornmeal beverage with chocolate and milk)

Milk Products

<u>Flavored Milks</u>
[2'-FL] = 0.12 g/100 g

11115000	Buttermilk, fat free (skim)
11115100	Buttermilk, low fat (1%)
11115200	Buttermilk, reduced fat (2%)
11115300	Buttermilk, whole
11115400	Kefir, NS as to fat content
11511000	Chocolate milk, NFS
11511100	Chocolate milk, ready to drink, whole
11511200	Chocolate milk, ready to drink, reduced fat (2%)
11511300	Chocolate milk, ready to drink, fat free (skim)
11511400	Chocolate milk, ready to drink, low fat (1%)
11511550	Chocolate milk, ready to drink, reduced sugar, NS as to milk

11511600	Nesquik, chocolate milk, ready to drink, low fat (1%)
11511610	Nesquik, chocolate milk, ready to drink, fat free (skim)
11511700	Nesquik, chocolate milk, ready to drink, low fat (1%), no sugar added
11512010	Hot chocolate / Cocoa, ready to drink
11512020	Hot chocolate / Cocoa, ready to drink, made with nonfat milk
11512100	Hot chocolate / Cocoa, ready to drink, with whipped cream
11512110	Hot chocolate / Cocoa, ready to drink, made with nonfat milk and whipped cream
11513000	Chocolate milk, made from dry mix, NS as to type of milk
11513100	Chocolate milk, made from dry mix with whole milk
11513150	Chocolate milk, made from dry mix with reduced fat milk (2%)
11513200	Chocolate milk, made from dry mix with low fat milk (1%)
11513300	Chocolate milk, made from dry mix with fat free milk (skim)
11513350	Chocolate milk, made from reduced sugar mix, NS as to type of milk
11513355	Chocolate milk, made from reduced sugar mix with whole milk
11513360	Chocolate milk, made from reduced sugar mix with reduced fat milk (2%)
11513365	Chocolate milk, made from reduced sugar mix with low fat milk (1%)
11513370	Chocolate milk, made from reduced sugar mix with fat free milk (skim)
11513380	Nesquik, chocolate milk, made from dry mix, NS as to type of milk
11513381	Nesquik, chocolate milk, made from dry mix with whole milk
11513382	Nesquik, chocolate milk, made from dry mix with reduced fat milk (2%)
11513383	Nesquik, chocolate milk, made from dry mix with low fat milk (1%)
11513384	Nesquik, chocolate milk, made from dry mix with fat free milk (skim)
11513390	Nesquik, chocolate milk, made from no sugar added dry mix, NS as to type of milk
11513391	Nesquik, chocolate milk, made from no sugar added dry mix with whole milk
11513392	Nesquik, chocolate milk, made from no sugar added dry mix with reduced fat milk (2%)
11513393	Nesquik, chocolate milk, made from no sugar added dry mix with low fat milk (1%)
11513394	Nesquik, chocolate milk, made from no sugar added dry mix with fat free milk (skim)
11514110	Hot chocolate / Cocoa, made with dry mix and whole milk
11514120	Hot chocolate / Cocoa, made with dry mix and reduced fat milk (2%)
11514130	Hot chocolate / Cocoa, made with dry mix and low fat milk (1%)
11514140	Hot chocolate / Cocoa, made with dry mix and fat free milk (skim)
11514320	Hot chocolate / Cocoa, made with no sugar added dry mix and whole milk
11514330	Hot chocolate / Cocoa, made with no sugar added dry mix and reduced fat milk (2%)
11514340	Hot chocolate / Cocoa, made with no sugar added dry mix and low fat milk (1%)
11514350	Hot chocolate / Cocoa, made with no sugar added dry mix and fat free milk (skim)
11519040	Strawberry milk, NFS
11519050	Strawberry milk, whole
11519105	Strawberry milk, reduced fat (2%)
11519200	Strawberry milk, low fat (1%)
11519205	Strawberry milk, fat free (skim)
11525000	Milk, malted, natural flavor, made with milk
11526000	Milk, malted, chocolate, made with milk
11541400	Milk shake with malt
11542100	Milk shake, fast food, chocolate
11542200	Milk shake, fast food, flavors other than chocolate
11543000	Milk shake, bottled, chocolate
11543010	Milk shake, bottled, flavors other than chocolate
11551050	Licuado / Batido (milk fruit drink)
11553100	Fruit smoothie, NFS
11553110	Fruit smoothie, with whole fruit and dairy
11553120	Fruit smoothie, with whole fruit and dairy, added protein
11553130	Fruit smoothie juice drink, with dairy
11560000	Yoo-hoo, chocolate milk drink
78101100	Fruit and vegetable smoothie

78101110 Fruit and vegetable smoothie, added protein
78101120 Fruit and vegetable smoothie, bottled
92171000 Coffee, bottled/canned
92171010 Coffee, bottled/canned, light

Dry Mixtures of Flavored Milks, Cocoa
(Adjusted for Not Being Reconstituted, 28 g powder to 240 mL of water)
[2'-FL] = 1.15 g/100 g
11830100 Hot chocolate / Cocoa, dry mix, not reconstituted
11830115 Hot chocolate / Cocoa, dry mix, no sugar added, not reconstituted
11830150 Cocoa powder, not reconstituted (no dry milk)
11830160 Chocolate beverage powder, dry mix, not reconstituted
11830165 Chocolate beverage powder, reduced sugar, dry mix, not reconstituted
11830260 Milk, malted, dry mix, not reconstituted
11830400 Strawberry beverage powder, dry mix, not reconstituted

