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October 20, 2022

Dr. Ellen Anderson
Regulatory Review Scientist
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

Dear Dr. Anderson,

Re: GRAS Notice No. GRN 0001051

In response to your email of October 4, 2022, below are our responses to your request for additional information regarding GRN 0001051. FDA's questions are italicized text and our responses are in plain text.

We hope the responses to your questions are satisfactory. We are looking forward to your completed evaluation. If you have any further questions or need clarification, please reach out to me at saori.akizuki@kyowa-kirin.co.jp.

Yours sincerely,

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Response to Questions from U.S. FDA – GRAS Notice No. GRN 001051 – 2'-Fucosyllactose (2'-FL)

OVERVIEW

Kyowa Hakko Bio Co., Ltd. (Kyowa) presents the following responses to the United States (U.S.) Food and Drug Administration's (FDA's) letter dated 03 October 2022, pertaining to questions from the Agency on the Generally Recognized as Safe (GRAS) uses of 2'-fucosyllactose (2'-FL) described in GRAS Notice No. GRN 001051.

RESPONSES

Question 1

1. *The intended uses of 2'-FL described in the notice include use in non-exempt, infant formula for term infants. Please identify the protein source(s) included in the intended infant formula (e.g., cow milk-based, soy-based, etc.).*

Response

As Kyowa is not a manufacturer of infant formula, the protein sources that will be included in infant formula products to which 2'-FL may be added will be determined by the infant formula manufacturer; however, it is anticipated that 2'-FL may be used with any protein source that is permitted for use in infant formula products in the U.S. The major protein sources used in infant formula products marketed in the U.S. include cow's milk protein–based products and soy protein–based products.

Question 2

2. *In section 3.3 on page 33 of the notice, it states, "2'-FL is intended to be added as a nutritional ingredient to non-exempt infant formula, as well as specified foods and beverages as described in Section 1.3 and defined under 21 CFR 170.3(n)…" We note that 2'-FL does not meet the regulatory definition of a "nutrient" in infant formula under 21 CFR 106.3. We also note that, while there is no regulatory definition of "nutrient" or "nutritional ingredient" for conventional foods and beverages, FDA refers to the Dietary Reference Intakes of the National Academy of Medicine (formerly the Institute of Medicine) in 21 CFR Part 101. In our review of the notice, we would refer to 2'-FL as an ingredient but not a "nutritional ingredient." For the administrative record, please revise this statement with regards to 2'-FL being described as a "nutritional ingredient."*

Response

Kyowa agrees with the FDA that 2'-FL should be referred to as an ingredient rather than a nutritional ingredient. Section 3.3 is updated as follows:

> "*2'-FL is intended to be added as an ingredient to non-exempt infant formula, as well as specified foods and beverages as described in Section 1.3 and defined under 21 CFR 170.3(n)…*"

Question 3

3. *Kyowa intends to use 2'-FL in food categories not previously included among the intended uses of 2'-FL in previous GRAS notices submitted to FDA. Several of the new uses have standards of identity as listed in 21 CFR Parts 131 (milk and cream), 136 (bakery products), and 145 (canned fruits). A footnote to Table 1.3-1 states, "2'-FL is intended for use in unstandardized products where standards of identity…do not permit its addition in standardized products." However, it is not clear what foods would be included among the expanded uses in Table 1.3-1. Please address the following:*

Question 3a

a. *Kyowa proposes use levels of 2'-FL at 24-48 g/kg (2.4-4.8% by weight) in conventional baked goods and baking mixes. Many of these foods have standards of identity (21 CFR Part 136). Given the many subcategories of foods that may fall within the broader heading of "baked goods and baking mixes," we request that you provide a clearer statement of the types of baked goods and baking mixes that are included in the intended uses of 2'-FL.*

   i. *Please clarify which subcategories of baked goods are likely to contain the 2'-FL ingredient. Subcategories of foods may be identified by the first three digits of the NHANES food code scheme.*

   ii. *Please clarify if some or all standardized foods were excluded from the estimates of dietary exposure presented in the notice.*

   iii. *Given the broad intake of "breads and baked goods, including gluten-free" and the impact on dietary exposure to 2'-FL from its consumption (28 to 57% of total mean dietary exposure for ages 1+ years, per page 36 of the notice), we recommend that you refine the dietary exposure estimate by narrowing down the foods considered within these broad categories.*

Response

3.a.i. The subcategories of baked goods in which 2'-FL is intended for use are summarized in Table 3-1 below. The intended uses have been generally categorized according to the first 3 digits of the applicable National Health and Nutrition Examination Survey (NHANES) food codes (as detailed in Appendix A).

Table 3-1 Subcategories of Baked Goods Included as Intended Uses for 2'-FL in the U.S.

Food Category (21 CFR §170.3) (U.S. FDA, 2020)	Food Uses[a]	Use Levels (g/L or g/kg)
Baked Goods and Baking Mixes	Breads (white, whole wheat, specialty, including gluten-free varieties)	24 to 48
	Bagels, rolls, and muffins	
	Biscuits	
	Cakes	
	Cookies	
	Pies	
	Cobblers, fritters, and crepes	
	Doughnuts	
	Crackers	
	Pancakes, waffles, and French toast	

2'-FL = 2'-fucosyllactose; CFR = *Code of Federal Regulations*; U.S. = United States.
[a] 2'-FL is intended for use in unstandardized products where standards of identity, as established under 21 CFR Parts §130 to 169, do not permit its addition in standardized products.

3.a.ii Bakery products with standards of identity include a variety of bread, rolls, and buns (*i.e.*, white, enriched, milk, raisin, and whole wheat). The standard of identity for bread, rolls, and buns laid out in 21 CFR 136.110(c)(18) states that "*other ingredients that do not change the basic identity or adversely affect the physical and nutritional characteristics of the food*" may be added to the bread products. All other varieties of bread, rolls, and buns with standards of identity must conform to the requirements prescribed under Part 136.110. It is expected that the addition of 2'-FL to bread products with standards of identity would comply with 21 CFR 136.110(c)(18) since its addition would not change the identity or the physical and nutritional characteristic of the bread product. Food codes pertaining to these standardized bakery products were included in the exposure assessment to accurately capture the pattern of consumption (as detailed in Appendix A).

3.a.iii The broad range of intake, and consequent contribution to total mean intakes from "breads and baked goods, including gluten-free" is due to the range being presented across all population subgroups (1+ years). The pattern of consumption varies across the individual population groups (*i.e.*, 28% contribution in the 20- to 64-year-old group, and 57% in the 4- to 11-year-old group), with the contribution in the overall population (2+ years) being 37%. It must be noted, however, that a number of assumptions were applied to render conservative intake estimates that would provide overestimates of actual consumption patterns. For example, it was assumed that all products contained 2'-FL at the maximum proposed use level whereas in reality this will not be the case, as the levels added to foods and beverages will vary depending on the product type. Furthermore, it is unlikely that 2'-FL will have 100% market penetration in all identified food categories. Considering these factors, and as the exposure estimates from all proposed uses for all population groups were within background exposure to 2'-FL from human milk in infants, a vulnerable population group, 2'-FL is considered to be safe for all population groups, and the dietary exposure estimate was not refined.

Question 3b

b. We note that the use levels of 2'-FL are up to 17 g/kg (1.7% by weight) in canned fruit. The specific standardized canned fruits are listed in 21 CFR Part 145. Many canned fruits have standards of identity that may preclude use of 2'-FL in this food category. Please clarify the intended use (e.g., provide examples of nonstandardized foods within this category), use level, and the specific types of foods considered in the dietary exposure estimates of 2'-FL from this food category.

Response

It is noted that the standards of identity for canned fruits listed in 21 CFR Part 145 do not permit the addition of 2'-FL (*i.e.*, canned applesauce, canned apricots, canned berries, canned cherries, canned figs, preserved figs, canned fruit cocktail, canned seedless grapes, canned grapefruit, canned peaches, canned pears, canned pineapple, canned plums, canned prunes). 2'-FL is intended for use in unstandardized canned fruits at a use level of 1.7 g/100 g. Examples of unstandardized canned fruit products include canned kumquat, canned orange, canned apple, canned lychee, canned papaya, canned cranberry, and canned rhubarb (see Appendix A for the list of food codes). Food codes for canned fruits with standards of identity were also included in the exposure assessment to generate conservative estimates for the intake of 2'-FL.

Question 3c

c. Kyowa proposes a use level for 2'-FL of up to 1.2 g/L (0.12% by volume) in evaporated or condensed milk. The standards of identity for evaporated milk (21 CFR 131.130), concentrated milk (21 CFR 131.115), and sweetened condensed milk (21 CFR 131.120) do not include use of 2'-FL in these foods. Please clarify the intended use in this food category, including the types of foods used in the estimates of dietary exposure.

Response

Under 21 CFR 131.130, evaporated milk is the liquid food obtained by partial removal of water only from milk that contains not less than 6.5% by weight of milk fat. Under 21 CFR 131.115, concentrated milk is the liquid food obtained by partial removal of water from milk with a milk fat content of not less than 7.5%. Under 21 CFR 131.120, sweetened condensed milk is the food obtained by partial removal of water only from a mixture of milk and safe and suitable nutritive carbohydrate sweeteners that contains not less than 8% milk fat. There are no provisions for optional ingredients in the standards of identity for evaporated milk, concentrated milk, or sweetened condensed milk that would permit the addition of 2'-FL. Therefore, 2'-FL is intended for use in unstandardized evaporated and condensed milk products such as the low-fat and fat-free varieties. Food codes for the standardized products were included in the exposure assessment as a conservative measure.

Question 4

4. *Please clarify if the intended uses of 2'-FL will be substitutional for other non-digestible carbohydrate ingredients in food or if it is intended to be added in combination with other non-digestible carbohydrate ingredients.*

Response

The use of Kyowa's 2'-FL in infant formula and other food uses is intended to be substitutional to other 2'-FL ingredients produced by other manufacturers and currently on the U.S. market; therefore, additive consumption of 2'-FL, beyond the estimated consumption levels detailed in Section 3.4 of GRN 001051, is not expected.

Kyowa is not a final food or infant formula product manufacturer; however, the company considers it likely that infant formula or food manufacturers may use a combination of human milk oligosaccharides (HMOs), or other poorly-digestible carbohydrates, to produce infant formula products or foods containing these ingredients in amounts and combinations that are compositionally similar to human milk. As new infant formula products are subject to premarket notification and other quality requirements under 21 CFR Part 106, the potential use of 2'-FL in combination with other non-digestible carbohydrates would be supported by data and information provided in accordance with the minimum quality requirements for infant formula under 21 CFR 106.96.

Question 5

5. *In the dietary exposure summary on page 36 of the notice, Kyowa cites estimated sources of contribution to dietary intakes of 2'-FL across the U.S. population.*

Question 5a

a. *Please clarify if the levels from contribution of "breads and baked goods" (28-57% total mean intakes) and "beverage whiteners" (1-47% to total mean intakes), were based on the range of exposures for individuals or specific age-gender subpopulations.*

Response

The contribution to the total mean intake of 2'-FL was presented as the range of exposures over the individual age and gender subgroups, excluding infants aged up to 12 months, hence the large variability in the contributions. It is noted that the contributions within the "total population" subgroup are a better representation of the general U.S. population. For the "total population" subgroup aged 2 years and older, "breads and baked goods" and "beverage whiteners" contributed 37% and 32%, respectively, to total mean 2'-FL intakes.

Question 5b

b. You state that 2'-FL for infants 7 to <12 months of age, "other baby foods" and "term infant formula" contribute approximately 45% of "total mean intake." Please provide the other dietary sources of 2'-FL for this population of older infants.

Response

Food uses that contributed >1% and their corresponding percent contributions to the total mean intake of 2'-FL in infants aged 7 to <12 months are presented in Table 5-1. The following proposed food uses contributed >0.1% and <1% to the total mean intakes: canned fruit, baby desserts, fruit juices and nectars, non-dairy milk, frozen dairy desserts, sports/isotonic/energy drinks, edible ices/sherbets/sorbet, non-dairy yogurt and fruit flavored drinks. The remaining proposed uses contributed <0.1% to mean 2'-FL intakes.

Table 5-1 Contribution of Individual Food Uses to Total Mean Intake of 2'-FL in Infants Aged 7 to <12 Months of Age

Proposed Food Use	Contribution to Total Mean Intake of 2'-FL (%)
Other baby foods	25.0
Term infant formula	20.0
Hot cereals (infant and toddler food)	16.2
Breads and baked goods, including gluten-free	12.2
Hot breakfast cereals (breakfast cereals)	6.0
Baby snacks	4.7
Unflavored milk	2.9
Yogurt	2.9
Hypoallergenic formula	2.1
Toddler formula	1.6
Baby juices	1.2
RTE breakfast cereals	1.1

2'-FL = 2'-fucosyllactose; RTE = ready to eat.

Question 6

6. The purity of the 2'-FL ingredient is ≤ 82% (dry basis), by calculation. Kyowa states that "other" components would comprise up to 18% of the dry weight of this ingredient. Kyowa states that other carbohydrates are present in minor amounts (with specified limits in parentheses) and are identified as D-lactose (≤5%), L-fucose (≤1%), D-glucose and D-galactose (≤1%), and difucosyllactose (≤1%). Kyowa also states that ash may be present at ≤0.5%. We note that all these components do not add up to 18%.

Question 6a

a. Please identify the remaining components present in the 2'-FL ingredient.

Response

Kyowa notes that the parameter "Fucosylgalactose" and its specification limit of ≤3% was accidentally omitted from the specifications table (Table 2.3.1-1) of GRN 001051. Kyowa also notes that the specification limits for all carbohydrates were incorrectly reported as on a wet basis and should have been on a dry basis. Kyowa further notes that the specification limit for purity of 2'-FL is ≥82% on a dry basis. The remaining compositional parameters for Kyowa's 2'-FL include ≤5% D-lactose, ≤1% L-fucose, ≤1% D-glucose and D-galactose, and ≤3% difucosyllactose, as well as ≤0.5% ash on a wet basis. Kyowa recognizes that the limits for the specified carbohydrates and ash do not add up to 18%.

Other minor, non-identified peaks were present in the high-performance liquid chromatography with pulsed amperometric detection (HPLC-PAD) chromatograms for 2'-FL, which Kyowa considers to account for the remainder of the ingredient. Kyowa therefore proposes to add the parameter "sum of other carbohydrates" with a limit of ≤10% to the final product specifications. "Sum of other carbohydrates" can be determined by calculation as follows:

Sum of other carbohydrates = 100 (% w/w dry matter [DM]) - 2'-FL (% w/w DM) - quantified carbohydrates (*i.e.*, D-lactose, L-fucose, D-glucose and D-galactose, fucosylgalactose, and difucosyllactose; % w/w DM) - ash (% w/w DM).

Note that the parameter "ash" is reported on a % wet basis in the specifications and Certificates of Analysis and needs to be converted to % DM for the calculation.

For clarity, Kyowa provides an updated Table 2.3.1-1 (specifications) and Table 2.3.3.1-1 (batch analyses data) below. Newly added and corrected information appears in red text.

Table 2.3.1-1 Physical and Chemical Specifications for 2'-FL

Specification Parameter	Specification	Method
Organoleptic		
Appearance	Powder	Visual observation
Color	White to off-white	General Notice, JP[a]
Physicochemical		
Identification	RT of standard ± 3%	HPLC-PAD (internal method)
Purity	≥82% dwb	HPLC-PAD (internal method)
Water	≤9.0 w/w%	JP 2.48[a]
Ash	≤0.5 w/w%	JP 2.44[a]
Residual protein	≤100 mg/kg (0.01%)	Bradford method
pH (25˚C, 5% solution)	4.0 to 9.0	JP 2.54[a]
Other Carbohydrates		
D-lactose	≤5 (dwb%)	HPLC-PAD (internal method)
L-fucose	≤1 (dwb%)	HPLC-PAD (internal method)
D-glucose and D-galactose	≤1 (dwb%)	HPLC-PAD (internal method)
Fucosylgalactose	≤3 (dwb%)	HPLC-PAD (internal method)

Table 2.3.1-1 Physical and Chemical Specifications for 2'-FL

Specification Parameter	Specification	Method
Difucosyllactose	≤3 (dwb%)	HPLC-PAD (internal method)
Sum of other carbohydrates	≤10 (dwb%)	By calculation[b]
Heavy Metals		
Arsenic	≤0.2 mg/kg	USP 233[c]
Cadmium	≤0.2 mg/kg	USP 233[c]
Lead	≤0.2 mg/kg	USP 233[c]
Mercury	≤0.2 mg/kg	USP 233[c]
Iron	≤10 mg/kg	USP 233[c]

2'-FL = 2'-fucosyllactose; DM = dry matter; dwb = dry weight basis; HPLC-PAD = high-performance liquid chromatography with pulsed amperometric detection; JP = Japanese Pharmacopoeia; RT = retention time; USP = United States Pharmacopoeia.
[a] Method is consistent with the compendial method specified in 17th edition of the Japanese Pharmacopeia (2016).
[b] Sum of other carbohydrates = 100 (% w/w DM) - 2'-FL (% w/w DM) - quantified carbohydrates (*i.e.*, D-lactose, L-fucose, D-glucose and D-galactose, fucosylgalactose, and difucosyllactose; % w/w DM) - ash (% w/w DM).
[c] Method is consistent with the compendial method specified in the United States Pharmacopeia 35th revision (2011).

Table 2.3.3.1-1 Summary of Chemical Batch Analyses for the Final 2'-FL Powdered Ingredient Produced with a Genetically Modified Strain of *Escherichia coli* W

Specification Parameter	Specification	Methods of Analysis	Manufacturing Lot					
			A	B	C	D	E	F
Properties								
Appearance	Powder	Visual observation	Complies	Complies	Complies	Complies	Complies	Complies
Color	White to off-white	JP 17; General Notice[a]	Complies	Complies	Complies	Complies	Complies	Complies
pH (25˚C, 5% solution)	4.0 to 9.0	JP 2.54[a]	6.3	6.4	6.2	5.7	6.1	6.2
Purity								
Identification	RT of standard ± 3%	HPLC-PAD (internal method)	Complies	Complies	Complies	Complies	Complies	Complies
Purity (dwb%)	≥82	HPLC-PAD (internal method)	92	92	92	91	96	94
Water (w/w%)	≤9.0	JP 2.48[a]	5.0	3.9	3.9	2.7	2.8	2.3
Ash (w/w%)	≤0.5	JP 2.44[a]	0.2	0.1	0.1	0.0	0.1	0.1
Residual proteins (mg/kg)	NS	Dot-blot (internal method)[b]	≤1 (LOQ)	≤1 (LOQ)	≤1 (LOQ)	≤1 (LOQ)	≤1 (LOQ)	≤1 (LOQ)
Residual proteins (mg/kg)	≤100	Bradford method	≤100[c]	NT	NT	NT	NT	NT
Other Carbohydrates								
D-lactose (dwb%)	≤5	HPLC-PAD (internal method)[d]	3.1	2.7	2.3	2.4	2.1	2.3
L-fucose (dwb%)	≤1	HPLC-PAD (internal method)[d]	≤0.05 (LOQ)	0.1	0.1	0.1	0.1	0.1
D-glucose and D-galactose (dwb%)	≤1	HPLC-PAD (internal method)[d]	0.2	0.1	0.1	0.2	≤0.05 (LOQ)	0.1
Fucosylgalactose (dwb%)	≤3	HPLC-PAD (internal method)[d]	0.8	0.5	0.4	0.9	0.1	0.8

Table 2.3.3.1-1 Summary of Chemical Batch Analyses for the Final 2'-FL Powdered Ingredient Produced with a Genetically Modified Strain of *Escherichia coli* W

Specification Parameter	Specification	Methods of Analysis	Manufacturing Lot					
			A	B	C	D	E	F
Difucosyllactose (dwb%)	≤3	HPLC-PAD (internal method)[d]	0.5	1.4	0.9	1.0	1.1	1.0
Sum of other carbohydrates (dwb%)	≤10	By calculation[e]	3.15	3.1	4.1	4.4	0.45	1.6
Mass balance	NA	By calculation[f]	100	100	100	100	100	100
Heavy Metals								
Arsenic (mg/kg)	≤0.2	USP 233[g,h]	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)
Cadmium (mg/kg)	≤0.2	USP 233[g,h]	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)
Lead (mg/kg)	≤0.2	USP 233[g,h]	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)
Mercury (mg/kg)	≤0.2	USP 233[g,h]	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)
Iron (mg/kg)	≤10	USP 233[g,h]	0.1	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)	≤0.05 (LOQ)

2'-FL = 2'-fucosyllactose; DM = dry matter; dwb = dry weight basis; HPLC-PAD = high-performance liquid chromatography with pulsed amperometric detection; JP = Japanese Pharmacopeia; LOQ = limit of quantification; NA = not applicable; NS = not specified; ppm = parts per million; RT = retention time; USP = United States Pharmacopeia.

[a] Method is consistent with the compendial method specified in 17th edition of the Japanese Pharmacopeia (2016).

[b] Limit of detection = 1 mg/kg.

[c] Evaluated using a limit test at 100 ppm.

[d] LOQ = 0.05 % (w/w).

[e] Sum of other carbohydrates = 100 (% w/w DM) - 2'-FL (% w/w DM) - quantified carbohydrates (*i.e.*, D-lactose, L-fucose, D-glucose and D-galactose, fucosylgalactose, and difucosyllactose; % w/w DM) - ash (% w/w DM).

[f] Mass balance = Sum of 2'-FL (purity), ash, D-lactose, L-fucose, D-glucose and D-galactose, fucosylgalactose, difucosyllactose, and sum of other carbohydrates.

[g] LOQ = 0.05 mg/kg.

[h] Method is consistent with the compendial method specified in the United States Pharmacopeia 35th revision (2011).

Question 6b

b. Batch analyses suggest purity from 91-96% of 2'-FL. Given the specification of ≤ 82% is much lower than the results of batch analyses, we request that you consider adjusting the stated specifications to more closely match the results of batch analyses. If variation is expected in the composition of 2'-FL that is not reflected in in batch analyses, please discuss sources of variation in the composition of the ingredient.

Response

Kyowa wishes to maintain the specified purity limit of ≥82% dry basis for their 2'-FL ingredient. As discussed in response to Question 6a above, the remaining composition of Kyowa's 2'-FL ingredient can be defined by the specified carbohydrate impurities (*i.e.*, ≤5% D-lactose, ≤1% L-fucose, ≤1% D-glucose and D-galactose, ≤3% fucosylgalactose**,** and ≤3% difucosyllactose) and the newly added parameter "sum of other carbohydrates" with a limit of ≤10% to account for the minor, unidentified carbohydrate peaks.

Potential variation in the composition of Kyowa's 2'-FL may come from residual raw materials lactose and glucose, as well as variation in the levels of identified carbohydrates and minor unidentified carbohydrate impurities. The levels of all of these carbohydrate impurities are controlled by specification limits.

Furthermore, all of the carbohydrates present in Kyowa's 2'-FL ingredient would result from residual raw materials or carbohydrate by-products produced during the synthesis of 2'-FL. As humans have the same metabolic pathway for the production of 2'-FL, minor carbohydrate by-products would also be expected to be present in human breast milk. Exposures to these carbohydrates from the intended uses of Kyowa's 2'-FL ingredient are expected to be insignificant compared to background exposures and are not expected to pose safety concerns.

As discussed in Section 2.3.1 of GRN 001051, Kyowa notes that the proposed purity specification for Kyowa's 2'-FL produced using a genetically modified strain of ***Escherichia*** *coli* W is similar to the purity of 2'-FL produced using a genetically modified strain of *E. coli* K-12 (*i.e.*, ≥82% dry basis *vs.* ≥82% relative area under the curve; as specified in GRN 749 and notified to the Agency as GRAS with no questions) (DuPont Nutrition & Health, 2017; U.S. FDA, 2018a).

Question 7

7. *For water, ash, and pH, the specification is listed in terms of the method number associated with the Japanese Pharmacopeia. Although Section 2.3.1 provides a description of the method (Karl-Fischer titration) to determine water content, the other methods are only identified by number. For the administrative record, please provide a brief description of the method or comparable AOAC method for ash and pH.*

Response

Ash

The method of analysis for ash is Japanese Pharmacopeia (JP) 2.44, Residue on Ignition Test (SJP, 2016). This test is harmonized with the European Pharmacopoeia and the United States Pharmacopeia (USP).

Procedure: Take approximately 1 g of sample and weigh precisely in a porcelain crucible that has been pre-baked and previously weighed. Add 3 mL of concentrated sulfuric acid to carbonize the sample and heat until no more smoke is produced. Then add 1 mL concentrated sulfuric acid and heat again until no more smoke is produced. Ignite the sample at 600 ± 50°C for at least 16 hours. Determine the ash content by weighing the sample after it has been cooled in a desiccator. Determine the ash content of 2 samples, and the final value is calculated as the average of the two.

pH

The method of analysis for ash is JP 2.54, pH Determination (SJP, 2016).

Procedure: Prepare a 50 mg/mL sample solution and measure with a pH meter at 25°C. The temperature for pH measurement was incorrectly reported as 20°C in GRN 001051. The correct temperature is 25°C.

Question 8

8. Residual protein is determined by the dot-blot (internal) method. In Section 2.3.1, it is noted that the method was developed and concluded to be suitable for its intended use by Kyowa. The batch analyses show this result is consistently below the LOQ (≤1 mg/kg); however, the specification for residual protein is ≤10 mg/kg.

Question 8a

a. For clarity, please provide a brief description of the dot blot (internal) method and its validation.

Response

Test Method: Prepare 100 mg/mL sample solution and 0.1 µg/mL bovine serum albumin (BSA) standard solution. The proteins in 1 mL of the sample and standard solutions are collected on a polyvinylidene difluoride (PVDF) membrane using a Bio-Dot device, stained with Amido Black solution, and the color of the BSA standard solution (equivalent to 1 part per million [ppm]) is used as the comparison color.

Evaluation Criteria: The color of the sample solution is not darker than that of the standard solution (1 ppm) (coloration is confirmed visually). If the color of the sample solution is darker than that of the standard solution, dilute the sample solution 10-fold and repeat the measurement.

Question 8b

b. Other than the comparison with protein specifications in previous GRNs, please also discuss what proteins, if any, have been detected or anticipated to be present, to justify the need for 10 mg/kg limit. In your response, please address the ability of the method of manufacture to reliably remove of residual protein.

Response

No proteins have been detected in batch analyses for Kyowa's 2'-FL ingredient. Sources of potential protein include the production microorganism. 2'-FL is secreted into the medium by the production organism and intact cells are removed with a ceramic filter followed by purification with a series of cationic resin and anionic resin ion exchangers, and a series of microfiltration steps and an ultrafiltration membrane (molecular weight cut-off of 6,000 Da), which effectively remove any residual microorganism, endotoxins, and residual proteins. Batch analyses data demonstrate the reliability of the purification processes to remove residual proteins, as results for all batches were below the limit of quantification (LOQ) (≤1 mg/kg) of the Dot-Blot method.

Despite the sensitivity of the Dot-Blot method, it is more technically challenging than other colorimetric methods (*e.g.*, Bradford assay). Although the Bradford assay is less sensitive than the Dot-Blot method, there are no safety concerns with the low-level residual protein that are present in the ingredient. Therefore, Kyowa has changed analytical methods to the Bradford assay, which is an internationally recognized standard method. The test for residual proteins in 2'-FL was conducted as a limit test at 100 ppm and no residual proteins were detected in 4 lots of Kyowa's 2'-FL. The results are provided in Table 8-1 below, and the results for Lot A have been added in red font to Table 2.3.3.1-1 reproduced above in response to FDA Question 6a.

Additionally, as Kyowa has changed analytical methods, they have set a new specification limit of ≤100 mg/kg residual proteins using the Bradford method. The specifications have been updated in Table 2.3.1-1 reproduced above in response to FDA Question 6a, with changes marked in red font.

Table 8-1 Summary of Residual Protein Analyses for the Final 2'-FL Powdered Ingredient Produced with a Genetically Modified Strain of *Escherichia coli* W

Specification Parameter	Specification	Methods of Analysis	Manufacturing Lot			
			A	G	H	I
Residual proteins (mg/kg)	≤100	Bradford method	≤100[a]	≤100[a]	≤100[a]	≤100[a]

2'-FL = 2'-fucosyllactose; ppm = parts per million.
[a] Evaluated using a limit test at 100 ppm.

Question 9

9. The specified limit (≤0.5 mg/kg) for ash is higher than the levels reflected in the results of batch analyses. We recommend that you reduce the limit for ash or address why such variation (not reflected in batch analyses) may be expected in total ash levels.

Response

After the 2'-FL containing solution is passed through the cationic resin and anionic resin ion exchangers, the solution may contain residues of acid from the resin regeneration chemicals. The acid is neutralized with NaOH, which forms inorganic salts such as sodium chloride. Such inorganic salts will contribute to the ash content. The specified limit (≤0.5 mg/kg) for ash is higher than the results of the batch analyses as it takes into consideration potential fluctuations resulting from the formation of inorganic salts as described above.

Question 10

10. Table 2.3.3.1-1 lists specifications and results of batch analyses for heavy metals, citing USP 35 (2011) for the method used in these analyses. While USP 35 chapter 233 "elemental impurities-procedures" describes analytical procedures that are suitable for evaluating limits described in USP 232 (drugs) and USP 2232 (dietary supplements), the limits supported may not be appropriate for food ingredients.

Question 10a

a. Please state the analytical method used and confirm that is validated and fit for purpose for elemental analysis of the 2'-FL food ingredients.

Response

The analytical method used for assessment of heavy metals is based on USP 233. Kyowa confirms that this method is suitable for assessing heavy metals in food. Kyowa also notes that "dietary supplement" ingredients are legally defined as food ingredients in the U.S. and there is no scientific basis to infer that a method validated for use on a dietary supplement ingredient would not be similarly suitable for a high-purity food ingredient. A short description of the analytical method is provided below.

Analytical Method: Dissolve the sample in the diluent to prepare a 20 mg/mL sample solution. The sample solution and the calibration curve solution are tested by inductively coupled plasma mass spectrometry. The concentration is determined from the intensity ratio in each element.

Intensity Ratio: Ratio of the counts per second (CPS) of an element to the CPS of an internal standard.

Question 10b

b. The specified limits (each ≤0.2 mg/kg) for arsenic, cadmium, lead, and mercury are much higher than the levels reflected in the results of batch analyses. We recommend that you reduce the limits to reflect results of batch analyses.

Response

Kyowa would like to maintain their current specified limits for arsenic, cadmium, lead, and mercury.

Kyowa notes that their specification limit for lead (≤0.2 mg/kg) is comparable to or less than lead specifications for other 2'-FL ingredients that were concluded to be GRAS and notified to the FDA without questions (GRN 546, 650 – Glycom A/S, 2014, 2016; U.S. FDA, 2015a, 2016).

Kyowa's specification limit for arsenic (≤0.2 mg/kg) is comparable to specification limits for other 2'-FL ingredients that were concluded to be GRAS and notified to the FDA without questions (GRN 571, 749, 897, 929 – Jennewein Biotechnologie GmbH, 2015, 2020; DuPont Nutrition & Health, 2017, 2019; U.S. FDA, 2015b, 2018a, 2020a, 2021a).

Kyowa's specification limit for cadmium (≤0.2 mg/kg) is comparable to the specification limit for other 2'-FL ingredients that were concluded to be GRAS and notified to the FDA without questions (GRN 571, 929 – Jennewein Biotechnologie GmbH, 2015, 2020; U.S. FDA, 2015b, 2021a).

Kyowa's specification limit for mercury (≤0.2 mg/kg) is comparable to or less than the specification limit for other 2'-FL ingredients that were concluded to be GRAS and notified to the FDA without questions (GRN 571, 749, 897, 929 – Jennewein Biotechnologie GmbH, 2015, 2020; DuPont Nutrition & Health, 2017, 2019; U.S. FDA, 2015b, 2018a, 2020a, 2021a).

Therefore, on the basis that the limits for arsenic, cadmium, lead, and mercury are comparable to limits for other 2'-FL ingredients concluded to be GRAS and notified to the FDA without questions, Kyowa does not expect any safety concerns from these limits and proposes to maintain the specification limits for arsenic, cadmium, lead, and mercury at ≤0.2 mg/kg each.

Question 11

11. As noted on page 45 of the notice, 2'-FL is not purified by crystallization. Kyowa states that other GRNs (GRNs 000546, 000571, 000735, and 000929) have described 2'-FL that is concentrated but not crystallized. Although you note similar processes (e.g., ion exchange, filtration) are used in other GRAS notices, the specific purification steps may differ between manufacturers. We request that you provide a clear narrative that discusses the removal of unwanted impurities that arise from the fermentation/production of 2'-FL using the method of manufacture described in GRN 001051. We would look for the narrative to support the schematic overview shown in Figure 2.2.3-1.