Milk-Based Meal Replacement Beverages or Diet beverages
[2'-FL] = 0.12 g/100 g
95101000 Boost, nutritional drink, ready-to-drink
95101010 Boost Plus, nutritional drink, ready-to-drink
95102000 Carnation Instant Breakfast, nutritional drink, regular, ready-to-drink
95103000 Ensure, nutritional shake, ready-to-drink
95103010 Ensure Plus, nutritional shake, ready-to-drink
95104000 Glucerna, nutritional shake, ready-to-drink
95105000 Kellogg's Special K Protein Shake
95106000 Muscle Milk, ready-to-drink
95106010 Muscle Milk, light, ready-to-drink
95110000 Slim Fast Shake, meal replacement, regular, ready-to-drink
95110010 Slim Fast Shake, meal replacement, sugar free, ready-to-drink
95110020 Slim Fast Shake, meal replacement, high protein, ready-to-drink
95120000 Nutritional drink or meal replacement, ready-to-drink, NFS
95120010 Nutritional drink or meal replacement, high protein, ready-to-drink, NFS
95120020 Nutritional drink or meal replacement, high protein, light, ready-to-drink, NFS

Powdered Milk-Based Meal Replacement Beverages
(Adjusted for Not Being Reconstituted, 16 g powder to 240 mL of water or milk)
[2'-FL] = 1.92 g/100 g
95220000 Nutritional drink mix or meal replacement, powder, NFS
95220010 Nutritional drink mix or meal replacement, high protein, powder, NFS

Not Reconstituted Milk-Based Meal Replacement Beverages
(Adjusted for Not Being Reconstituted, 20 g powder to 240 mL of milk)
[2'-FL] = 1.56 g/100 g
95201000 Carnation Instant Breakfast, nutritional drink mix, regular, powder
95201010 Carnation Instant Breakfast, nutritional drink mix, sugar free, powder

Not Reconstituted Milk-Based Meal Replacement Beverages
(Adjusted for not being reconstituted, 26 g powder to 227 mL of water)
[2'-FL] = 1.20 g/100 g
95202010 Muscle Milk, light, powder
95210000 Slim Fast Shake Mix, powder
95210010 Slim Fast Shake Mix, sugar free, powder
95210020 Slim Fast Shake Mix, high protein, powder

Not Reconstituted Milk-Based Meal Replacement Beverages
(Adjusted for not being reconstituted, 70 g powder to 454 mL of water)
[2'-FL] = 0.90 g/100 g

95202000 Muscle Milk, regular, powder

Yogurt
[2'-FL] = 0.53 g/100 g

11410000 Yogurt, NS as to type of milk or flavor
11411010 Yogurt, plain, NS as to type of milk
11411100 Yogurt, plain, whole milk
11411200 Yogurt, plain, low fat milk
11411300 Yogurt, plain, nonfat milk
11411400 Yogurt, Greek, plain, whole milk
11411410 Yogurt, Greek, plain, low fat
11411420 Yogurt, Greek, plain, nonfat milk
11420000 Yogurt, vanilla, NS as to type of milk
11421000 Yogurt, vanilla, whole milk
11422000 Yogurt, vanilla, low fat milk
11422100 Yogurt, vanilla, low fat milk, light
11423000 Yogurt, vanilla, nonfat milk
11424000 Yogurt, vanilla, nonfat milk, light
11424500 Yogurt, Greek, vanilla, whole milk
11424510 Yogurt, Greek, vanilla, low fat
11424520 Yogurt, Greek, vanilla, nonfat
11425000 Yogurt, chocolate, NS as to type of milk
11426000 Yogurt, chocolate, whole milk
11427000 Yogurt, chocolate, nonfat milk
11428000 Yogurt, Greek, chocolate, nonfat
11430000 Yogurt, fruit, NS as to type of milk
11431000 Yogurt, fruit, whole milk
11432000 Yogurt, fruit, low fat milk
11432500 Yogurt, fruit, low fat milk, light
11433000 Yogurt, fruit, nonfat milk
11433500 Yogurt, fruit, nonfat milk, light
11434000 Yogurt, Greek, fruit, whole milk
11434010 Yogurt, Greek, fruit, low fat
11434020 Yogurt, Greek, fruit, nonfat

Mixtures Containing Yogurt
(Adjusted for a Yogurt Content of 34.6% to 93.2%)
[2'-FL] = 0.18 to 0.49 g/100 g

11446000 Fruit and low fat yogurt parfait
83115000 Yogurt dressing

Processed Fruits and Fruit Juices

Fruit Drinks
[2'-FL] = 0.12 g/100 g

64134015 Fruit smoothie, with whole fruit (no dairy)
64134020 Fruit smoothie, with whole fruit (no dairy), added protein
64134030 Fruit smoothie juice drink (no dairy)
64134100 Fruit smoothie, light

64134200	Fruit smoothie, bottled
64200100	Fruit nectar, NFS
64201010	Apricot nectar
64201500	Banana nectar
64202010	Cantaloupe nectar
64203020	Guava nectar
64204010	Mango nectar
64205010	Peach nectar
64210010	Papaya nectar
64213010	Passion fruit nectar
64215010	Pear nectar
64221010	Soursop (Guanabana) nectar
92307500	Iced Tea / Lemonade juice drink
92307510	Iced Tea / Lemonade juice drink, light
92307520	Iced Tea / Lemonade juice drink, diet
92432000	Fruit juice drink, citrus, carbonated
92433000	Fruit juice drink, noncitrus, carbonated
92510610	Fruit juice drink
92510650	Tamarind drink (Refresco de tamarindo)
92510720	Fruit punch, made with fruit juice and soda
92510730	Fruit punch, made with soda, fruit juice, and sherbet or ice cream
92510955	Lemonade, fruit juice drink
92510960	Lemonade, fruit flavored drink
92511015	Fruit flavored drink
92511250	Fruit juice beverage, 40-50% juice, citrus
92512090	Pina Colada, nonalcoholic
92512110	Margarita mix, nonalcoholic
92513000	Fruit flavored smoothie drink, frozen (no dairy)
92513010	Fruit flavored smoothie drink, frozen, light (no dairy)
92530410	Fruit flavored drink, with high vitamin C
92530510	Cranberry juice drink, with high vitamin C
92530610	Fruit juice drink, with high vitamin C
92531030	Sunny D
92541010	Fruit flavored drink, powdered, reconstituted
92542000	Fruit flavored drink, with high vitamin C, powdered, reconstituted
92550030	Fruit juice drink, with high vitamin C, light
92550035	Fruit juice drink, light
92550040	Fruit juice drink, diet
92550110	Cranberry juice drink, with high vitamin C, light
92550200	Grape juice drink, light
92550350	Orange juice beverage, 40-50% juice, light
92550360	Apple juice beverage, 40-50% juice, light
92550370	Lemonade, fruit juice drink, light
92550380	Pomegranate juice beverage, 40-50% juice, light
92550610	Fruit flavored drink, with high vitamin C, diet
92550620	Fruit flavored drink, diet
92552000	Fruit flavored drink, with high vitamin C, powdered, reconstituted, diet
92552010	Fruit flavored drink, powdered, reconstituted, diet
92552020	Sunny D, reduced sugar
92552030	Capri Sun, fruit juice drink
92582100	Fruit juice drink, with high vitamin C, plus added calcium
92582110	Sunny D, added calcium