Response

The broth is inactivated with heat and acid to avoid contamination of microorganisms other than the production strain. The intact production strain cells are removed using a ceramic filter and the obtained solution is passed through a series of cationic resin and anionic resin ion exchangers to remove a wide range of positively and negatively charged impurities, *e.g*., inorganic salts, organic acids, nucleic acids, proteins, endotoxins, *etc*. The solution is then filtered using a microfiltration membrane to remove any potential microorganisms and concentrated using an evaporator. The concentrated solution is decolorized with activated carbon, and then filtered in a series of filtration steps using a microfiltration membrane and an ultra-filtration membrane (molecular weight cut-off of 6,000 Da) to remove residual endotoxins, as well as any residual protein and organic impurities. The obtained solution is then further concentrated using an evaporator, filtered through a microfiltration membrane, and then spray-dried.

Question 12

12. *In Table 1.3-1, a proposed food use for 2'-FL is in formula intended for pregnant women ("mum" formulas, -9 to 0 months). However, there is no accompanying narrative that supports the safe consumption of 2'-FL in a product specifically targeted to pregnant women who are a vulnerable subpopulation. We also note that in the study by Elison et al., 2016, volunteers were excluded if they were pregnant, seeking pregnancy, and nursing. Thus, it is unclear if safety and tolerance of 2'-FL have been specifically examined in pregnant women. Please provide a narrative that discusses the consumption of 2'-FL by pregnant women and why this is not expected to be a safety concern. As part of this discussion, we suggest including information on how the gut microbiome changes during pregnancy and if this impacts the absorption, distribution, metabolism, or excretion of 2'-FL in this subpopulation.*

Response

As discussed in Section 1.3 of GRN 001051, Kyowa proposed to use their 2'-FL ingredient in the same food uses and at the same use levels (with the exception of cereal and granola bars) as previously concluded to be GRAS by other notifiers, and Kyowa also proposed some additional food uses. The proposed food use of "formula intended for pregnant women ('mum' formulas, -9 to 0 months)" at a use level of 0.6 g/100 g (equivalent to 6 g/kg) has previously been concluded to be GRAS and notified to the FDA without questions in GRNs 735 and 852 (Glycosyn, LLC and Friesland Campino Domo B.V., 2018; BASF SE, 2019; U.S. FDA, 2018b, 2019a). Kyowa reviewed GRNs 735 and 852 to identify a narrative supporting safety of this use; however, no supporting safety information specific to consumption of 2'-FL by pregnant or lactating women was provided in GRNs 735 or 852 (Glycosyn, LLC and Friesland Campino Domo B.V., 2018; BASF SE, 2019; U.S. FDA, 2018b, 2019a).

The study published by Elison *et al.* (2016) was conducted primarily to investigate the effects of 2'-FL and lacto-*N*-neotetraose (LNnT) on compositional changes in the gastrointestinal microbiota, as well as tolerance to the study product, in healthy adults. Pregnant or lactating women, and women seeking to become pregnant, were excluded from the study; although the basis for this exclusion is not stated, a likely reason is to reduce between-subject variability in the study population and the fact that it is standard practice to avoid this population group in clinical trials.

The gastrointestinal microbiota has been reported to differ between pregnant and non-pregnant women, although a high degree of variability exists in both populations (Koren *et al.*, 2012). The optimal gut microbiome is not known; however, decreased diversity has been linked to a disruption of the normal gut microbiota and a higher diversity has been suggested to correlate with a healthier microbiome (Maher *et al.*, 2020). In a recent systematic review, the gut microbiome of pregnant women was reported to be influenced by maternal diet in all 5 studies identified (Maher *et al.*, 2020). Four of the identified studies evaluated the effects of dietary carbohydrate intake on maternal gut microbiota, and in all 4 studies higher dietary fiber intake was positively associated with increased gut microbiota diversity and richness. Although 2' -FL is not a dietary fiber, it is a poorly-digestible carbohydrate that is resistant to hydrolysis by digestive enzymes in the upper digestive tract (Engfer *et al.*, 2000; Gnoth *et al.*, 2000), and is either partially fermented by the intestinal microbiota or excreted unchanged in the feces (Brand-Miller *et al.*, 1995, 1998; Chaturvedi *et al.*, 2001; Coppa *et al.*, 2001; Albrecht *et al.*, 2011; Kuntz *et al*., 2019). Elison *et al.* (2016) reported that the consumption of 2'-FL by healthy adults resulted in an increase in relative abundance of Actinobacteria and *Bifidobacterium*. Given that consumption of dietary fiber did not have an adverse effect on the gut microbiota of pregnant women, but rather resulted in increased diversity of the microbiota, and given that consumption of 2'-FL by healthy adults increased the abundance of Actinobacteria and *Bifidobacterium* and had no adverse effects on microbiota, no adverse effects on gut microbiota diversity would be expected from the consumption of 2'-FL.

No studies were identified in which 2'-FL was consumed by pregnant women. However, as discussed above, 2'-FL is a poorly-digestible carbohydrate and studies conducted with other poorly-digestible carbohydrates in pregnant women can be used to support the safe use of 2'-FL in this population group. In a recent meta-analysis of studies involving supplementation of pregnant women with probiotics or prebiotics (*i.e.,* galactooligosaccharides [GOS] or fructooligosaccharides [FOS]), the authors reported no serious health concerns regarding maternal or infant health and concluded that prebiotics are "*safe to use during and after pregnancy and lactation*" (Sheyholislami and Connor, 2021).

Based on the safe consumption of other poorly-digestible carbohydrates by pregnant women, the lack of observations indicative of potential adverse effects reported in any of the pre-clinical studies or human studies in infants included in GRN 001051, as well as the increased permeability and sensitivity of the infant gastrointestinal tract compared to adults, no adverse effects attributable to the consumption of 2'-FL by pregnant women are anticipated to occur. As 2'-FL intakes from all proposed conditions of use in GRN 001051 are within the range of background exposure from human milk in infants, a vulnerable population group, 2'-FL is considered to be safe for all population groups, including pregnant women.

Question 13

13. *In Table 3.4.2.1-2, the dietary exposure for toddlers (1-3 years; 640 mg/kg bw/d) is listed as being above the dietary exposure for infants (0-6 months; 570 mg/kg bw/d). However, we note that Laursen 2021 states,[1] "Complementary feeding, due to the introduction of dietary fibers and new protein sources, induces a shift in the gut microbiota and metabolism away from the milk-adapted and toward a more mature and diverse adult-like community…" and "the complementary feeding period coincides with a phase of drastic changes in the gut microbiota…, including a rapid decline in HMO-degrading Bifidobacterium species." Please provide a narrative that discusses the safety and tolerability of 2'-FL consumption by toddlers given that the dietary exposure for toddlers (i.e., for all proposed food uses) is higher than for infants who may have gut microbiota adapted for HMO-degradation (0-6 months).*

[1] Laursen MF. Gut Microbiota Development: Influence of Diet from Infancy to Toddlerhood [published online ahead of print, 2021 Aug 30]. Ann Nutr Metab. 2021;1-14. doi:10.1159/000517912

Response

The use level of 2'-FL previously concluded to be GRAS in term (non-exempt) infant formula and toddler formula of 2.4 g/L corresponds to the representative mean concentration of 2'-FL in mature human milk. Based on the estimated intake calculations presented in GRN 001051, dietary exposure in toddlers from all proposed conditions of use of 2'-FL (640 mg/kg body weight/day) is within the mean range of background exposure of breastfed infants (197 to 770 mg/kg body weight/day) and well below the highest estimated exposure of breastfed infants of Secretor mothers (1,254 mg/kg body weight/day) calculated using concentrations of 2'-FL reported in mature human milk and assuming a standard infant body weight of 6.7 kg (World Health Organization [WHO] Growth Chart[1]; average of 50th percentile for boys and girls at 4 months) and a milk consumption of 1.2 L/day (Butte *et al.*, 2002; da Costa *et al.*, 2010; Nielsen *et al.*, 2011; EFSA, 2013). The estimates of consumption of 2'-FL from all proposed uses were calculated conservatively, under the assumption that all food products within a food category contain 2'-FL at the maximum specified level of use. However, 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. Therefore, the estimates of consumption of 2'-FL as presented in GRN 001051 are expected to be higher than actual consumption levels.

Background intakes of 2'-FL by breastfed infants were calculated in GRN 001051 using a mean range of 1.1 to 4.3 g 2'-FL/L in mature human milk. This range is consistent with a recent review of HMO concentrations throughout lactation, in which mean 2'-FL concentrations in human milk were reported to be up to 4,102 mg/L during the fourth month of lactation, and up to 1,882 mg/L during the sixth month of lactation (Thum *et al.*, 2021). Thus, data on the levels in human milk continue to support the safe background dietary mean intakes of 2'-FL at up to 735 mg/kg body weight/day (assuming a body weight of 6.7 kg and milk consumption of 1.2 L/day).

[1] https://www.cdc.gov/growthcharts/who_charts.htm.

As noted by Laursen (2021), the introduction of complementary feeding, which introduces dietary fibers and proteins, induces a change in the composition of the gut microbiota as more and different substrates become available for the microbiota. This change in microbial composition is to be expected, as Laursen (2021) also notes that diet is a "*key factor influencing the gut microbiota development in early life*." If HMO consumption decreases, then it is expected that populations of HMO-consuming bacteria in the gastrointestinal tract will also decreased in abundance, as the bacteria would have less substrate to consume.

Laursen (2021) further notes that breastfeeding maintains *Bifidobacterium* species as the dominant organism in the gut microbiota, as "*due to the human milk oligosaccharide (HMO) content, breast milk represents a strong selective factor for shaping the early infancy microbiota, dominated by specific Bifidobacterium species*." In contrast, formula feeding is associated with a gut microbiota characterized by a higher prevalence of potentially pathogenic taxa, which are reported to likely be the result of the lack of HMOs and a higher protein content in infant formula. However, in a recent human study, the consumption of infant formula with added 2'-FL and LNnT resulted in an infant gut microbiota more similar to that of breastfed infants with higher relative abundances of *Bifidobacterium* (Berger *et al.*, 2020), demonstrating that the gut microbiota of infants is influenced by the availability of HMOs, including 2'-FL. Based on the results of this study, it would be expected that HMO-degrading *Bifidobacterium* species in the gut microbiota would persist and potentially increase in abundance as long as 2'-FL was available from the diet. Furthermore, it is likely that the infant gut has bacteria adapted to HMO degradation due to consumption of HMOs, and that the level of HMO degradation would change with the level of HMO consumption, rather than age alone. Therefore, if dietary intakes of 2'-FL in toddlers were the same as or potentially higher than dietary intakes of 2'-FL in formula fed infants aged 0 to 6 months, it would be expected that the gut microbiota would maintain a high abundance of HMO-degrading *Bifidobacterium* species that are capable of metabolizing 2'-FL due to its availability.

In addition, there is no evidence to suggest that decreasing levels of 2'-FL or HMOs in general in human milk over the course of lactation could be due to reduced tolerance of the breastfed child to HMOs, or that introduction of HMOs in the diet of older children could be disadvantageous.

Kyowa notes that the use of 2'-FL in toddler formula and foods at levels encompassing those included in GRN 001051 have previously been concluded to be GRAS and notified to the FDA without objection in GRNs 546, 571, 735, 749, 815, 852, 897, 929, and 932 (Glycom A/S, 2014, 2018; Jennewein Biotechnologie GmbH, 2015, 2020; DuPont Nutrition & Health, 2017, 2019; Glycosyn, LLC and Friesland Campino Domo B.V., 2018; BASF SE, 2019; Advanced Protein Technologies, Corp., 2020; U.S. FDA, 2015a,b, 2018a,b, 2019a,b, 2020a, 2021a,b). As 2'-FL intakes in toddlers reported in these GRAS Notices, as well as in GRN 001051, from all proposed conditions of use are within background exposure from human milk in infants, a vulnerable population group, and considering that it is expected that the gut microbiota would maintain a high abundance of HMO-degrading *Bifidobacterium* species that are capable of metabolizing 2'-FL due to its availability, 2'-FL is considered to be safe for all population groups, including toddlers.

Question 14

14. *In the clinical study by Elison et al., 2016, in which the highest 2'-FL dose was 20 g/p/d, the authors state, "Compared with placebo, most of the changes in GSRS [Gastrointestinal Symptom Rating Scale] scores were insignificant, again with the exception of the of the intervention group receiving the highest dose of 2'FL, who reported increased nausea, rumbling, bloating, passing of gas, diarrhoea, loose stools and urgency to pass stools…" Despite these observed gastrointestinal symptoms, the study authors concluded, "the daily uptake of up to 20 g of the HMO 2'FL . . . is perfectly safe in adults."*

Question 14a

a. *In Table 3.4.2.1-1, Kyowa reports several population groups which are expected to have a dietary exposure to 2'-FL at or above 20 g/p/d at the 90th percentile: female adults, male adults, and the elderly. Given that there does not appear to be published data to support safety and tolerance of 2'-FL above 20 g/p/d, and that Elison et al., 2016 concluded that up to 20 g/p/d was safe, please provide a narrative that discusses the safety and tolerability of 2'-FL at dietary exposures above 20 g/p/d.*

Response

Dietary exposure estimates included in GRN 001051 range from 20.0 to 20.6 g/person/day in the stated population groups. These estimates of consumption are calculated conservatively, under the assumption that all food products within a food category contain 2'-FL at the maximum specified level of use. However, the levels added to specific foods will vary and it is unlikely that 2'-FL will have 100% market penetration in all identified food categories. Therefore, the estimates consumption of 2'-FL as presented in GRN 001051 are expected to overestimate actual consumption levels.

In the study reported by Elison *et al.* (2016), the doses provided to study subjects were chosen to be within the range of average consumption by infants on a body weight basis. The study products, 2'-FL, LNnT, or 2'-FL with LNnT at doses of 0 (2 g glucose placebo), 5, 10, or 20 g/day were provided as plastic bottles containing pre-measured amounts of powdered study product. The subjects were instructed to mix the powder with water and consume the product with breakfast daily for 2 weeks. This type of bolus consumption (*i.e.,* a full daily dose consumed entirely during 1 eating occasion) would result in a higher concentration of 2'-FL in the gastrointestinal tract, which is a likely cause of the mild gastrointestinal effects reported by Elison *et al.* (2016). Bolus consumption of 2'-FL is not representative of the consumption of 2'-FL as proposed by Kyowa as an ingredient in infant, toddler, or "mum" formula, or as an ingredient in conventional foods and beverages. Under Kyowa's proposed conditions of use, as indicated in GRN 001051, the intake of 2'-FL would be distributed throughout the day, resulting in lower concentrations of the ingredient in the gastrointestinal tract at any time compared to a bolus consumption of up to 20 g 2'-FL. The adverse effects reported by Elison *et al.* (2016), while mild, monitorable, transient, and reversible, are therefore not representative of effects that might be expected upon dietary consumption of 2'-FL and would not be expected to occur in population groups consuming a conservative estimate of 20.6 g 2'-FL over the course of a day.

As discussed in GRN 001051, on the basis of the chemical and structural identity to 2'-FL from human milk, the intakes of Kyowa's 2'-FL under the conditions of intended use in comparison to the natural background dietary exposure to 2'-FL from the consumption of human milk is pivotal in the assessment of the safety of Kyowa's 2'-FL ingredient. The estimated dietary intakes of 20.0 to 20.6 g/person/day (equivalent to 209 to 273 mg/kg body weight/day) in female adults, male adults, and the elderly are within the average range of 2'-FL intakes from mature human milk (197 to 770 mg/kg body weight/day), and below maximum 2'-FL intakes from mature Secretor milk (1,254 mg/kg body weight/day). As 2'-FL intakes from all proposed conditions of use are within background exposure from human milk in infants, a vulnerable population group, 2'-FL is considered to be safe for all population groups, including female adults, male adults, and the elderly.

Question 14b

b. For a 60-kg adult, the corresponding dietary exposure on a body weight basis of 20 g/p/d is 333 mg/kg bw/d. In Table 3.4.2.1-2, we note that children (4-11 years) have a dietary exposure to 2'-FL at the 90th percentile (i.e., 411 mg/kg bw/d) that is significantly higher than 333 mg/kg bw/d. Given that Elison et al., 2016 reported that adults experienced a range of GI symptoms at this dose and did not include volunteers younger than 18 years, please provide a narrative that discusses the safety and tolerability of 2'-FL in children at dietary exposures as high as 411 mg/kg bw/d.

Response

As noted above, 2'-FL was consumed as a bolus dose in the study by Elison *et al.* (2016). This type of bolus consumption (*i.e.,* a full daily dose consumed entirely during 1 eating occasion) would result in a higher concentration of 2'-FL in the gastrointestinal tract, which is a likely cause of the mild gastrointestinal effects reported by Elison *et al.* (2016). Bolus consumption of 2'-FL is not representative of consumption of 2'-FL from Kyowa's proposed conditions of use. Under Kyowa's proposed conditions of use, as indicated in GRN 001051, the intake of 2'-FL would be distributed throughout the day, resulting in lower concentrations of the ingredient in the gastrointestinal tract at any time compared to a bolus consumption of up to 20 g 2'-FL. The adverse effects reported by Elison *et al.* (2016), while mild, monitorable, transient, and reversible, are therefore not representative of effects that might be expected upon dietary consumption of 2'-FL and would not be expected to occur in children consuming foods with 2'-FL throughout the day.

Kyowa notes that the adult dose of 20 g 2'-FL/day would be equivalent to a dose of 333 mg 2'-FL/kg body weight/day for a 60-kg adult. Although the estimated consumption of 2'-FL in children under Kyowa's intended conditions of use is higher than the equivalent adult dose on a body weight basis (*i.e.*, 411 mg/kg body weight/day in children 4 to 11 years of age), this level of consumption is well within the average range of 2'-FL intakes from mature human milk (197 to 770 mg/kg body weight/day) and substantially below maximum 2'-FL intakes in breastfed infants from mature Secretor milk (1,254 mg/kg body weight/day). As 2'-FL intakes from all proposed conditions of use are within background exposure from human milk in infants, a vulnerable population group, 2'-FL is considered to be safe for all population groups, including children.

Question 14c

c. If 2'-FL is added to foods that also contain other non-digestible carbohydrates or dietary fibers (e.g., energy bars) or if 2'-FL is consumed by those who already have a high fiber diet, the cumulative effects on the gastrointestinal tract should be considered. While gastrointestinal symptoms are often associated with the high intake of dietary fiber, it is often assumed that consumers are aware of such properties, and it can be argued that the intake of dietary fiber is self-limiting. However, a consumer may be less likely to associate these symptoms with products that contain an HMO such as 2'-FL (i.e., a naturally occurring component of human milk). Please discuss the safety and tolerability of 2'-FL considering the potential for additive and cumulative gastrointestinal effects when 2'-FL is consumed with other non-digestible carbohydrates and/or dietary fiber in the diet.

Response

Kyowa is a manufacturer of ingredients rather than final consumer food and beverage products; however, the company considers it likely that food or beverage manufacturers may include a combination of HMOs or other poorly-digestible carbohydrates in final food products. For infant formula specifically, any new infant formula containing new HMOs, a new HMO combination, or a new combination of HMOs and other poorly-digestible carbohydrates in the U.S. would be subject to Section 412 of the *Federal Food, Drug, and Cosmetic Act* (FFDCA) (21 USC §350[a]), which would ensure that any combination of HMOs or other poorly-digestible carbohydrates would be supported by tolerance and safety testing in infants (U.S. FDA, 2022a).

The combined use of 2'-FL and other non-digestible carbohydrates or dietary fibers also may occur in other food and beverage products, where such uses are permitted. The safety and expected tolerability of the combined intake of different HMOs and other poorly-digestible carbohydrates have been addressed in previous GRAS Notices to which the FDA responded with no questions (GRNs 815, 833, 880, 881, 932, 951, and 1014) (Glycom A/S, 2018, 2019a,b,c; Advanced Protein Technologies, Corp., 2020; DuPont Nutrition & Biosciences, 2020; Chr. Hansen, Inc., 2021; U.S. FDA, 2019b,c, 2020b,c, 2021b, 2021c, 2022b). As noted in a response to questions posed by the FDA regarding GRN 815, other poorly-digestible carbohydrate sources of dietary fiber (*i.e.,* FOS, GOS, and inulin) are GRAS for use in various food and beverage products, and recent GRAS evaluations have raised no safety concerns regarding their combined addition to foods (GRN 815, 849, 990 – Glycom A/S, 2018; Intrinsic Organics, LLC, 2019; Tata Chemicals Limited, 2020; U.S. FDA, 2019b,d, 2021d).

It has been reported that average consumption of dietary fiber in adult Americans is approximately 15 g/day, while recommended fiber intake is 25 to 30 g/day (UCSF, 2022). Although the Institute of Medicine (IOM) did not include 2'-FL or other HMOs in their consideration of isolated fibers, it was concluded that excess consumption of other poorly-digestible carbohydrates is likely to be self-limiting, and an upper limit for consumption was not set (IOM, 2005). In addition, adverse effects reported in pre-clinical and clinical studies of poorly-digestible carbohydrates have been generally limited to those indicative of high concentrations of poorly-digestible material in the lower gastrointestinal tract attributable to either very high dietary consumption in animal studies or large bolus doses consumed in human studies (*i.e.*, Elison *et al.*, 2016). As discussed above, bolus consumption of 2'-FL is not representative of consumption of 2'-FL from Kyowa's proposed conditions of use. Under Kyowa's proposed conditions of use, as indicated in GRN 001051, the intake of 2'-FL would be distributed throughout the day, resulting in lower concentrations of the ingredient in the gastrointestinal tract at any time, which would not be expected to result in adverse

gastrointestinal effects. Furthermore, considering the low background dietary intakes of fiber, the consumption of 2'-FL spaced throughout the day from Kyowa's proposed conditions of use would not be expected to result in adverse gastrointestinal effects. Thus, Kyowa is of the opinion that the potential for additive and cumulative gastrointestinal effects when 2'-FL is consumed with other non-digestible carbohydrates and/or dietary fiber in the diet is limited and does not represent a safety concern.

Question 15

15. *On page 52, Kyowa discusses the results of the unpublished 90-day toxicity study performed using the 2'-FL ingredient as the test article. Specifically, Kyowa states, "Several statistically significant differences were reported with respect to food consumption, functional observation, clinical biochemistry, organ weights, gross necropsy, and histopathology." Kyowa notes that these effects were considered by the study authors to be "incidental and not toxicologically relevant"; however, without information beyond what is currently provided in the notice, some of these observations could appear counter to a GRAS conclusion for Kyowa's 2'-FL ingredient. Please provide a brief explanation of some of the main statistically significant changes that were observed in this study and why they are not expected to be a safety concern.*

Response

A summary of the statistically significant changes in the high-dose group (2,000 mg/kg body weight/day) compared to the control and a discussion of their toxicological relevance are provided below.

Females in the 2,000 mg/kg body weight/day dose group consumed statistically significantly ($P<0.01$) less food on Day 35; however, there were no further statistically significant differences before or after, and the reported significant difference had no influence on body weight change. Hence, this difference was not considered to be toxicologically significant.

There were no significant differences in functional observations. This parameter was incorrectly reported in the study summary in GRN 001051.

Males in the 2,000 mg/kg body weight/day dose group experienced a statistically significant reduction in the number of urinations ($P<0.01$ in the parametric procedure) and defecations ($P<0.05$ in the non-parametric procedure). However, the changes were minor (*i.e.*, the difference between the mean in the high-dose group and that in the control was ≤1.0) and were considered to have no toxicological implications.

Sodium levels measured in the blood of females in the 2,000 mg/kg body weight/day group were statistically significantly higher than the control. However, the difference between the control and high-dose group (142 ± 1 and 140 ± 1 mmol/L, respectively) was small and the study authors concluded it to be of no toxicological significance.

The absolute weight of the pituitary gland of males in the 2,000 mg/kg body weight/day dose group was statistically significantly decreased compared to the control group. However, this was not considered to be toxicologically significant as there were no corresponding changes in relative weight or macroscopic or microscopic changes.

There were no abnormal gross findings noted in any of the animals. This parameter was incorrectly reported in the study summary in GRN 001051.

Histopathological changes were judged by the study authors to be incidental, as the observed changes are commonly found in healthy rats and/or there were no substantial differences in the degree or frequency of the changes between the control and 2,000 mg/kg body weight/day group.

Question 16

16. *On page 81, Kyowa discusses the clinical trial by Leung et al., 2020 which investigated the effects of "young child formulas" on respiratory and gastrointestinal infections in Chinese children (1-2.5 years). As stated in the notice, the study authors reported a statistically significant increase in the duration of upper respiratory tract infections in children consuming formula containing 2'-FL at 3.0 g/L. Please discuss why this finding is not expected to be a safety concern and comment on any additional published studies that have investigated the safety of 2'-FL consumption by children.*

Response

In the study conducted by Leung *et al.* (2020), Chinese children 1 to 2.5 years of age (n=114/group) were provided for 6 months with the control formula (standard milk formula, supplemented with 4 g GOS/L) or test formulas containing bioactive proteins, GOS (4 g/L), 2'-FL (3 g/L), and milk fat at levels typically found in human breast milk; milk formula containing lower levels of bioactive proteins; or milk formula supplemented with 2'-FL (3 g/L) only. Based on a statistical power analysis included in the publication, this study was adequately powered to detect changes in the primary outcomes, upper respiratory tract infection (URTI) incidence and gastrointestinal tract infection (GITI) duration in the study population.

Parents/caretakers were instructed to record signs of illness in a diary and to return to the clinic for evaluation by a pediatrician and collection of nasal swabs upon observation of signs of respiratory illness. New cases of URTI were defined as a runny nose and/or cough persisting for >2 days, beginning ≥7 days after the previous episode.

The authors reported no statistically significant differences in the primary outcomes (URTI incidence and GITI duration) among the 3 study groups. The authors noted that subjects consuming the formula containing 2'-FL only had longer (but not more frequent) URTI, as well as a significantly higher number of cough episodes, runny nose episodes, and days with fever. Notably, although there were statistically significant increases in these parameters in subjects given formula supplemented with 2'-FL only, the magnitudes of these increases were small[2] and their biological relevance was not discussed, other than the authors noted that the total fever days in the group given formula supplemented with 2'-FL only was very low (2.5 ± 3.1). The authors reported no difference in the nasal microbiome or pathogen profiles[3] as assessed from swabs collected from subjects throughout the study and upon report of signs of respiratory illness. Furthermore, significant increases in duration of URTI, episodes of cough or runny nose, and days with fever were not reported in the other group given formula containing 2'-FL at 3 g/L with GOS and other bioactive compounds compared to the control formula group. Statistical comparisons between the 3 test formula groups were not presented.

[2] Magnitude of increase compared to control formula: duration of URTI (1.6 days), number of cough episodes (3.3 episodes), number of runny nose episodes (2.5 episodes), number of days with fever (0.6 days).
[3] It is noted in the supplementary material to this publication that nasal pathogen analysis included analysis for 16 RNA viruses, 2 DNA viruses, and 3 types of "atypical bacteria".

However, when considered as adverse events, there were no significant differences compared to control formula in the number of URTI; percent of subjects experiencing cases of acute bronchiolitis, bronchitis, or otitis media; percent of subjects experiencing isolated fevers; or the percent of subjects experiencing viral infections (not meeting the definition of URTI or gastrointestinal infection). Furthermore, the investigators judged that none of the adverse events were product-related and this conclusion was confirmed by an independent data safety monitoring board.

Kyowa notes that Leung *et al.* (2020) concluded that the study formulas were safe and supported normal growth in toddlers. In addition, the concentration of 2'-FL in the formulas administered in this study (3.0 g/L) is higher than Kyowa's proposed use level in toddler formula of 2.4 g/L, which corresponds to the mean concentration of 2'-FL reported in mature human milk and which has been concluded to be GRAS by Kyowa and in previous GRAS Notices for 2'-FL to which the FDA has responded with no questions. Kyowa therefore concludes that the results of the study published by Leung *et al.* (2020) do not indicate a potential safety concern for 2'-FL under Kyowa's proposed conditions of use.

The results of an intervention study conducted in healthy infants and children 2 months to 4 years of age with documented cow's milk protein allergy that was included in GRN 001051 and GRN 000897 provide additional support for the safe consumption of formula containing 2'-FL and LNnT in young children (DuPont Nutrition & Health, 2019; Nowak-Wegrzyn *et al*., 2019). In this study, a whey-based extensively hydrolyzed formula (EHF) supplemented with 2'-FL and LNnT at concentrations of 1.0 and 0.5 g/L, respectively, was evaluated in a cross-over double-blind placebo-controlled food challenge (DBPCFC) followed by an open-label period of consumption of the test formula (minimum of 240 mL/day) for an additional 7 to 9 days during which tolerability and safety were assessed. A total of 55 subjects completed the 1-week open challenge, with an average consumption of 302 ± 161 mL formula/day. No treatment-related gastrointestinal symptoms (flatulence, abnormal stool frequency/consistency, reactions, increased spitting-up or vomiting), reactions requiring early discontinuation, or serious adverse events were reported. In addition, the favorable results of other studies previously reviewed by the FDA in GRAS Notices submitted to the Agency of 2'-FL in infant populations, which are inherently more vulnerable due to their younger age, provide additional support for the safety of 2'-FL in older children (Marriage *et al.*, 2015; Goehring *et al.*, 2016; Kajzer *et al.*, 2016; Puccio *et al.*, 2017; Storm *et al.*, 2019).

Question 17

17. *On pages 5 and 39, Kyowa indicates that 2'-FL has a proposed intended use in oral nutritional supplements. However, the recommended conditions of use are given as, "2 g 2'-FL/45 g powdered serving or 250 mL ready to consume product, consumed twice per day for a total daily intake of 4 g 2'-FL/day" (emphasis added). This recommended intake pattern could imply a dose or therapeutic effect. Furthermore, it implies that intake greater than twice per day (4 g 2'-FL/day) may have adverse effects. If Kyowa expects 2'-FL to have a therapeutic effect when consumed in oral nutritional supplements, please clarify why 2'-FL should not be considered as a drug.*

Response

Kyowa's intended use level is based on oral nutrition products containing 2'-FL that are already on the U.S. market. The typical conditions of use as indicated above were provided to permit calculation of intakes for the purposes of assessing safety of the intended use and resulting consumption. Based on this calculation, it is anticipated that the total daily consumption from this use would be 4 g/day. However, as oral nutritional beverages containing Kyowa's 2'-FL are not intended for therapeutic use, this consumption level represents a "typical use level" rather than a recommended daily dose.

Question 18

18. One of Kyowa's stated intended uses for 2'-FL is in enteral tube feeds. We note that consumers requiring enteral tube feeds consist of vulnerable subpopulations suffering from a range of ailments that may preclude assessing the safety of ingredients such as 2'-FL in those specific subpopulations. Please clarify if the population expected to receive 2'-FL through enteral tube feeds will be under the care of a physician and/or other medical supervision.

Response

Kyowa is not a final food product manufacturer; however, the company anticipates that people who receive 2'-FL by enteral tube feeding would use the product under the guidance of their physician or health care professional.

Question 19

19. On page 80, Kyowa discusses newly identified clinical studies in infants that utilize test formulas containing 2'-FL. We note that Vandenplas et al., 2020; Roman et al., 2020; and Storm et al., 2019 report on test formulas that contain 2'-FL at levels below the proposed use level of 2.4 g/L. Please clarify how these studies support Kyowa's GRAS conclusion for 2'-FL at a use level of 2.4 g/L.

Response

Although the concentrations of 2'-FL used in the studies reported by Vandenplas *et al*. (2020), Roman e*t al*. (2020), and Storm *et al*. (2019) are lower than Kyowa's proposed use level in infant formula of 2.4 g/L, which has been concluded by Kyowa and by previous notifiers to be safe and suitable and GRAS, these 3 studies add to the overall body of evidence demonstrating the safe consumption of 2'-FL by infants. The studies published by Storm *et al.* (2019) and Roman *et al.* (2020) also were included to support the safety of 2'-FL in GRNs 897, 929, and 1014 (DuPont Nutrition & Health, 2019; Jennewein Biotechnologie GmbH, 2020; Chr. Hansen, Inc., 2021; U.S. FDA, 2020a, 2021a, 2022b).

Question 20

20. Please state whether the Escherichia coli production strain has been deposited in a recognized culture collection and provide the deposit designation.

Response

Kyowa has deposited the production strain at the National Biological Resource Center (NBRC). The deposition number is NITE SD_00487.

Question 21

21. Please indicate whether the E. coli production strain is expected to produce antimicrobials or secondary metabolites.

Response

The host strain, *E. coli* W, is a Gram-negative, rod-shaped, facultative anaerobe that has been used in the industrial production of amino acids for foods, feeds, medicines, and various other applications for nearly 80 years (Archer *et al.*, 2011; UniProt, 2021). Based on the long history of safe use of the host strain in food manufacturing, production of antimicrobials or secondary metabolites is not expected. Furthermore, the genetic changes made by Kyowa to the host strain are well-characterized and not related to the production of antimicrobials or secondary metabolites.

Question 22

22. Please indicate whether the E. coli production strain is expected to be resistant to antibiotics.

Response

Two antibiotic resistance genes are used during the genetic manipulations to produce the production strain, an ampicillin-resistance gene (which encodes beta-lactamase) and the chloramphenicol resistance gene (which encodes chloramphenicol acetyl transferase). Following selection of the desired genetic traits using the antibiotic resistance genes, both antibiotic resistant genes are removed from the production organism. The absence of the ampicillin-resistant gene and chloramphenicol-resistant gene in the production organism is confirmed by plating with ampicillin or chloramphenicol and confirming ampicillin or chloramphenicol sensitivity.