Frozen Fruit Drinks

(Adjusted for Not Being Reconstituted, 1 Cup Juice Mix to 3 Cups Water)
[2'-FL] = 0.48 g/100 g

92511000 Lemonade, frozen concentrate, not reconstituted

Concentrated Fruit Drinks
(Adjusted for Not Being Reconstituted, 55 mL of Frozen Concentrate to Produce a 240 mL Beverage)
[2'-FL] = 0.64 g/100 g

92512040 Frozen daiquiri mix, frozen concentrate, not reconstituted
92512050 Frozen daiquiri mix, from frozen concentrate, reconstituted

Powdered Fruit Drinks
(Adjusted for Not Being Reconstituted, 16 g Powder to 240 mL of Water)
[2'-FL] = 1.92 g/100 g

92900100 Fruit flavored drink, with high vitamin C, powdered, not reconstituted
92900110 Fruit flavored drink, powdered, not reconstituted
92900200 Fruit flavored drink, powdered, not reconstituted, diet

Mixtures Containing Fruit Drinks
(Adjusted for a Fruit Drink Content of 50% to 74.7%)
[2'-FL] = 0.06 to 0.09 g/100 g

92530950 Vegetable and fruit juice drink, with high vitamin C
92550400 Vegetable and fruit juice drink, with high vitamin C, diet
92550405 Vegetable and fruit juice drink, with high vitamin C, light
93301213 Vodka and lemonade

Fruit Juices
[2'-FL] = 0.12 g/100 g

61201020 Grapefruit juice, 100%, NS as to form
61201220 Grapefruit juice, 100%, canned, bottled or in a carton
61201225 Grapefruit juice, 100%, with calcium added
61201620 Grapefruit juice,100%, frozen, reconstituted
61204000 Lemon juice, 100%, NS as to form
61204200 Lemon juice, 100%, canned or bottled
61207000 Lime juice, 100%, NS as to form
61207200 Lime juice, 100%, canned or bottled
61210000 Orange juice, 100%, NFS
61210220 Orange juice, 100%, canned, bottled or in a carton
61210250 Orange juice, 100%, with calcium added, canned, bottled or in a carton
61210620 Orange juice, 100%, frozen, reconstituted
61210820 Orange juice, 100%, with calcium added, frozen, reconstituted
61213220 Tangerine juice, 100%
61213800 Fruit juice blend, citrus, 100% juice
61213900 Fruit juice blend, citrus, 100% juice, with calcium added
64100100 Fruit juice, NFS
64100110 Fruit juice blend, 100% juice
64100200 Cranberry juice blend, 100% juice
64100220 Cranberry juice blend, 100% juice, with calcium added
64101010 Apple cider
64104010 Apple juice, 100%
64104030 Apple juice, 100%, with calcium added
64104600 Blackberry juice, 100%
64105400 Cranberry juice, 100%, not a blend
64116020 Grape juice, 100%

64116060 Grape juice, 100%, with calcium added
64120010 Papaya juice, 100%
64121000 Passion fruit juice, 100%
64124020 Pineapple juice, 100%
64126000 Pomegranate juice, 100%
64132010 Prune juice, 100%
64132500 Strawberry juice, 100%
64133100 Watermelon juice, 100%

Frozen Fruit Juices
(Adjusted for Not Being Reconstituted, 1 Cup Juice Mix to 3 Cups Water)
[2'-FL] = 0.48 g/100 g
61210720 Orange juice, 100%, frozen, not reconstituted

Mixtures Containing Fruit Juices
(Adjusted for a Fruit Juice Content of 3.6% to 75.3%)
[2'-FL] = <0.01 to 0.09 g/100 g
78101000 Vegetable and fruit juice, 100% juice, with high vitamin C
93301032 Cape Cod
93301040 Daiquiri
93301075 Greyhound
93301085 Kamikaze
93301111 Martini, flavored
93301115 Mimosa
93301132 Orange Blossom
93301139 Salty Dog
93301140 Screwdriver
93301141 Seabreeze
93301200 Pina Colada
93301230 Sloe gin fizz
93301270 Fruit punch, alcoholic
93301275 Champagne punch
93301280 Singapore Sling
93301310 Mai Tai
93301320 Tequila Sunrise
93301330 Gin Rickey
93301370 Fuzzy Navel
93301600 Gin fizz
93302100 Zombie

Sweet Sauces, Toppings, and Syrups

Syrups Used to Flavor Milk Beverages
(Adjusted for a Syrup Content of 12.5 to 13.3%)
[2'-FL] = 0.09 g/100 g
11513400 Chocolate milk, made from syrup, NS as to type of milk
11513500 Chocolate milk, made from syrup with whole milk
11513550 Chocolate milk, made from syrup with reduced fat milk (2%)
11513600 Chocolate milk, made from syrup with low fat milk (1%)
11513700 Chocolate milk, made from syrup with fat free milk (skim)
11513750 Chocolate milk, made from syrup with non-dairy milk
11513800 Chocolate milk, made from light syrup, NS as to type of milk
11513801 Chocolate milk, made from light syrup with whole milk