Kyowa has conducted antimicrobial susceptibility testing for the parental strain, *E. coli* W, and the modified production strain. Testing was conducted in accordance with the European Food Safety Authority (EFSA) *Guidance on the characterisation of microorganisms used as feed additives or as production organisms* (EFSA, 2018) and the Clinical and Laboratory Standard Institute (CLSI) guidelines (CLSI, 2004). The results of the testing demonstrated that *E. coli* W and the genetically modified *E. coli* W production strain were susceptible to all antibiotics tested (*i.e.,* ampicillin, gentamycin, kanamycin, streptomycin, ciprofloxacin, colistin, tetracycline, and fosfomycin).

Kyowa also conducted a search of the genetically modified *E. coli* W production organism genome for genes encoding proteins involved in antimicrobial resistance using the ResFinder database. No sequences were identified that are homologous to sequences encoding proteins relevant to resistance to sulphonamide, nitroimidazole, oxazolidinone, quinolone, rifampicin, fusidic acid, tetracycline, colistin, phenicol, β-lactam, trimethoprim, fosfomycin, aminoglycoside, or glycopeptide antimicrobials. The gene *mdfa*, which encodes a multidrug efflux pump that confers resistance to macrolide antimicrobials was identified (100% sequence homology) in the genome of the production organism. However, this gene is widely distributed in the genome of the parental strain, *E. coli* W and other safe *E. coli* strains (*i.e*., B and K strains), and importantly, the production organism is not present in Kyowa's final 2'-FL ingredient. Thus, the *mdfa* gene is not an acquired element, but is intrinsic to the *E. coli* W strain and is therefore not considered to be a safety concern (EFSA, 2018).

Kyowa therefore confirms that the *E. coli* W-derived production strain does not contain any elements expected to confer resistance to antibiotics.

Question 23

23. On page 14, section 2.2.1.2 of the notice, it states that 5 genes are deleted from the parental strain. For the administrative record, please provide a brief description of the deleted gene sequences.

Response

Kyowa inserted 5 heterologous genes into 5 genomic loci which are not involved in the production of 2'-FL. The description of deleted gene products are as follows. Galactokinase, which catalyzes the phosphorylation of α-D-galactose to galactose-1-phosphate; aldose 1-epimerase, which catalyzes the isomerisation of α-D-glucose to β-D-glucose; a hypothetical protein with unspecified function; N-acetylglucosamine phosphotransferase system permease, which is a transmembrane protein that facilitates the uptake and phosphorylation of N-acetylglucosamine; a transmembrane channel that permits movement of water in and out of the cell; and an uncharacterized transmembrane transporter protein.

Question 24

24. On page 16 of the notice, it states that the final step of the fermentation process is a "heat treatment (sterilization)" step. For the administrative record, please describe this step, including the time and temperature parameters used.

Response

The heat treatment (sterilization) step consists of heating the fermentation broth to over 70°C for no more than 40 minutes.

The final step of the fermentation process is updated as follows: The production of 2'-FL is stopped *via* heat treatment (sterilization at over 70°C for no more than 40 minutes), after which the broth is cooled and acidified.

Question 25

25. For the administrative record, please identify any materials used in the production and formulation of 2'-FL that are derived from major allergens (other than cow milk allergens) and state whether these will be present in the final product. If none, please provide a statement confirming this.

Response

None of the raw materials used in the production and formulation of 2'-FL are derived from major allergens (other than lactose derived from milk). Therefore, no materials derived from major allergens or allergens are present in the final product.

Question 26

26. For the administrative record, please briefly specify how the purity of the E. coli production strain is ensured.

Response

The purity, identity, and productivity of the production strain is confirmed when the master cell bank is prepared. Cells from the master cell bank are inoculated to produce the working frozen cell bank. The master cell bank and the working frozen cell bank are stored in a deep freezer that is temperature controlled and monitored. The purity is controlled by monitoring the metabolic activity of the production strain (*i.e.*, productivity), which is determined by analyzing the production of 2'-FL. The productivity is assessed by analyzing the 2'-FL content using high-performance liquid chromatography (HPLC) as an in-process control step of the manufacturing process. Hence, the purity of the production strain is ensured as part of the manufacturing process.

Question 27

27. On pages 20, 24, and 49 of the notice, Kyowa lists a specification for "Cronobacter spp. (Enterobacter sakazakii)". Kyowa states that the method used is ISO 22964:2017, which corresponds to "Microbiology of the Food Chain - Horizontal Method for the Detection of Cronobacter spp." For the administrative record, please clarify whether you test for the presence of Cronobacter spp. or C. sakazakii, specifically. If it is the former, please state whether presumptive positives are further analyzed to determine if the isolate is C. sakazakii.

Response

The method ISO 22964:2017 is used to determine the presence of *Cronobacter* spp. only. If *Cronobacter* spp. is detected, the batch does not meet the specification and cannot be sold. Hence, no further analysis is conducted.

Question 28

28. On page 20 of the notice, Kyowa states: "Analysis of 6 lots of 2'-FL (5 of which were non-consecutive)…" Please indicate which lots are non-consecutive.

Response

Lots A, B, C, D, and F are non-consecutive.

Question 29

29. *We note the following general comments for the administrative record. No further action or response is necessary from Kyowa regarding these comments:*

    a. *On page 29, Kyowa lists medical foods among the intended uses previously concluded to be GRAS. We would like to note that some "medical food" uses were in conventional foods (that did not meet the definition of medical foods) and/or were removed from the scope of the respective notices. Such changes in the intended uses would have been reflected in amendments to the respective GRAS notices. These amendments should be available as part of the records in FDA's online GRAS Notice Inventory.*

    b. *On page 32, Kyowa discusses the concentration of 2'-FL in human milk and states that milk levels summarized in Table 3.2-1 were determined in GRN 000546. Since the proposed use level of 2.4 g 2'-FL/L has been previously concluded to be GRAS, we note the following for informational purposes: Since the closure of GRN 000546, additional information on 2'-FL concentrations in human milk have been published in the literature, including several systematic reviews, and we suggest including this information in future GRAS notices for HMO ingredients.*

    c. *While we are not aware of any citizen petition (submitted under 21 CFR 10.30) to FDA to label 2'-FL as a dietary fiber, the estimated dietary exposure to 2'-FL in GRN 001051 suggests uses analogous to fiber ingredients.*

Response

No response required.

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Appendix A
Representative Food Codes for Proposed Food Uses of 2'-Fucosyllactose in the U.S. (2017-2018 NHANES Data)

Representative Food Codes for Proposed Food Uses of 2'-Fucosyllactose in the U.S. (2017-2018 NHANES Data)

Baked Goods and Baking Mixes

Breads and baked goods, including gluten-free
[2'-FL] = 4.8 g/100 g

13252600	Tiramisu
51000100	Bread, NS as to major flour
51000110	Bread, NS as to major flour, toasted
51000180	Bread, made from home recipe or purchased at a bakery, NS as to major flour
51000190	Bread, made from home recipe or purchased at a bakery, toasted, NS as to major flour
51000200	Roll, NS as to major flour
51000300	Roll, hard, NS as to major flour
51000400	Roll, bran, NS as to type of bran
51101000	Bread, white
51101010	Bread, white, toasted
51101050	Bread, white, made from home recipe or purchased at a bakery
51101060	Bread, white, made from home recipe or purchased at a bakery, toasted
51102010	Bread, white with whole wheat swirl
51102020	Bread, white with whole wheat swirl, toasted
51105010	Bread, Cuban
51105040	Bread, Cuban, toasted
51106010	Bread, native, water, Puerto Rican style
51106020	Bread, native, water, toasted, Puerto Rican style
51106200	Bread, lard, Puerto Rican style
51106210	Bread, lard, toasted, Puerto Rican style
51106300	Bread, caressed, Puerto Rican style
51106310	Bread, caressed, toasted, Puerto Rican style
51107010	Bread, French or Vienna
51107040	Bread, French or Vienna, toasted
51108010	Focaccia, Italian flatbread, plain
51108100	Naan, Indian flatbread
51109010	Bread, Italian, Grecian, Armenian
51109040	Bread, Italian, Grecian, Armenian, toasted
51109100	Bread, pita
51109110	Bread, pita, toasted
51109150	Bread, pita with fruit
51109200	Bread, pita with fruit, toasted
51111010	Bread, cheese
51111040	Bread, cheese, toasted
51113010	Bread, cinnamon
51113100	Bread, cinnamon, toasted

51115010 Bread, cornmeal and molasses
51115020 Bread, cornmeal and molasses, toasted
51119010 Bread, egg, Challah
51119040 Bread, egg, Challah, toasted
51121015 Garlic bread, NFS
51121025 Garlic bread, from fast food / restaurant
51121035 Garlic bread, from frozen
51121045 Garlic bread, with parmesan cheese, from fast food / restaurant
51121055 Garlic bread, with parmesan cheese, from frozen
51121065 Garlic bread, with melted cheese, from fast food / restaurant
51121075 Garlic bread, with melted cheese, from frozen
51121110 Bread, onion
51121120 Bread, onion, toasted
51122000 Bread, reduced calorie and/or high fiber, white or NFS
51122010 Bread, reduced calorie and/or high fiber, white or NFS, toasted
51122100 Bread, reduced calorie and/or high fiber, white or NFS, with fruit and/or nuts
51122110 Bread, reduced calorie and/or high fiber, white or NFS, with fruit and/or nuts, toasted
51122300 Bread, white, special formula, added fiber
51122310 Bread, white, special formula, added fiber, toasted
51123010 Bread, high protein
51123020 Bread, high protein, toasted
51127010 Bread, potato
51127020 Bread, potato, toasted
51129010 Bread, raisin
51129020 Bread, raisin, toasted
51130510 Bread, white, low sodium or no salt
51130520 Bread, white, low sodium or no salt, toasted
51133010 Bread, sour dough
51133020 Bread, sour dough, toasted
51134000 Bread, sweet potato
51134010 Bread, sweet potato, toasted
51135000 Bread, vegetable
51135010 Bread, vegetable, toasted
51140100 Bread, dough, fried
51150000 Roll, white, soft
51153000 Roll, white, hard
51154010 Roll, white, hot dog bun
51154100 Roll, white, hamburger bun
51154510 Roll, diet
51154550 Roll, egg bread
51154600 Roll, cheese
51155000 Roll, French or Vienna
51156500 Roll, garlic
51157000 Roll, white, hoagie, submarine

51158100	Roll, Mexican, bolillo
51159000	Roll, sour dough
51165000	Coffee cake, yeast type
51180010	Bagel
51180030	Bagel, with raisins
51180080	Bagel, with fruit other than raisins
51183990	Breadsticks, NFS
51184000	Breadsticks, hard, NFS
51184100	Breadsticks, hard, reduced sodium
51184200	Breadsticks, soft, NFS
51184210	Breadsticks, soft, from fast food / restaurant
51184220	Breadsticks, soft, from frozen
51184230	Breadsticks, soft, with parmesan cheese, from fast food / restaurant
51184240	Breadsticks, soft, with parmesan cheese, from frozen
51184250	Breadsticks, soft, topped with melted cheese
51184260	Breadsticks, soft, stuffed with melted cheese
51185000	Croutons
51186010	Muffin, English
51186100	Muffin, English, with raisins
51186130	Muffin, English, cheese
51186160	Muffin, English, with fruit other than raisins
51187000	Melba toast
51187020	Anisette toast
51188500	Zwieback toast
51300050	Bread, whole grain white
51300060	Bread, whole grain white, toasted
51300100	Bagel, whole grain white
51300110	Bread, whole wheat
51300120	Bread, whole wheat, toasted
51300140	Bread, whole wheat, made from home recipe or purchased at bakery
51300150	Bread, whole wheat, made from home recipe or purchased at bakery, toasted
51300175	Bread, chappatti or roti, wheat
51300180	Bread, puri, wheat
51300185	Bread, paratha, wheat
51300210	Bread, whole wheat, with raisins
51300220	Bread, whole wheat, with raisins, toasted
51300300	Bread, sprouted wheat
51300310	Bread, sprouted wheat, toasted
51301010	Bread, wheat or cracked wheat
51301020	Bread, wheat or cracked wheat, toasted
51301040	Bread, wheat or cracked wheat, made from home recipe or purchased at bakery
51301050	Bread, wheat or cracked wheat, made from home recipe or purchased at bakery, toasted
51301120	Bread, wheat or cracked wheat, with raisins
51301130	Bread, wheat or cracked wheat, with raisins, toasted

51301510	Bread, wheat or cracked wheat, reduced calorie and/or high fiber
51301520	Bread, wheat or cracked wheat, reduced calorie and/or high fiber, toasted
51301540	Bread, French or Vienna, whole wheat
51301550	Bread, French or Vienna, whole wheat, toasted
51301600	Bread, pita, whole wheat
51301610	Bread, pita, whole wheat, toasted
51301620	Bread, pita, wheat or cracked wheat
51301630	Bread, pita, wheat or cracked wheat, toasted
51301700	Bagel, wheat
51301750	Bagel, whole wheat
51301800	Bagel, wheat, with raisins
51301805	Bagel, whole wheat, with raisins
51301820	Bagel, wheat, with fruit and nuts
51301900	Bagel, wheat bran
51302500	Muffin, English, wheat bran
51302520	Muffin, English, wheat bran, with raisins
51303010	Muffin, English, wheat or cracked wheat
51303030	Muffin, English, whole wheat
51303050	Muffin, English, wheat or cracked wheat, with raisins
51303070	Muffin, English, whole wheat, with raisins
51303100	Muffin, English, whole grain white
51306000	Breadsticks, hard, whole wheat
51320010	Roll, wheat or cracked wheat
51320060	Roll, wheat or cracked wheat, hot dog bun
51320070	Roll, wheat or cracked wheat, hamburger bun
51320500	Roll, whole wheat
51320550	Roll, whole wheat, hot dog bun
51320560	Roll, whole wheat, hamburger bun
51320700	Roll, whole grain white
51320710	Roll, whole grain white, hot dog bun
51320720	Roll, whole grain white, hamburger bun
51401010	Bread, rye
51401020	Bread, rye, toasted
51401030	Bread, marble rye and pumpernickel
51401040	Bread, marble rye and pumpernickel, toasted
51401200	Muffin, English, rye
51404010	Bread, pumpernickel
51404020	Bread, pumpernickel, toasted
51404500	Bagel, pumpernickel
51404550	Muffin, English, pumpernickel
51407010	Bread, black
51407020	Bread, black, toasted
51420000	Roll, rye
51421000	Roll, pumpernickel

51501010	Bread, oatmeal
51501020	Bread, oatmeal, toasted
51501040	Bread, oat bran
51501050	Bread, oat bran, toasted
51501080	Bagel, oat bran
51502010	Roll, oatmeal
51503000	Muffin, English, oat bran
51503040	Muffin, English, oat bran, with raisins
51601010	Bread, multigrain, toasted
51601020	Bread, multigrain
51601210	Bread, multigrain, with raisins
51601220	Bread, multigrain, with raisins, toasted
51602010	Bread, multigrain, reduced calorie and/or high fiber
51602020	Bread, multigrain, reduced calorie and/or high fiber, toasted
51620000	Roll, multigrain
51620020	Roll, multigrain, hot dog bun
51620030	Roll, multigrain, hamburger bun
51630000	Bagel, multigrain
51630100	Bagel, multigrain, with raisins
51630200	Muffin, English, multigrain
51801010	Bread, barley
51801020	Bread, barley, toasted
51804010	Bread, soy
51804020	Bread, soy, toasted
51805010	Bread, sunflower meal
51805020	Bread, sunflower meal, toasted
51806010	Bread, rice
51806020	Bread, rice, toasted
51807000	Injera, Ethiopian bread
51808000	Bread, gluten free
51808010	Bread, gluten free, toasted
51808050	Breadsticks, hard, gluten free
51808100	Roll, gluten free
52101000	Biscuit, NFS
52101040	Crumpet
52102040	Biscuit, from refrigerated dough
52103000	Biscuit, from fast food / restaurant
52104010	Biscuit, home recipe
52104040	Biscuit, wheat
52104100	Biscuit, cheese
52104200	Biscuit with fruit
52105100	Scone
52105200	Scone, with fruit
53100050	Cake batter, raw, chocolate