11513802	Chocolate milk, made from light syrup with reduced fat milk (2%)
11513803	Chocolate milk, made from light syrup with low fat milk (1%)
11513804	Chocolate milk, made from light syrup with fat free milk (skim)
11513805	Chocolate milk, made from light syrup with non-dairy milk
11513850	Chocolate milk, made from sugar free syrup, NS as to type of milk
11513851	Chocolate milk, made from sugar free syrup with whole milk
11513852	Chocolate milk, made from sugar free syrup with reduced fat milk (2%)
11513853	Chocolate milk, made from sugar free syrup with low fat milk (1%)
11513854	Chocolate milk, made from sugar free syrup with fat free milk (skim)
11513855	Chocolate milk, made from sugar free syrup with non-dairy milk
91301130	Fruit flavored syrup used for milk beverages

Non-Exempt Infant and Follow-On Formula

Infant Formula

[2'-FL] = 0.24 g/100 g

11710000	Infant formula, NFS
11710050	Similac Expert Care Alimentum, infant formula, NS as to form
11710051	Similac Expert Care Alimentum, infant formula, ready-to-feed
11710053	Similac Expert Care Alimentum, infant formula, prepared from powder, made with water, NFS
11710054	Similac Expert Care Alimentum, infant formula, prepared from powder, made with tap water
11710055	Similac Expert Care Alimentum, infant formula, prepared from powder, made with plain bottled water
11710056	Similac Expert Care Alimentum, infant formula, prepared from powder, made with baby water
11710350	Similac Advance, infant formula, NS as to form
11710351	Similac Advance, infant formula, ready-to-feed
11710352	Similac Advance, infant formula, prepared from liquid concentrate, made with water, NFS
11710353	Similac Advance, infant formula, prepared from powder, made with water, NFS
11710354	Similac Advance, infant formula, prepared from liquid concentrate, made with tap water
11710355	Similac Advance, infant formula, prepared from liquid concentrate, made with plain bottled water
11710356	Similac Advance, infant formula, prepared from liquid concentrate, made with baby water
11710357	Similac Advance, infant formula, prepared from powder, made with tap water
11710358	Similac Advance, infant formula, prepared from powder, made with plain bottled water
11710359	Similac Advance, infant formula, prepared from powder, made with baby water
11710360	Similac Advance Organic, infant formula, NS as to form
11710361	Similac Advance Organic, infant formula, ready-to-feed
11710363	Similac Advance Organic, infant formula, prepared from powder, made with water, NFS
11710367	Similac Advance Organic, infant formula, prepared from powder, made with tap water
11710368	Similac Advance Organic, infant formula, prepared from powder, made with plain bottled water
11710369	Similac Advance Organic, infant formula, prepared from powder, made with baby water
11710370	Similac Sensitive, infant formula, NS as to form
11710371	Similac Sensitive, infant formula, ready-to-feed
11710372	Similac Sensitive, infant formula, prepared from liquid concentrate, made with water, NFS
11710373	Similac Sensitive, infant formula, prepared from powder, made with water, NFS
11710374	Similac Sensitive, infant formula, prepared from liquid concentrate, made with tap water
11710375	Similac Sensitive, infant formula, prepared from liquid concentrate, made with plain bottled water
11710376	Similac Sensitive, infant formula, prepared from liquid concentrate, made with baby water
11710377	Similac Sensitive, infant formula, prepared from powder, made with tap water
11710378	Similac Sensitive, infant formula, prepared from powder, made with plain bottled water
11710379	Similac Sensitive, infant formula, prepared from powder, made with baby water
11710380	Similac Sensitive for Spit-Up, infant formula, NS as to form
11710381	Similac Sensitive for Spit-Up, infant formula, ready-to-feed

11710383	Similac Sensitive for Spit-Up, infant formula, prepared from powder, made with water, NFS
11710387	Similac Sensitive for Spit-Up, infant formula, prepared from powder, made with tap water
11710388	Similac Sensitive for Spit-Up, infant formula, prepared from powder, made with plain bottled water
11710389	Similac Sensitive for Spit-Up, infant formula, prepared from powder, made with baby water
11710620	Enfamil PREMIUM Newborn, infant formula, NS as to form
11710621	Enfamil PREMIUM Newborn, infant formula, ready-to-feed
11710626	Enfamil PREMIUM Newborn, infant formula, prepared from powder, made with water, NFS
11710627	Enfamil PREMIUM Newborn, infant formula, prepared from powder, made with tap water
11710628	Enfamil PREMIUM Newborn, infant formula, prepared from powder, made with plain bottled water
11710629	Enfamil PREMIUM Newborn, infant formula, prepared from powder, made with baby water
11710630	Enfamil PREMIUM Infant, infant formula, NS as to form
11710631	Enfamil PREMIUM Infant, infant formula, ready-to-feed
11710632	Enfamil PREMIUM Infant, infant formula, prepared from liquid concentrate, made with water, NFS
11710633	Enfamil PREMIUM Infant, infant formula, prepared from liquid concentrate, made with tap water
11710634	Enfamil PREMIUM Infant, infant formula, prepared from liquid concentrate, made with plain bottled water
11710635	Enfamil PREMIUM Infant, infant formula, prepared from liquid concentrate, made with baby water
11710636	Enfamil PREMIUM Infant, infant formula, prepared from powder, made with water, NFS
11710637	Enfamil PREMIUM Infant, infant formula, prepared from powder, made with tap water
11710638	Enfamil PREMIUM Infant, infant formula, prepared from powder, made with plain bottled water
11710639	Enfamil PREMIUM Infant, infant formula, prepared from powder, made with baby water
11710640	Enfamil PREMIUM LIPIL, infant formula, NS as to form
11710642	Enfamil PREMIUM LIPIL, infant formula, prepared from liquid concentrate, made with water, NFS
11710643	Enfamil PREMIUM LIPIL, infant formula, prepared from powder, made with water, NFS
11710644	Enfamil PREMIUM LIPIL, infant formula, prepared from liquid concentrate, made with tap water
11710645	Enfamil PREMIUM LIPIL, infant formula, prepared from liquid concentrate, made with plain bottled water
11710646	Enfamil PREMIUM LIPIL, infant formula, prepared from liquid concentrate, made with baby water
11710647	Enfamil PREMIUM LIPIL, infant formula, prepared from powder, made with tap water
11710648	Enfamil PREMIUM LIPIL, infant formula, prepared from powder, made with plain bottled water
11710649	Enfamil PREMIUM LIPIL, infant formula, prepared from powder, made with baby water
11710650	Enfamil LIPIL, infant formula, NS as to form
11710651	Enfamil LIPIL, infant formula, ready-to-feed
11710652	Enfamil LIPIL, infant formula, prepared from liquid concentrate, made with water, NFS
11710653	Enfamil LIPIL, infant formula, prepared from powder, made with water, NFS
11710654	Enfamil LIPIL, infant formula, prepared from liquid concentrate, made with tap water
11710655	Enfamil LIPIL, infant formula, prepared from liquid concentrate, made with plain bottled water
11710656	Enfamil LIPIL, infant formula, prepared from liquid concentrate, made with baby water
11710657	Enfamil LIPIL, infant formula, prepared from powder, made with tap water
11710658	Enfamil LIPIL, infant formula, prepared from powder, made with plain bottled water
11710659	Enfamil LIPIL, infant formula, prepared from powder, made with baby water
11710660	Enfamil A.R. Lipil, infant formula, NS as to form
11710661	Enfamil A.R. Lipil, infant formula, ready-to-feed
11710663	Enfamil A.R. LIPIL, infant formula, prepared from powder, made with water, NFS
11710664	Enfamil A.R. LIPIL, infant formula, prepared from powder, made with tap water
11710670	Enfamil Gentlease LIPIL, infant formula, NS as to form
11710671	Enfamil Gentlease LIPIL, infant formula, ready-to-feed
11710673	Enfamil Gentlease LIPIL, infant formula, prepared from powder, made with water, NFS
11710677	Enfamil Gentlease LIPIL, infant formula, prepared from powder, made with tap water
11710678	Enfamil Gentlease LIPIL, infant formula, prepared from powder, made with plain bottled water
11710679	Enfamil Gentlease LIPIL, infant formula, prepared from powder, made with baby water
11710910	Gerber Good Start Gentle Plus, infant formula, NS as to form
11710911	Gerber Good Start Gentle Plus, infant formula, ready-to-feed

11710912	Gerber Good Start Gentle Plus, infant formula, prepared from liquid concentrate, made with water, NFS
11710913	Gerber Good Start Gentle Plus, infant formula, prepared from powder, made with water, NFS
11710914	Gerber Good Start Gentle Plus, infant formula, prepared from liquid concentrate, made with tap water
11710915	Gerber Good Start Gentle Plus, infant formula, prepared from liquid concentrate, made with plain bottled water
11710916	Gerber Good Start Gentle Plus, infant formula, prepared from liquid concentrate, made with baby water
11710917	Gerber Good Start Gentle Plus, infant formula, prepared from powder, made with tap water
11710918	Gerber Good Start Gentle Plus, infant formula, prepared from powder, made with plain bottled water
11710919	Gerber Good Start Gentle Plus, infant formula, prepared from powder, made with baby water
11710920	Gerber Good Start Protect Plus, infant formula, NS as to form
11710923	Gerber Good Start Protect Plus, infant formula, prepared from powder, made with water, NFS
11710927	Gerber Good Start Protect Plus, infant formula, prepared from powder, made with tap water
11710928	Gerber Good Start Protect Plus, infant formula, prepared from powder, made with plain bottled water
11710929	Gerber Good Start Protect Plus, infant formula, prepared from powder, made with baby water
11710960	America's Store Brand, infant formula, NS as to form
11710961	America's Store Brand, infant formula, prepared from liquid concentrate, made with water, NFS
11710962	America's Store Brand, infant formula, prepared from powder, made with water, NFS
11710963	America's Store Brand, infant formula, ready-to-feed
11710964	America's Store Brand, infant formula, prepared from liquid concentrate, made with tap water
11710965	America's Store Brand, infant formula, prepared from liquid concentrate, made with plain bottled water
11710966	America's Store Brand, infant formula, prepared from liquid concentrate, made with baby water
11710967	America's Store Brand, infant formula, prepared from powder, made with tap water
11710968	America's Store Brand, infant formula, prepared from powder, made with plain bottled water
11710969	America's Store Brand, infant formula, prepared from powder, made with baby water

Follow-On Formula

[2'-FL] = 0.24 g/100 g

11710480	Similac Go and Grow, infant formula, NS as to form
11710481	Similac Go and Grow, infant formula, prepared from powder, made with water, NFS
11710482	Similac Go and Grow, infant formula, prepared from powder, made with tap water
11710483	Similac Go and Grow, infant formula, prepared from powder, made with plain bottled water
11710484	Similac Go and Grow, infant formula, prepared from powder, made with baby water

Meal Replacement Products

[2'-FL] = 0.2 g/100 g

11710800	Pediasure, infant formula, NS as to form
11710801	Pediasure, infant formula, ready-to-feed
11710805	Pediasure Fiber, infant formula, NS as to form
11710806	Pediasure Fiber, infant formula, ready-to-feed

Baby Foods

Growing Up (Toddler) Milks

[2'-FL] = 0.2 g/100 g

11710680	Enfamil Enfagrow PREMIUM Next Step LIPIL, infant formula, NS as to form
11710681	Enfamil Enfagrow PREMIUM Next Step LIPIL, infant formula, ready-to-feed