53100070 Cake batter, raw, not chocolate
53100100 Cake or cupcake, NS as to type
53101100 Cake, angel food, without icing or filling
53101200 Cake, angel food, with icing or filling
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
53102800 Cake or cupcake, Black Forest
53103000 Cake, Boston cream pie
53104100 Cake or cupcake, carrot, without icing or filling
53104260 Cake or cupcake, carrot, with icing or filling
53104300 Cake, carrot, diet
53104400 Cake or cupcake, coconut, with icing or filling
53104500 Cheesecake
53104550 Cheesecake with fruit
53104600 Cheesecake, chocolate
53105270 Cake or cupcake, chocolate, devil's food or fudge, with icing or filling
53105275 Cake or cupcake, chocolate, devil's food or fudge, without icing or filling
53105300 Cake or cupcake, German chocolate, with icing or filling
53105500 Cake, chocolate, with icing, diet
53106500 Cake, cream, without icing or topping
53108200 Snack cake, chocolate, with icing or filling
53108220 Snack cake, chocolate, with icing or filling, reduced fat and calories
53109200 Snack cake, not chocolate, with icing or filling
53109220 Snack cake, not chocolate, with icing or filling, reduced fat and calories
53109300 Cake, Dobos Torte
53110000 Cake, fruit cake, light or dark, holiday type cake
53111000 Cake or cupcake, gingerbread
53112100 Ice cream cake
53113000 Cake, jelly roll
53114000 Cake or cupcake, lemon, without icing or filling
53114100 Cake or cupcake, lemon, with icing or filling
53115100 Cake or cupcake, marble, without icing or filling
53115200 Cake or cupcake, marble, with icing or filling
53115310 Cake or cupcake, nut, without icing or filling
53115320 Cake or cupcake, nut, with icing or filling
53115410 Cake or cupcake, oatmeal
53115450 Cake or cupcake, peanut butter
53116000 Cake, pound, without icing or filling
53116020 Cake, pound, with icing or filling
53116270 Cake, pound, chocolate
53116350 Cake, pound, Puerto Rican style

53116390 Cake, pound, reduced fat, cholesterol free
53116500 Cake or cupcake, pumpkin, without icing or filling
53116510 Cake or cupcake, pumpkin, with icing or filling
53116550 Cake or cupcake, raisin-nut
53116570 Cake, Ravani
53116600 Cake, rice flour, without icing or filling
53116650 Cake, Quezadilla, El Salvadorian style
53117100 Cake or cupcake, spice, without icing or filling
53117200 Cake or cupcake, spice, with icing or filling
53118100 Cake, sponge, without icing or filling
53118200 Cake, sponge, with icing or filling
53118300 Cake, sponge, chocolate
53118410 Rum cake, without icing
53118500 Cake, torte
53118550 Cake, tres leche
53119000 Cake, pineapple, upside down
53120270 Cake or cupcake, white, with icing or filling
53120275 Cake or cupcake, white, without icing or filling
53121270 Cake or cupcake, yellow, with icing or filling
53121275 Cake or cupcake, yellow, without icing or filling
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
53124110 Cake or cupcake, zucchini
53200100 Cookie, batter or dough, raw
53201000 Cookie, NFS
53202000 Cookie, almond
53203000 Cookie, applesauce
53203500 Cookie, biscotti
53204000 Cookie, brownie, NS as to icing
53204010 Cookie, brownie, without icing
53204100 Cookie, brownie, with icing or filling
53204840 Cookie, brownie, reduced fat, NS as to icing
53204860 Cookie, brownie, fat free, NS as to icing
53205250 Cookie, butterscotch, brownie
53205260 Cookie, bar, with chocolate
53206000 Cookie, chocolate chip
53206020 Cookie, chocolate chip, made from home recipe or purchased at a bakery
53206030 Cookie, chocolate chip, reduced fat
53206100 Cookie, chocolate chip sandwich
53206500 Cookie, chocolate, made with rice cereal
53206550 Cookie, chocolate, made with oatmeal and coconut, no bake

53207000 Cookie, chocolate or fudge
53207020 Cookie, chocolate or fudge, reduced fat
53207050 Cookie, chocolate, with chocolate filling or coating, fat free
53208000 Cookie, marshmallow, chocolate-covered
53208200 Cookie, marshmallow pie, chocolate covered
53209005 Cookie, chocolate, with icing or coating
53209010 Cookie, sugar wafer, chocolate-covered
53209015 Cookie, chocolate sandwich
53209020 Cookie, chocolate sandwich, reduced fat
53209100 Cookie, chocolate, sandwich, with extra filling
53209500 Cookie, chocolate and vanilla sandwich
53210000 Cookie, chocolate wafer
53210900 Cookie, graham cracker with chocolate and marshmallow
53211000 Cookie bar, with chocolate, nuts, and graham crackers
53215500 Cookie, coconut
53220000 Cookie, fruit-filled bar
53220010 Cookie, fruit-filled bar, fat free
53220030 Cookie, fig bar
53220040 Cookie, fig bar, fat free
53222010 Cookie, fortune
53222020 Cookie, cone shell, ice cream type, wafer or cake
53223000 Cookie, gingersnaps
53223100 Cookie, granola
53224000 Cookie, ladyfinger
53224250 Cookie, lemon bar
53225000 Cookie, macaroon
53226000 Cookie, marshmallow, with coconut
53226500 Cookie, marshmallow, with rice cereal, no bake
53226550 Cookie, marshmallow, with rice cereal and chocolate chips
53226600 Cookie, marshmallow and peanut butter, with oat cereal, no bake
53228000 Cookie, meringue
53230000 Cookie, molasses
53231000 Cookie, Lebkuchen
53231400 Cookie, multigrain, high fiber
53233000 Cookie, oatmeal
53233010 Cookie, oatmeal, with raisins
53233040 Cookie, oatmeal, reduced fat, NS as to raisins
53233050 Cookie, oatmeal sandwich, with creme filling
53233060 Cookie, oatmeal, with chocolate chips
53233080 Cookie, oatmeal sandwich, with peanut butter and jelly filling
53233100 Cookie, oatmeal, with chocolate and peanut butter, no bake
53234000 Cookie, peanut butter
53234100 Cookie, peanut butter, with chocolate
53234250 Cookie, peanut butter with rice cereal, no bake

53235000 Cookie, peanut butter sandwich
53235500 Cookie, with peanut butter filling, chocolate-coated
53235600 Cookie, Pfeffernusse
53236000 Cookie, Pizzelle
53236100 Cookie, pumpkin
53237000 Cookie, raisin
53237010 Cookie, raisin sandwich, cream-filled
53237500 Cookie, rum ball, no bake
53238000 Cookie, sandwich-type, not chocolate or vanilla
53239000 Cookie, shortbread
53239010 Cookie, shortbread, reduced fat
53239050 Cookie, shortbread, with icing or filling
53239100 Pocky
53240000 Cookie, animal
53240010 Cookie, animal, with frosting or icing
53241500 Cookie, butter or sugar
53241510 Marie biscuit
53241600 Cookie, butter or sugar, with fruit and/or nuts
53242000 Cookie, sugar wafer
53242500 Cookie, toffee bar
53243000 Cookie, vanilla sandwich
53243010 Cookie, vanilla sandwich, extra filling
53243050 Cookie, vanilla sandwich, reduced fat
53244010 Cookie, butter or sugar, with chocolate icing or filling
53244020 Cookie, butter or sugar, with icing or filling other than chocolate
53246000 Cookie, tea, Japanese
53247000 Cookie, vanilla wafer
53247050 Cookie, vanilla wafer, reduced fat
53247500 Cookie, vanilla with caramel, coconut, and chocolate coating
53251100 Cookie, rugelach
53260030 Cookie, chocolate chip, sugar free
53260200 Cookie, oatmeal, sugar free
53260300 Cookie, sandwich, sugar free
53260400 Cookie, sugar or plain, sugar free
53260500 Cookie, sugar wafer, sugar free
53260600 Cookie, peanut butter, sugar free
53261000 Cookie, gluten free
53270100 Cookies, Puerto Rican style
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
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
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
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
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
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
53341500 Pie, buttermilk
53341750 Pie, chess

53342000 Pie, chocolate cream
53342070 Pie, chocolate cream, individual size or tart
53343000 Pie, coconut cream
53343070 Pie, coconut cream, individual size or tart
53344000 Pie, custard
53344070 Pie, custard, individual size or tart
53344200 Mixed fruit tart filled with custard or cream cheese
53344300 Dessert pizza
53345000 Pie, lemon cream
53345070 Pie, lemon cream, individual size or tart
53346000 Pie, peanut butter cream
53346500 Pie, pineapple cream
53347000 Pie, pumpkin
53347070 Pie, pumpkin, individual size or tart
53347500 Pie, sour cream, raisin
53347600 Pie, squash
53348000 Pie, strawberry cream
53348070 Pie, strawberry cream, individual size or tart
53360000 Pie, sweet potato
53365000 Pie, vanilla cream
53370000 Pie, chiffon, not chocolate
53371000 Pie, chiffon, chocolate
53373000 Pie, black bottom
53381000 Pie, lemon meringue
53381070 Pie, lemon meringue, individual size or tart
53382000 Pie, chocolate-marshmallow
53385000 Pie, pecan
53385070 Pie, pecan, individual size or tart
53385500 Pie, oatmeal
53386000 Pie, pudding, flavors other than chocolate
53387000 Pie, Toll house chocolate chip
53390000 Pie, shoo-fly
53390100 Pie, tofu with fruit
53391000 Pie shell
53391100 Pie shell, graham cracker
53391150 Pie shell, chocolate wafer
53391200 Vanilla wafer dessert base
53400200 Blintz, cheese-filled
53400300 Blintz, fruit-filled
53410100 Cobbler, apple
53410200 Cobbler, apricot
53410300 Cobbler, berry
53410500 Cobbler, cherry
53410800 Cobbler, peach

53410850	Cobbler, pear
53410880	Cobbler, plum
53410900	Cobbler, rhubarb
53415100	Crisp, apple, apple dessert
53415120	Fritter, apple
53415200	Fritter, banana
53415220	Fritter, berry
53415300	Crisp, blueberry
53415400	Crisp, cherry
53415500	Crisp, peach
53430000	Crepe, NS as to filling
53430100	Crepe, chocolate filled
53430200	Crepe, fruit filled
53441210	Basbousa
53520000	Doughnut, NFS
53520100	Doughnut, cake type, plain
53520120	Doughnut, chocolate
53520130	Doughnut, cake type, powdered sugar
53520135	Doughnut, cake type, with icing
53520140	Doughnut, cake type, chocolate icing
53520160	Doughnut, chocolate, with chocolate icing
53520170	Doughnut holes
53520200	Churros
53520510	Beignet
53521110	Doughnut, yeast type
53521130	Doughnut, yeast type, with chocolate icing
53521140	Doughnut, jelly
53521210	Doughnut, custard-filled
53521230	Doughnut, custard-filled, with icing
53610100	Coffee cake, crumb or quick-bread type
53610170	Coffee cake, crumb or quick-bread type, with fruit
53610200	Coffee cake, crumb or quick-bread type, cheese-filled
54001000	Crackers, NFS
54102010	Graham crackers
54102015	Graham crackers (Teddy Grahams)
54102020	Graham crackers, chocolate covered
54102050	Crackers, oatmeal
54102060	Crackers, Cuban
54102100	Graham crackers, reduced fat
54102200	Graham crackers, sandwich, with filling
54103000	Crackers, breakfast biscuit
54200100	Crackers, butter, reduced sodium
54201010	Crackers, matzo, reduced sodium
54202020	Crackers, saltine, reduced sodium

54204020	Crackers, wheat, reduced sodium
54204030	Crackers, woven wheat, reduced sodium
54301010	Crackers, butter, plain
54301020	Crackers, butter, flavored
54301030	Crackers, butter (Ritz)
54301100	Crackers, butter, reduced fat
54304000	Crackers, cheese
54304005	Crackers, cheese (Cheez-It)
54304020	Crackers, cheese (Goldfish)
54304100	Crackers, cheese, reduced fat
54304110	Crackers, cheese, reduced sodium
54304150	Crackers, cheese, whole grain
54305010	Crackers, crispbread
54305020	Crackers, flatbread
54307000	Crackers, matzo
54308000	Crackers, milk
54313000	Crackers, oyster
54318500	Rice cake
54319000	Crackers, rice
54319005	Crackers, rice and nuts
54319020	Popcorn cake
54319500	Rice paper
54325000	Crackers, saltine
54325010	Crackers, saltine, reduced fat
54325060	Crackers, saltine, multigrain
54326000	Crackers, multigrain
54328000	Crackers, sandwich
54328100	Crackers, sandwich, peanut butter filled
54328105	Crackers, sandwich, peanut butter filled (Ritz)
54328110	Crackers, sandwich, reduced fat, peanut butter filled
54328120	Crackers, whole grain, sandwich, peanut butter filled
54328200	Crackers, sandwich, cheese filled
54328210	Crackers, sandwich, cheese filled (Ritz)
54336000	Crackers, water
54336100	Crackers, wonton
54337010	Crackers, woven wheat
54337020	Crackers, woven wheat, plain (Triscuit)
54337030	Crackers, woven wheat, flavored (Triscuit)
54337060	Crackers, woven wheat, reduced fat
54338000	Crackers, wheat
54338010	Crackers, wheat, plain (Wheat Thins)
54338020	Crackers, wheat, flavored (Wheat Thins)
54338100	Crackers, wheat, reduced fat
54339000	Crackers, corn

54340100 Crackers, gluten free, plain
54340110 Crackers, gluten free, flavored
54402700 Pita chips
54440010 Bagel chips
55100005 Pancakes, NFS
55100010 Pancakes, plain, from frozen
55100015 Pancakes, plain, reduced fat, from fozen
55100020 Pancakes, with fruit, from frozen
55100025 Pancakes, with chocolate, from frozen
55100030 Pancakes, whole grain, from frozen
55100035 Pancakes, whole grain, reduced fat, from frozen
55100040 Pancakes, gluten free, from frozen
55100050 Pancakes, plain, from fast food / restaurant
55100055 Pancakes, with fruit, from fast food / restaurant
55100060 Pancakes, with chocolate, from fast food / restaurant
55100065 Pancakes, whole grain, from fast food / restaurant
55100070 Pancakes, whole grain and nuts, from fast food / restaurant
55100080 Pancakes, from school, NFS
55101000 Pancakes, plain
55101015 Pancakes, plain, reduced fat
55103000 Pancakes, with fruit
55103020 Pancakes, pumpkin
55103100 Pancakes, with chocolate
55105000 Pancakes, buckwheat
55105100 Pancakes, cornmeal
55105200 Pancakes, whole grain
55105205 Pancakes, whole grain, reduced fat
55106000 Pancakes, gluten free
55200010 Waffle, NFS
55200020 Waffle, plain, from frozen
55200030 Waffle, plain, reduced fat, from frozen
55200040 Waffle, fruit, from frozen
55200050 Waffle, chocolate, from frozen
55200060 Waffle, whole grain, from frozen
55200070 Waffle, whole grain, reduced fat, from frozen
55200080 Waffle, whole grain, fruit, from frozen
55200090 Waffle, gluten free, from frozen
55200100 Waffle, plain, from fast food / restaurant
55200110 Waffle, chocolate, from fast food / restaurant
55200120 Waffle, fruit, from fast food / restaurant
55200130 Waffle, whole grain, from fast food / restaurant
55200200 Waffle, from school, NFS
55201000 Waffle, plain
55203000 Waffle, fruit

55203600 Waffle, chocolate
55203700 Waffle, cinnamon
55204000 Waffle, cornmeal
55205000 Waffle, whole grain
55208000 Waffle, gluten free
55211050 Waffle, plain, reduced fat
55212000 Waffle, whole grain, reduced fat
55300010 French toast, NFS
55300020 French toast, plain, from frozen
55300030 French toast, whole grain, from frozen
55300040 French toast, gluten free, from frozen
55300050 French toast, plain, from fast food / restaurant
55300055 French toast, whole grain, from fast food / restaurant
55300060 French toast, from school, NFS
55301000 French toast, plain
55301010 French toast, plain, reduced fat
55301015 French toast, whole grain
55301020 French toast, whole grain, reduced fat
55301025 French toast, gluten free
55301030 French toast sticks, NFS
55301031 French toast sticks, plain, from frozen
55301040 French toast sticks, plain, from fast food / restaurant
55301048 French toast sticks, from school, NFS
55301050 French toast sticks, plain
55301055 French toast sticks, whole grain
55310100 Fried bread, Puerto Rican style
55400010 Crepe, NFS
55401000 Crepe, plain
55501000 Chinese pancake
55610300 Dumpling, plain
55702100 Dosa (Indian), plain
91550100 Coconut cream cake, Puerto Rican style