11710683	Enfamil Enfagrow PREMIUM Next Step LIPIL, infant formula, prepared from powder, made with water, NFS
11710687	Enfamil Enfagrow PREMIUM Next Step LIPIL, infant formula, prepared from powder, made with tap water
11710688	Enfamil Enfagrow PREMIUM Next Step LIPIL, infant formula, prepared from powder, made with plain bottled water
11710689	Enfamil Enfagrow PREMIUM Next Step LIPIL, infant formula, prepared from powder, made with baby water
11710690	Enfamil Gentlease Next Step LIPIL, infant formula, NS as to form
11710693	Enfamil Gentlease Next Step LIPIL, infant formula, prepared from powder, made with water, NFS
11710697	Enfamil Gentlease Next Step LIPIL, infant formula, prepared from powder, made with tap water
11710698	Enfamil Gentlease Next Step LIPIL, infant formula, prepared from powder, made with plain bottled water
11710699	Enfamil Gentlease Next Step LIPIL, infant formula, prepared from powder, made with baby water
11710930	Gerber Good Start 2 Gentle Plus, infant formula, NS as to form
11710933	Gerber Good Start 2 Gentle Plus, infant formula, prepared from powder, made with water, NFS
11710937	Gerber Good Start 2 Gentle Plus, infant formula, prepared from powder, made with tap water
11710938	Gerber Good Start 2 Gentle Plus, infant formula, prepared from powder, made with plain bottled water
11710939	Gerber Good Start 2 Gentle Plus, infant formula, prepared from powder, made with baby water
11710940	Gerber Good Start 2 Protect Plus, infant formula, NS as to form
11710943	Gerber Good Start 2 Protect Plus, infant formula, prepared from powder, made with water, NFS
11710947	Gerber Good Start 2 Protect Plus, infant formula, prepared from powder, made with tap water
11710948	Gerber Good Start 2 Protect Plus, infant formula, prepared from powder, made with plain bottled water
11710949	Gerber Good Start 2 Protect Plus, infant formula, prepared from powder, made with baby water

Ready-to-Eat, Ready-to-Serve, Hot Cereals

[2'-FL] = 1.09 g/100 g

57820000	Cereal, baby food, jarred, NFS
57820100	Rice cereal, baby food, jarred, NFS
57822000	Mixed cereal with applesauce and bananas, baby food, jarred
57823000	Oatmeal with applesauce and bananas, baby food, jarred
57824000	Rice cereal with applesauce and bananas, baby food, jarred
57824500	Rice cereal with mixed fruit, baby food, jarred

Yogurt and Juice Beverages, Identified as "Baby" Drinks

[2'-FL] = 1.0 g/100 g

67202000	Apple juice, baby food
67202010	Apple juice, with added calcium, baby food
67203000	Apple-fruit juice blend, baby food
67203200	Apple-banana juice, baby food
67203400	Apple-cherry juice, baby food
67203500	Apple-grape juice, baby food
67203600	Apple-peach juice, baby food
67203700	Apple-prune juice, baby food
67203800	Grape juice, baby food
67204000	Mixed fruit juice, not citrus, baby food
67204100	Mixed fruit juice, not citrus, with added calcium, baby food
67205000	Orange juice, baby food
67211000	Orange-apple-banana juice, baby food
67212000	Pear juice, baby food
67230000	Apple-sweet potato juice, baby food
67230500	Orange-carrot juice, baby food

67250100 Banana juice with lowfat yogurt, baby food
67250150 Mixed fruit juice with lowfat yogurt, baby food
67260000 Fruit juice and water drink, with high vitamin C and added calcium, baby food

Desserts, "Junior Type"
[2'-FL] = 1.09 g/100 g

13310000 Custard pudding, flavor other than chocolate, baby food, NS as to strained or junior
13311000 Custard pudding, baby food, flavor other than chocolate, strained
13312000 Custard pudding, baby food, flavor other than chocolate, junior
67100100 Fruit, baby food, NFS
67100110 Fruit bar, with added vitamin C, baby food, toddler
67100200 Tropical fruit medley, baby food, strained
67100300 Apples, baby food, toddler
67101000 Apple-raspberry, baby food, NS as to strained or junior
67101020 Apple-raspberry, baby food, junior
67102000 Applesauce, baby food, NS as to strained or junior
67102020 Applesauce, baby food, junior
67104000 Applesauce and apricots, baby food, NS as to strained or junior
67104020 Applesauce and apricots, baby food, junior
67104030 Applesauce with bananas, baby food, NS as to strained or junior
67104060 Applesauce with bananas, baby food, junior
67104080 Applesauce with cherries, baby food, junior
67104090 Applesauce with cherries, baby food, NS as to strained or junior
67108000 Peaches, baby food, NS as to strained or junior
67108020 Peaches, baby food, junior
67109000 Pears, baby food, NS as to strained or junior
67109020 Pears, baby food, junior
67113000 Apples and pears, baby food, NS as to strained or junior
67113020 Apples and pears, baby food, junior
67114000 Pears and pineapple, baby food, NS as to strained or junior
67114020 Pears and pineapple, baby food, junior
67304000 Plums, baby food, NS as to strained or junior
67304020 Plums, baby food, junior
67307000 Apricots, baby food, NS as to strained or junior
67307020 Apricots, baby food, junior
67308000 Bananas, baby food, NS as to strained or junior
67308020 Bananas, baby food, junior
67309000 Bananas and pineapple, baby food, NS as to strained or junior
67309020 Bananas and pineapple, baby food, junior
67309030 Bananas and strawberry, baby food, junior
67404000 Fruit dessert, baby food, NS as to strained or junior
67404020 Fruit dessert, baby food, junior
67404050 Fruit Supreme dessert, baby food
67404550 Cherry cobbler, baby food, junior
67405000 Peach cobbler, baby food, NS as to strained or junior
67405020 Peach cobbler, baby food, junior
67412000 Dutch apple dessert, baby food, NS as to strained or junior
67412020 Dutch apple dessert, baby food, junior
67414100 Mango dessert, baby food
67415000 Tutti-fruitti pudding, baby food, NS as to strained or junior
67415020 Tutti-fruitti pudding, baby food, junior
67430000 Fruit flavored snack, baby food
67430500 Yogurt and fruit snack, baby food

Baby Crackers, Pretzels, Cookies, and Snack Items

[2'-FL] = 5.7 g/100 g

53801000	Cereal bar with fruit filling, baby food
53803050	Cookie, fruit, baby food
53803100	Cookie, baby food
53803250	Cookie, teething, baby
53803300	Cookie, rice, baby
54350000	Crackers, baby food
54350010	Gerber Finger Foods, Puffs, baby food
54350020	Finger Foods, Puffs, baby food
54360000	Crunchy snacks, corn based, baby food
54408100	Pretzel, baby food
57830100	Gerber Graduates Finger Snacks Cereal, baby food

Table 10. Proposed Conventional Food Categories and Intended Use

Proposed Food Category	Food Uses	Maximum 2'-FL Use Level (g/serving)	RACC[a] (g or mL)	Maximum 2'-FL Use Levels (g/100 g)
Beverages and Beverage Bases	Energy drinks	0.28	360	0.08
	Fitness water and thirst quenchers, sports and isotonic drinks	0.28	360	0.08
Breakfast Cereals	Ready-to-eat breakfast cereals for adults and children	1.2	15 (puffed) 40 (high-fiber) 60 (biscuit-types)	8.0 3.0 2.0
	Hot cereals for adults and children	1.2	40 (dry) ~250 prepared	0.48 (as consumed)
Dairy Product Analogs	Milk substitutes such as soy milk and imitation milks	0.28	240	0.12
Frozen Dairy Desserts and Mixes	Frozen desserts including ice creams* and frozen yogurts, frozen novelties	1.2	~70	1.7
Gelatins, Puddings, and Fillings	Dairy-based puddings, custards, and mousses	1.2	~70	1.7
	Fruit pie filling	1.2	85	1.41
	"Fruit prep" such as fruit filling in bars, cookies, yogurt, and cakes	1.2	~40	3.0
Grain Products and Pastas	Bars, including snack bars, meal-replacement bars, and breakfast bars	0.48	40	1.20
Jams and Jellies, Commercial	Jellies and jams, fruit preserves*, and fruit butters	1.2	~20	6.0
Milk, Whole and Skim	All *Acidophilus* or fortified milks, non-fat and low-fat milk fluids, including fluid milk and reconstituted milk powder*	0.28	240	0.12
Milk Products	Flavored milks, including chocolate milk, coffee drinks, cocoa, smoothies (dairy and fruit-based), other fruit and dairy combinations, yogurt drinks, and fermented milk drinks including kefir**	0.28	240	0.12

	Milk-based meal replacement beverages or diet beverages**	0.28	240	0.12
	Yogurt*, **	1.2	225	0.53
	Formula intended for pregnant women ("mum" formulas, -9 to 0 months)	1.2	200[b]	0.6
Processed Fruits and Fruit Juiced	Fruit drinks, including vitamin and mineral-fortified products	0.28	240	0.12
	Fruit juices*	0.28	240	0.12
Sweet sauces, Toppings, and Syrups	Syrups used to flavor milk beverages	0.28	40	0.70
Other Categories				
Non-Exempt Infant and Follow-On Formula	Infant formula (0 to 6 months), including ready-to-drink formula or formula prepared from powder	0.24	100[b]	0.24 (0.40 g/100 kcal)[c]
	Follow-on formula (6-12 months), including ready-to-drink formula or formula prepared from powder	0.24	100[b]	0.24 (0.40 g/100 kcal)[c]
Baby Foods	Meal replacement products such as PediaSure®	0.24	120[b]	0.2
	Growing-up (toddler) milks (12-36 months)	0.24	120[b]	0.2
	Ready-to-eat, ready-to-serve, hot cereals	1.2	15 (dry) 110 (ready-to-serve)	1.09 (as consumed)
	Yogurt and juice beverages identified as "baby" drinks	1.2	120	1.0
	Desserts including fruit desserts, cobblers, yogurt/fruit combinations ("junior type" desserts)	1.2	110	1.09
	Baby crackers, pretzels, cookies, and snack items	0.4	7	5.7
Medical Foods	Oral nutritional supplements and enteral tube feeding (11 years and older)	4.0	200[b]	2.0

[a] Reference Amounts Customarily Consumed per Eating Occasion (RACC), based on values established in 21 CFR 101.12. Note: when a range of values is reported for a proposed food use, particular foods within that food use may differ with respect to their RACC.

[b] No RACC value exists; therefore, approximate serving sizes are provided according to food manufacturer instructions.

[c] The intended use level in infant formula and baby meal replacement products is 2.4 g per L (0.24 g per 100 mL), or 0.40 g per 100 kcal. For a 100 mL formula that contains 60 kcal, the conversion is as follows:

$$\frac{100\ mL}{60\ kcal} \times \frac{0.24\ g}{100\ mL} = 0.004 \frac{g}{kcal}\ or\ 0.40 \frac{g}{100 kcal}$$

* 2'-FL is intended for use in unstandardized products when standards of identity do not permit its addition.

** Includes ready-to-drink and powder forms.

From: Richard Kraska
To: Morissette, Rachel
Subject: RE: Response on GRN 737
Date: Monday, February 12, 2018 3:21:58 PM
Attachments: image011.png
GRAS.2FL.PDF

Hi Rachel

Sorry about the omission. The letter is attached.

Do you have an idea when you will be making a final response?