Beverages and Beverage Bases

Soft drinks (regular and diet)
[2'-FL] = 0.12 g/100 g

92400000 Soft drink, NFS
92400100 Soft drink, NFS, diet
92410310 Soft drink, cola
92410315 Soft drink, cola, reduced sugar
92410320 Soft drink, cola, diet
92410340 Soft drink, cola, decaffeinated

92410350 Soft drink, cola, decaffeinated, diet
92410360 Soft drink, pepper type
92410370 Soft drink, pepper type, diet
92410390 Soft drink, pepper type, decaffeinated
92410400 Soft drink, pepper type, decaffeinated, diet
92410410 Soft drink, cream soda
92410420 Soft drink, cream soda, diet
92410510 Soft drink, fruit flavored, caffeine free
92410520 Soft drink, fruit flavored, diet, caffeine free
92410550 Soft drink, fruit flavored, caffeine containing
92410560 Soft drink, fruit flavored, caffeine containing, diet
92410610 Soft drink, ginger ale
92410620 Soft drink, ginger ale, diet
92410710 Soft drink, root beer
92410720 Soft drink, root beer, diet
92410810 Soft drink, chocolate flavored
92410820 Soft drink, chocolate flavored, diet
92411510 Soft drink, cola, fruit or vanilla flavored
92411520 Soft drink, cola, chocolate flavored
92411610 Soft drink, cola, fruit or vanilla flavored, diet
92411620 Soft drink, cola, chocolate flavored, diet

Enhanced, fortified, or flavored waters (including carbonated waters)
[2'-FL] = 0.12 g/100 g

92410110 Carbonated water, sweetened
92410250 Carbonated water, sweetened, with low-calorie or no-calorie sweetener
94100200 Water, bottled, sweetened, with low calorie sweetener
94100300 Water, bottled, flavored (Capri Sun Roarin' Waters)
94210100 Water, bottled, flavored (Propel Water)
94210200 Water, bottled, flavored (Glaceau Vitamin Water)
94210300 Water, bottled, flavored (SoBe Life Water)
94220215 Water, bottled, flavored, sugar free (Glaceau Vitamin Water)
94220310 Water, bottled, flavored, sugar free (SoBe)

Non-milk-based meal replacement drinks
[2'-FL] = 0.5 g/100 g

95120050 Nutritional drink or shake, liquid, soy-based

Foods adjusted for being present in dried form
Reconstitution factor of 7
[2'-FL] = 3.5 g/100 g

95201600 Nutritional powder mix (Isopure)
95201700 Nutritional powder mix (Kellogg's Special K20 Protein Water)

Sports, isotonic, or energy drinks
[2'-FL] = 0.12 g/100 g

95310200 Energy drink (Full Throttle)
95310400 Energy drink (Monster)
95310500 Energy drink (Mountain Dew AMP)
95310550 Energy drink (No Fear)
95310555 Energy drink (No Fear Motherload)
95310560 Energy drink (NOS)
95310600 Energy drink (Red Bull)
95310700 Energy drink (Rockstar)
95310750 Energy drink (SoBe Energize Energy Juice Drink)
95310800 Energy drink (Vault)
95311000 Energy Drink
95312400 Energy drink, low calorie (Monster)
95312410 Energy drink, sugar free (Monster)
95312500 Energy drink, sugar free (Mountain Dew AMP)
95312550 Energy drink, sugar free (No Fear)
95312555 Energy drink, sugar-free (NOS)
95312560 Energy drink (Ocean Spray Cran-Energy Juice Drink)
95312600 Energy drink, sugar-free (Red Bull)
95312700 Energy drink, sugar free (Rockstar)
95312800 Energy drink, sugar free (Vault)
95312900 Energy drink (XS)
95312905 Energy drink (XS Gold Plus)
95313200 Energy drink, sugar free
95320200 Sports drink (Gatorade G)
95320500 Sports drink (Powerade)
95321000 Sports drink, NFS
95322200 Sports drink, low calorie (Gatorade G2)
95322500 Sports drink, low calorie (Powerade Zero)
95323000 Sports drink, low calorie
95330100 Fluid replacement, electrolyte solution
95330500 Fluid replacement, 5% glucose in water

Foods adjusted for being present in dried form
Reconstitution factor of 16.625
[2'-FL] = 1.995 g/100 g

92900300 Sports drink, dry concentrate, not reconstituted

Protein drinks
[2'-FL] = 0.5 g/100 g

Foods adjusted for being present in dried form
Reconstitution factor of 6 to 10
[2'-FL] = 3 to 5 g/100 g

95201200	Nutritional powder mix (EAS Whey Protein Powder)
95201300	Nutritional powder mix (EAS Soy Protein Powder)
95201500	Nutritional powder mix, high protein (Herbalife)
95210020	Nutritional powder mix, high protein (Slim Fast)
95220010	Nutritional powder mix, high protein, NFS
95230000	Nutritional powder mix, whey based, NFS
95230010	Nutritional powder mix, protein, soy based, NFS
95230020	Nutritional powder mix, protein, light, NFS
95230030	Nutritional powder mix, protein, NFS

Breakfast Cereals

Hot breakfast cereals (*e.g.*, oatmeal, grits), instant and RTE
[2'-FL] = 3.1 g/100 g

56200300	Cereal, cooked, NFS
56200990	Grits, NS as to regular, quick, or instant, NS as to fat
56201000	Grits, NS as to regular, quick, or instant, no added fat
56201040	Grits, NS as to regular, quick, or instant, fat added
56201050	Grits, regular or quick, made with water, NS as to fat
56201051	Grits, regular or quick, made with water, no added fat
56201052	Grits, regular or quick, made with water, fat added
56201055	Grits, regular or quick, made with milk, NS as to fat
56201056	Grits, regular or quick, made with milk, no added fat
56201057	Grits, regular or quick, made with milk, fat added
56201065	Grits, regular or quick, made with non-dairy milk, NS as to fat
56201066	Grits, regular or quick, made with non-dairy milk, no added fat
56201067	Grits, regular or quick, made with non-dairy milk, fat added
56201090	Grits, with cheese, NS as to fat
56201091	Grits, with cheese, no added fat
56201092	Grits, with cheese, fat added
56201210	Grits, instant, made with water, no added fat
56201220	Grits, instant, made with water, fat added
56201230	Grits, instant, made with water, NS as to fat
56201340	Grits, instant, made with milk, fat added
56201342	Grits, instant, made with milk, no added fat

56201344 Grits, instant, made with milk, NS as to fat
56201350 Grits, instant, made with non-dairy milk, NS as to fat
56201355 Grits, instant, made with non-dairy milk, no added fat
56201360 Grits, instant, made with non-dairy milk, fat added
56201515 Cornmeal mush, NS as to fat
56201516 Cornmeal mush, no added fat
56201517 Cornmeal mush, fat added
56201540 Cornmeal, Puerto Rican Style
56201600 Masa harina, cooked
56202900 Oatmeal, from fast food, plain
56202905 Oatmeal, from fast food, maple flavored
56202910 Oatmeal, from fast food, fruit flavored
56202920 Oatmeal, from fast food, other flavors
56202960 Oatmeal, NS as to regular, quick, or instant, NS as to fat
56203000 Oatmeal, NS as to regular, quick, or instant, no added fat
56203040 Oatmeal, NS as to regular, quick, or instant, fat added
56203055 Oatmeal, regular or quick, made with water, NS as to fat
56203056 Oatmeal, regular or quick, made with water, no added fat
56203057 Oatmeal, regular or quick, made with water, fat added
56203065 Oatmeal, regular or quick, made with milk, NS as to fat
56203066 Oatmeal, regular or quick, made with milk, no added fat
56203067 Oatmeal, regular or quick, made with milk, fat added
56203075 Oatmeal, regular or quick, made with non-dairy milk, NS as to fat
56203076 Oatmeal, regular or quick, made with non-dairy milk, no added fat
56203077 Oatmeal, regular or quick, made with non-dairy milk, fat added
56203085 Oatmeal, instant, plain, made with water, NS as to fat
56203086 Oatmeal, instant, plain, made with water, no added fat
56203087 Oatmeal, instant, plain, made with water, fat added
56203095 Oatmeal, instant, plain, made with milk, NS as to fat
56203096 Oatmeal, instant, plain, made with milk, no added fat
56203097 Oatmeal, instant, plain, made with milk, fat added
56203105 Oatmeal, instant, plain, made with non-dairy milk, NS as to fat
56203106 Oatmeal, instant, plain, made with non-dairy milk, no added fat
56203107 Oatmeal, instant, plain, made with non-dairy milk, fat added
56203125 Oatmeal, instant, maple flavored, NS as to fat
56203130 Oatmeal, instant, maple flavored, no added fat
56203135 Oatmeal, instant, maple flavored, fat added
56203150 Oatmeal, instant, fruit flavored, NS as to fat
56203155 Oatmeal, instant, fruit flavored, no added fat
56203160 Oatmeal, instant, fruit flavored, fat added
56203170 Oatmeal, instant, other flavors, NS as to fat
56203175 Oatmeal, instant, other flavors, no added fat
56203180 Oatmeal, instant, other flavors, fat added
56203500 Oatmeal, reduced sugar, plain, NS as to fat

56203510	Oatmeal, reduced sugar, plain, no added fat
56203520	Oatmeal, reduced sugar, plain, fat added
56203540	Oatmeal, made with milk and sugar, Puerto Rican style
56203550	Oatmeal, reduced sugar, flavored, NS as to fat
56203555	Oatmeal, reduced sugar, flavored, no added fat
56203560	Oatmeal, reduced sugar, flavored, fat added
56203600	Oatmeal, multigrain, NS as to fat
56203610	Oatmeal, multigrain, no added fat
56203620	Oatmeal, multigrain, fat added
56205050	Rice, cream of, cooked, no added fat
56205080	Rice, creamed, made with milk and sugar, Puerto Rican style
56205090	Rice, cream of, cooked, fat added
56205092	Rice, cream of, cooked, NS as to fat
56205094	Rice, cream of, cooked, made with milk
56206990	Cream of wheat, NS as to regular, quick, or instant, NS as to fat
56207000	Cream of wheat, NS as to regular, quick, or instant, no added fat
56207005	Cream of wheat, NS as to regular, quick, or instant, fat added
56207015	Cream of wheat, regular or quick, made with water, NS as to fat
56207016	Cream of wheat, regular or quick, made with water, no added fat
56207017	Cream of wheat, regular or quick, made with water, fat added
56207021	Cream of wheat, regular or quick, made with milk, NS as to fat
56207022	Cream of wheat, regular or quick, made with milk, no added fat
56207023	Cream of wheat, regular or quick, made with milk, fat added
56207025	Cream of wheat, regular or quick, made with non-dairy milk, NS as to fat
56207026	Cream of wheat, regular or quick, made with non-dairy milk, no added fat
56207027	Cream of wheat, regular or quick, made with non-dairy milk, fat added
56207030	Cream of wheat, instant, made with water, no added fat
56207050	Wheat, cream of, cooked, made with milk and sugar, Puerto Rican style
56207060	Cream of wheat, instant, made with water, fat added
56207070	Cream of wheat, instant, made with water, NS as to fat
56207094	Cream of wheat, instant, made with milk, fat added
56207095	Cream of wheat, instant, made with milk, no added fat
56207096	Cream of wheat, instant, made with milk, NS as to fat
56207101	Cream of wheat, instant, made with non-dairy milk, NS as to fat
56207102	Cream of wheat, instant, made with non-dairy milk, no added fat
56207103	Cream of wheat, instant, made with non-dairy milk, fat added
56207190	Whole wheat cereal, cooked, NS as to fat
56207200	Whole wheat cereal, cooked, no added fat
56207210	Whole wheat cereal, cooked, fat added
56207370	Wheat cereal, chocolate flavored, cooked
56208500	Oat bran cereal, cooked, no added fat
56208510	Oat bran cereal, cooked, fat added
56208520	Oat bran cereal, cooked, NS as to fat
56209000	Cream of rye

58174000 Upma, Indian breakfast dish
75217520 Hominy, cooked

RTE breakfast cereals – Puffed cereals
[2'-FL] = 8 g/100 g

57124200 Cereal, chocolate flavored, frosted, puffed corn
57126000 Cereal (Kellogg's Cocoa Krispies)
57128000 Cereal (General Mills Cocoa Puffs)
57132000 Cereal (General Mills Chex Corn)
57137000 Cereal, corn puffs
57151000 Cereal, crispy rice
57216000 Cereal, frosted rice
57301500 Cereal (Kashi 7 Whole Grain Puffs)
57303100 Cereal (General Mills Kix)
57303105 Cereal (General Mills Honey Kix)
57306500 Cereal (Malt-O-Meal Golden Puffs)
57326000 Cereal (Barbara's Puffins)
57335550 Cereal (General Mills Reese's Puffs)
57336000 Cereal (General Mills Chex Rice)
57337000 Cereal, rice flakes
57339000 Cereal (Kellogg's Rice Krispies)
57339500 Cereal (Kellogg's Rice Krispies Treats Cereal)
57340000 Cereal, puffed rice
57347000 Cereal (Kellogg's Corn Pops)
57407100 Cereal (General Mills Trix)
57416000 Cereal, puffed wheat, plain
57416010 Cereal, puffed wheat, sweetened

RTE breakfast cereals – High-fiber cereals
[2'-FL] = 3 g/100 g

57000100 Cereal, oat, NFS
57100100 Cereal, ready-to-eat, NFS
57101000 Cereal (Kellogg's All-Bran)
57103000 Cereal (Post Alpha-Bits)
57103100 Cereal (General Mills Cheerios Apple Cinnamon)
57104000 Cereal (Kellogg's Apple Jacks)
57106060 Cereal (General Mills Cheerios Banana Nut)
57106260 Cereal (General Mills Cheerios Berry Burst)
57117000 Cereal (Quaker Cap'n Crunch)
57117500 Cereal (Quaker Christmas Crunch)
57119000 Cereal (Quaker Cap'n Crunch's Crunchberries)
57120000 Cereal (Quaker Cap'n Crunch's Peanut Butter Crunch)

57123000 Cereal (General Mills Cheerios)
57124030 Cereal (General Mills Chex Chocolate)
57124050 Cereal (General Mills Chex Cinnamon)
57124100 Cereal (General Mills Cheerios Chocolate)
57124300 Cereal (General Mills Lucky Charms Chocolate)
57125000 Cereal (General Mills Cinnamon Toast Crunch)
57125010 Cereal (General Mills 25% Less Sugar Cinnamon Toast Crunch)
57125900 Cereal (General Mills Honey Nut Clusters)
57127000 Cereal (Post Cocoa Pebbles)
57130000 Cereal (General Mills Cookie Crisp)
57134000 Cereal, corn flakes
57135000 Cereal (Kellogg's Corn Flakes)
57139000 Cereal (General Mills Count Chocula)
57143500 Cereal (Post Great Grains, Cranberry Almond Crunch)
57148000 Cereal (Kellogg's Crispix)
57206700 Cereal (General Mills Fiber One)
57206710 Cereal (General Mills Fiber One Honey Clusters)
57206715 Cereal (General Mills Fiber One Raisin Bran Clusters)
57211000 Cereal (General Mills Frankenberry)
57213000 Cereal (Kellogg's Froot Loops)
57213010 Cereal (Kellogg's Froot Loops Marshmallow)
57213850 Cereal (General Mills Cheerios Frosted)
57214000 Cereal (Kellogg's Frosted Mini-Wheats)
57221700 Cereal, fruit rings
57221810 Cereal (General Mills Cheerios Fruity)
57223000 Cereal (Post Fruity Pebbles)
57230000 Cereal (Post Grape-Nuts)
57231200 Cereal (Post Great Grains Raisins, Dates, and Pecans)
57237100 Cereal (Post Honey Bunches of Oats Honey Roasted)
57237200 Cereal (Post Honey Bunches of Oats with Vanilla Bunches)
57237300 Cereal (Post Honey Bunches of Oats with Almonds)
57238000 Cereal (Post Honeycomb)
57240100 Cereal (General Mills Chex Honey Nut)
57241000 Cereal (General Mills Cheerios Honey Nut)
57241200 Cereal (Post Shredded Wheat Honey Nut)
57243000 Cereal (Kellogg's Honey Smacks)
57301505 Cereal (Kashi Autumn Wheat)
57301510 Cereal (Kashi GOLEAN)
57301511 Cereal (Kashi GOLEAN Crunch)
57301512 Cereal (Kashi GOLEAN Crunch Honey Almond Flax)
57301530 Cereal (Kashi Heart to Heart Honey Toasted Oat)
57303200 Cereal (Kellogg's Krave)
57304100 Cereal (Quaker Life)
57305100 Cereal (General Mills Lucky Charms)