Thanks
Rich

Richard Kraska, Ph.D., DABT
Chief Scientific Officer and Executive Vice President
Co-Founder
GRAS Associates, LLC
27499 Riverview Center Parkway
Bonita Springs, FL 34134
T: 239-444-1724 | C: 216-470-7280 | F: 239-444-1723| E: kraska@gras-associates.com

www.gras-associates.com

From: Morissette, Rachel [mailto:Rachel.Morissette@fda.hhs.gov]
Sent: Monday, February 12, 2018 11:44 AM
To: Richard Kraska <kraska@gras-associates.com>
Subject: FW: Response on GRN 737

Dear Rich,

In your response letter to our questions you mention that Dr. Lönnerdal provided a letter discussing his concurrence with the Expert Panel's conclusion. However, I did not see this letter among the attachments that you sent. Can you please send a scanned copy of that letter containing his original signature?

Thank you.

Rachel

Rachel Morissette, Ph.D.
Consumer Safety Officer

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
U.S. Food and Drug Administration
rachel.morissette@fda.hhs.gov

From: Richard Kraska [mailto:kraska@gras-associates.com]
Sent: Friday, January 05, 2018 10:56 AM
To: Morissette, Rachel <Rachel.Morissette@fda.hhs.gov>
Subject: Response on GRN 737

Hi Rachel

Attached please find our letter responding to your questions. Please confirm your receipt of this message.

In response to FDA comments, we have added Dr. Bo Lönnerdal to the expert panel. Dr. Lönnerdal is a recognized expert in pediatric nutrition.

Other attachments included are:

- CVs for all four members of the expert panel
- A short statement of qualification for the members of the expert panel
- A correction of Table 10 in the dossier
- A corrected, non-confidential report for the dietary intake estimate to be used to correct Appendix 8

Thank you for your help and we hope these responses are useful in the review.

Regards
Rich

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DAVIS, CALIFORNIA 95616-8669

January 2, 2018

Richard Kraska, Ph.D., DABT
Chief Scientific Officer and Executive Vice President
GRAS Associates, LLC
27499 Riverview Center Parkway
Bonita Springs, FL 34134

Dear Dr. Kraska,

I have reviewed all the material in the GRAS notice on 2'-fucosyl lactose that you have submitted to FDA. I have considerable expertise in bioactive components in breast milk and have conducted many clinical studies on breast-fed infants and infants fed formula with various added bioactive ingredients of different origin.

I agree with the opinion of the Expert Panel that the Glycosyn and Friesland Campina product is safe and that the proposed uses of 2'-FL in infant formulas and conventional foods for toddlers, children and adults, and in medical foods are safe.

Sincerely

(b) (6)

Bo Lönnerdal, Ph.D.
Distinguished Professor Emeritus of Nutrition & Internal Medicine

From: Richard Kraska
To: Morissette, Rachel; "Katrina Emmel"
Cc: lewis@gras-associates.com
Subject: RE: GRN 000735 medical food uses follow-up to our phone call
Date: Thursday, April 05, 2018 1:40:01 PM
Attachments: image013.png
image037.png

Rachel

That's great. We look forward to your final letter. Thanks again.

Rich

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From: Morissette, Rachel [mailto:Rachel.Morissette@fda.hhs.gov]
Sent: Thursday, April 5, 2018 1:37 PM
To: Richard Kraska <kraska@gras-associates.com>; 'Katrina Emmel' <emmel@gras-associates.com>
Cc: lewis@gras-associates.com
Subject: RE: GRN 000735 medical food uses follow-up to our phone call

Hi Richard,

The email below is sufficient for us to move ahead with your letter. The letter will reference the date we received your request to withdraw and will likely contain a footnote explaining that the intended uses were withdrawn. The filing letter included these uses so the response letter needs to address this discrepancy. However, there will not be any details in the letter beyond the fact that the company requested the uses to be withdrawn and the date that happened.

Best,

Rachel

Rachel Morissette, Ph.D.
Consumer Safety Officer

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
U.S. Food and Drug Administration
rachel.morissette@fda.hhs.gov

From: Richard Kraska [mailto:kraska@gras-associates.com]
Sent: Thursday, April 05, 2018 1:24 PM
To: Morissette, Rachel <Rachel.Morissette@fda.hhs.gov>; 'Katrina Emmel' <emmel@gras-associates.com>
Cc: lewis@gras-associates.com
Subject: RE: GRN 000735 medical food uses follow-up to our phone call

Hi Rachel

Our client has authorized the withdrawal of the medical food use from the GRN. What documentation do you need to officially do this? If you require a formal letter can we forward that to you by email?

One other question: will your "no questions" letter discuss this withdrawal or will it be silent on medical foods?

Thanks for all your help on this notice.

Regards
Rich

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From: Morissette, Rachel [mailto:Rachel.Morissette@fda.hhs.gov]
Sent: Thursday, April 5, 2018 11:32 AM
To: Richard Kraska <kraska@gras-associates.com>; 'Katrina Emmel' <emmel@gras-associates.com>
Subject: GRN 000735 medical food uses follow-up to our phone call

Dear Richard,

Thank you for meeting with us today to discuss the inclusion of medical foods in the intended uses for GRN 000735. Just to briefly recap, we are requesting that Glycosyn and FrieslandCampina withdraw the intended uses in medical foods in GRN 000735 because these uses do not appear to meet the Orphan Drug Act's (21 U.S.C. 360ee(b)(3)) definition of a medical food as follows:

"A food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation."

While the notice does mention that the administration would be under a physician's supervision for the dietary management of a disease or condition, the notice does not mention the need for distinctive nutritional requirements established by a medical evaluation. Currently, there are very few cases that meet this high standard and qualify as medical foods, with one example being the PKU diet that I mentioned. We acknowledge that FDA's interpretation of and policy regarding medical foods is evolving and we are referring companies to our 2016 Guidance About Medical Foods to show FDA's thinking on this topic.

You mentioned that you would like to take a few days to discuss this issue with your clients, which we agreed would be fine. I also mentioned that should the companies decide to withdraw those intended uses and come back later outside the review of this notice, we would suggest setting up a pre-submission meeting with our medical foods staff to discuss the next steps.

Please let me know if you have any questions.

Best regards,

Rachel

Rachel Morissette, Ph.D.
Consumer Safety Officer

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FDA U.S. FOOD & DRUG ADMINISTRATION