57305150 Cereal, frosted oat cereal with marshmallows
57305160 Cereal (Malt-O-Meal Blueberry Muffin Tops)
57305165 Cereal (Malt-O-Meal Cinnamon Toasters)
57305170 Cereal (Malt-O-Meal Coco-Roos)
57305174 Cereal (Malt-O-Meal Colossal Crunch)
57305175 Cereal (Malt-O-Meal Cocoa Dyno-Bites)
57305180 Cereal (Malt-O-Meal Corn Bursts)
57305210 Cereal (Malt-O-Meal Frosted Flakes)
57305300 Cereal (Malt-O-Meal Fruity Dyno-Bites)
57305400 Cereal (Malt-O-Meal Honey Graham Squares)
57305500 Cereal (Malt-O-Meal Honey Nut Toasty O's)
57305600 Cereal (Malt-O-Meal Marshmallow Mateys)
57306700 Cereal (Malt-O-Meal Toasted Oat Cereal)
57306800 Cereal (Malt-O-Meal Tootie Fruities)
57308400 Cereal (General Mills Cheerios Multigrain)
57316380 Cereal (General Mills Cheerios Oat Cluster Crunch)
57316385 Cereal (General Mills Cheerios Protein)
57316710 Cereal (Quaker Honey Graham Oh's)
57327450 Cereal (Quaker Toasted Oat Bran)
57327500 Cereal (Quaker Oatmeal Squares)
57341200 Cereal (Kellogg's Smart Start Strong)
57341300 Cereal (Kellogg's Smorz)
57344000 Cereal (Kellogg's Special K)
57344001 Cereal (Kellogg's Special K Blueberry)
57344005 Cereal (Kellogg's Special K Chocolatey Delight)
57344010 Cereal (Kellogg's Special K Red Berries)
57344015 Cereal (Kellogg's Special K Fruit & Yogurt)
57344020 Cereal (Kellogg's Special K Vanilla Almond)
57344025 Cereal (Kellogg's Special K Cinnamon Pecan)
57348000 Cereal, frosted corn flakes
57349000 Cereal (Kellogg's Frosted Flakes)
57355000 Cereal (Post Golden Crisp)
57408100 Cereal (Uncle Sam)
57411000 Cereal (General Mills Chex Wheat)
57417000 Cereal (Post Shredded Wheat)
57418000 Cereal (General Mills Wheaties)

RTE breakfast cereals – Biscuit-type cereals
[2'-FL] = 2 g/100 g

57106050 Cereal (Post Great Grains Banana Nut Crunch)
57143000 Cereal (Kellogg's Cracklin' Oat Bran)
57207000 Cereal, bran flakes
57208000 Cereal (Kellogg's All-Bran Complete Wheat Flakes)

57209000 Cereal (Post Bran Flakes)
57224000 Cereal (General Mills Golden Grahams)
57227000 Cereal, granola
57228000 Granola, homemade
57229000 Cereal (Kellogg's Low Fat Granola)
57308190 Cereal, muesli
57309100 Cereal (Nature Valley Granola)
57316450 Cereal (General Mills Oatmeal Crisp with Almonds)
57320500 Cereal (Quaker Granola with Oats, Honey, and Raisins)
57321900 Cereal (Nature's Path Organic Flax Plus)
57329000 Cereal, raisin bran
57330000 Cereal (Kellogg's Raisin Bran)
57330010 Cereal (Kellogg's Raisin Bran Crunch)
57331000 Cereal (Post Raisin Bran)
57332100 Cereal (General Mills Raisin Nut Bran)
57401100 Cereal, toasted oat

Chewing gum

Chewing Gum
[2'-FL] = 30 g/100 g

91800100 Chewing gum, NFS
91801000 Chewing gum, regular
91802000 Chewing gum, sugar free

Coffee and Tea

Coffee
[2'-FL] = 1 g/100 g

92171000 Coffee, bottled/canned
92171010 Coffee, bottled/canned, light

Tea
[2'-FL] = 1 g/100 g

92309000	Tea, iced, bottled, black
92309010	Tea, iced, bottled, black, decaffeinated
92309020	Tea, iced, bottled, black, diet
92309030	Tea, iced, bottled, black, decaffeinated, diet
92309040	Tea, iced, bottled, black, unsweetened
92309050	Tea, iced, bottled, black, decaffeinated, unsweetened
92309500	Tea, iced, bottled, green
92309510	Tea, iced, bottled, green, diet
92309520	Tea, iced, bottled, green, unsweetened

Dairy Product Analogs

Milk substitutes such as soy milk and imitation milks
[2'-FL] = 0.12 g/100 g

11300100	Non-dairy milk, NFS
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
11350000	Almond milk, sweetened
11350010	Almond milk, sweetened, chocolate
11350020	Almond milk, unsweetened
11350030	Almond milk, unsweetened, chocolate
11360000	Rice milk
11370000	Coconut milk
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	Chocolate milk, made from dry mix with non-dairy milk (Nesquik)
11513395	Chocolate milk, made from no sugar added dry mix with non-dairy milk (Nesquik)
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
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
42401010	Coconut milk, used in cooking

Mixed foods containing milk substitutes
Adjusted for milk substitute content of 42.2 to 83.6%
[2'-FL] = 05 to 0.10 g/100 g

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 Cafe Mocha, with non-dairy milk
92102612	Coffee, Iced Cafe Mocha, decaffeinated, with non-dairy milk
92161002	Coffee, Cappuccino, with non-dairy milk
92162002	Coffee, Cappuccino, decaffeinated, with non-dairy milk

Beverages whiteners
[2'-FL] = 60 g/100 g

12200100	Coffee creamer, NFS
12210200	Coffee creamer, liquid
12210210	Coffee creamer, liquid, flavored
12210260	Coffee creamer, liquid, fat free
12210270	Coffee creamer, liquid, fat free, flavored
12210280	Coffee creamer, liquid, fat free, sugar free, flavored
12210310	Coffee creamer, liquid, sugar free, flavored
12210400	Coffee creamer, powder
12210420	Coffee creamer, powder, flavored
12210430	Coffee creamer, powder, fat free
12210440	Coffee creamer,powder, fat free, flavored
12210505	Coffee creamer,powder, sugar free, flavored

Non-dairy cream
[2'-FL] = 8 g/100 g

12210520 Coffee creamer, soy, liquid
42402010 Coconut cream, canned, sweetened

Non-dairy yogurt
[2'-FL] = 1.2 g/100 g

41420380 Yogurt, soy
42401100 Yogurt, coconut milk

Non-dairy frozen desserts
[2'-FL] = 1.7 g/100 g

41480020 Frozen dessert, non-dairy

Frozen Dairy Desserts and Mixes

Frozen desserts including ice creams and frozen yogurts, frozen novelties
[2'-FL] = 1.7 g/100 g

11459990 Frozen yogurt, NFS
11460000 Frozen yogurt, vanilla
11460100 Frozen yogurt, chocolate
11460500 Frozen yogurt, soft serve, vanilla
11460510 Frozen yogurt, soft serve, chocolate
11461200 Frozen yogurt sandwich
11461210 Frozen yogurt bar, vanilla
11461220 Frozen yogurt bar, chocolate
11461250 Frozen yogurt cone, chocolate
11461260 Frozen yogurt cone, vanilla
11461300 Frozen yogurt cone, vanilla, waffle cone
11461320 Frozen yogurt cone, chocolate, waffle cone
13110000 Ice cream, NFS
13110100 Ice cream, vanilla
13110102 Ice cream, vanilla, with additional ingredients
13110110 Ice cream, chocolate
13110112 Ice cream, chocolate, with additional ingredients
13110200 Ice cream, soft serve, vanilla
13110210 Ice cream, soft serve, chocolate
13110460 Gelato, vanilla
13110470 Gelato, chocolate
13120050 Ice cream bar, vanilla
13120100 Ice cream bar, vanilla, chocolate coated
13120110 Ice cream candy bar

13120140 Ice cream bar, chocolate
13120500 Ice cream sandwich, vanilla
13120510 Ice cream sandwich, chocolate
13120550 Ice cream cookie sandwich
13120730 Ice cream cone, scooped, vanilla
13120735 Ice cream cone, scooped, vanilla, waffle cone
13120740 Ice cream cone, NFS
13120770 Ice cream cone, scooped, chocolate
13120775 Ice cream cone, scooped, chocolate, waffle cone
13120782 Ice cream cone, soft serve, vanilla
13120784 Ice cream cone, soft serve, chocolate
13120786 Ice cream cone, soft serve, vanilla, waffle cone
13120788 Ice cream cone, soft serve, chocolate, waffle cone
13120790 Ice cream cone, vanilla, prepackaged
13120792 Ice cream cone, chocolate, prepackaged
13120800 Ice cream soda, flavors other than chocolate
13120810 Ice cream soda, chocolate
13121000 Ice cream sundae, NFS
13121100 Ice cream sundae, fruit topping
13121120 Banana split
13121300 Ice cream sundae, hot fudge topping
13121400 Ice cream sundae, caramel topping
13126000 Ice cream, fried
13130100 Light ice cream, NFS
13130300 Light ice cream, vanilla
13130310 Light ice cream, chocolate
13130700 Soft serve, blended with candy or cookies, from fast food
13135000 Light ice cream sandwich, vanilla
13135010 Light ice cream sandwich, chocolate
13140000 Light ice cream bar, vanilla
13140100 Light ice cream bar, vanilla, chocolate coated
13140115 Light ice cream bar, chocolate
13140700 Creamsicle
13140710 Creamsicle, light
13140900 Fudgesicle
13142100 Light ice cream cone, vanilla, prepackaged
13142110 Light ice cream cone, chocolate, prepackaged
13161600 Fudgesicle, light

Fruit and Water Ices

Edible ices, sherbet, and sorbet
[2'-FL] = 1.7 g/100 g

13150000	Sherbet, all flavors
63420105	Frozen fruit juice bar
63420205	Frozen fruit juice bar, no sugar added
63430150	Sorbet
91601000	Italian Ice
91601010	Italian Ice, no sugar added
91610900	Popsicle, NFS
91611000	Popsicle
91611100	Popsicle, no sugar added
91612000	Freezer pop
91621000	Snow cone
91621050	Snow cone, no sugar added

Gelatins, Puddings, and Fillings

Dairy-based puddings, custards, and mousses
[2'-FL] = 1.7 g/100 g

13200110	Pudding, chocolate, NFS
13210110	Pudding, bread
13210280	Pudding, flavors other than chocolate, NFS
13210300	Custard
13210350	Flan
13210370	Creme brulee
13210410	Pudding, rice
13210450	Firni, Indian pudding
13210520	Pudding, tapioca, made from dry mix
13220110	Pudding, flavors other than chocolate, made from dry mix
13220120	Pudding, chocolate, made from dry mix
13220210	Pudding, flavors other than chocolate, made from dry mix, sugar free
13220220	Pudding, chocolate, made from dry mix, sugar free
13230110	Pudding, flavors other than chocolate, ready-to-eat
13230120	Pudding, flavors other than chocolate, ready-to-eat, sugar free
13230130	Pudding, chocolate, ready-to-eat
13230140	Pudding, chocolate, ready-to-eat, sugar free
13230500	Pudding, tapioca, ready-to-eat
13241000	Banana pudding
13250000	Mousse
13252200	Milk dessert or milk candy, Puerto Rican style
13252500	Barfi or Burfi, Indian dessert

13252590 Trifle
91560100 Haupia

Fruit pie filling
[2'-FL] = 1.41 g/100 g

61113500 Lemon pie filling
63101210 Apple pie filling
63113030 Cherry pie filling
63203700 Blueberry pie filling

"Fruit Prep" such as fruit filling in bars, cookies, yogurt, and cakes
[2'-FL] = 3 g/100 g

Mixed foods containing fruit filling
Adjusted for fruit filling content of 26.3 to 61.2%
[2'-FL] = 0.79 to 1.84 g/100 g

53440000 Strudel, apple
53440300 Strudel, berry
53440500 Strudel, cherry
53440700 Strudel, peach
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
53453150 Empanada, Mexican turnover, fruit-filled
53453170 Empanada, Mexican turnover, pumpkin

Grain Products and Pastas

Cereal and granola bars including energy, protein, and meal replacement bars
[2'-FL] = 4 g/100 g

53710400 Cereal or granola bar (General Mills Fiber One Chewy Bar)
53710500 Cereal or granola bar (Kellogg's Nutri-Grain Cereal Bar)
53710502 Cereal or granola bar (Kellogg's Nutri-Grain Yogurt Bar)
53710504 Cereal or granola bar (Kellogg's Nutri-Grain Fruit and Nut Bar)
53710600 Milk 'n Cereal bar
53710700 Cereal or granola bar (Kellogg's Special K bar)

53710800 Cereal or granola bar (Kashi Chewy)
53710802 Cereal or granola bar (Kashi Crunchy)
53710810 Cereal or granola bar (KIND Fruit and Nut Bar)
53710900 Cereal or granola bar (General Mills Nature Valley Chewy Trail Mix)
53710902 Cereal or granola bar, with yogurt coating (General Mills Nature Valley Chewy Granola Bar)
53710904 Cereal or granola bar (General Mills Nature Valley Sweet and Salty Granola Bar)
53710906 Cereal or granola bar (General Mills Nature Valley Crunchy Granola Bar)
53711000 Cereal or granola bar (Quaker Chewy Granola Bar)
53711002 Cereal or granola bar (Quaker Chewy 90 Calorie Granola Bar)
53711004 Cereal or granola bar (Quaker Chewy 25% Less Sugar Granola Bar)
53711006 Cereal or granola bar (Quaker Chewy Dipps Granola Bar)
53711100 Cereal or granola bar (Quaker Granola Bites)
53712000 Snack bar, oatmeal
53712100 Cereal or Granola bar, NFS
53712200 Cereal or granola bar, lowfat, NFS
53712210 Cereal or granola bar, nonfat
53713000 Cereal or granola bar, reduced sugar, NFS
53713010 Cereal or granola bar, fruit and nut
53713100 Cereal or granola bar, peanuts , oats, sugar, wheat germ
53714200 Cereal or granola bar, chocolate coated, NFS
53714210 Cereal or granola bar, with coconut, chocolate coated
53714220 Cereal or granola bar with nuts, chocolate coated
53714230 Cereal or granola bar, oats, nuts, coated with non-chocolate coating
53714250 Cereal or granola bar, coated with non-chocolate coating
53714300 Cereal or granola bar, high fiber, coated with non-chocolate yogurt coating
53714400 Cereal or granola bar, with rice cereal
53714500 Breakfast bar, NFS
53714510 Breakfast bar, date, with yogurt coating
53714520 Breakfast bar, cereal crust with fruit filling, lowfat
53720100 Nutrition bar (Balance Original Bar)
53720200 Nutrition bar (Clif Bar)
53720210 Nutrition bar (Clif Kids Organic Zbar)
53720300 Nutrition bar (PowerBar)
53720400 Nutrition bar (Slim Fast Original Meal Bar)
53720500 Nutrition bar (Snickers Marathon Protein Bar)
53720600 Nutrition bar (South Beach Living Meal Bar)
53720610 Nutrition bar (South Beach Living High Protein Bar)
53720700 Nutrition bar (Tiger's Milk)
53720800 Nutrition bar (Zone Perfect Classic Crunch)
53729000 Nutrition bar or meal replacement bar, NFS

Infant and Toddler Foods

Term infant formula

[2'-FL] = 0.24 g/100 g

11710000	Infant formula, NFS
11710350	Infant formula, NS as to form (Similac Advance)
11710351	Infant formula, ready-to-feed (Similac Advance)
11710352	Infant formula, liquid concentrate, made with water, NFS (Similac Advance)
11710353	Infant formula, powder, made with water, NFS (Similac Advance)
11710354	Infant formula, liquid concentrate, made with tap water (Similac Advance)
11710355	Infant formula, liquid concentrate, made with plain bottled water (Similac Advance)
11710356	Infant formula, liquid concentrate, made with baby water (Similac Advance)
11710357	Infant formula, powder, made with tap water (Similac Advance)
11710358	Infant formula, powder, made with plain bottled water (Similac Advance)
11710359	Infant formula, powder, made with baby water (Similac Advance)
11710360	Infant formula, NS as to form (Similac Advance Organic)
11710361	Infant formula, ready-to-feed (Similac Advance Organic)
11710363	Infant formula, powder, made with water, NFS (Similac Advance Organic)
11710367	Infant formula, powder, made with tap water (Similac Advance Organic)
11710368	Infant formula, powder, made with plain bottled water (Similac Advance Organic)
11710369	Infant formula, powder, made with baby water (Similac Advance Organic)
11710370	Infant formula, NS as to form (Similac Sensitive)
11710371	Infant formula, ready-to-feed (Similac Sensitive)
11710372	Infant formula, liquid concentrate, made with water, NFS (Similac Sensitive)
11710373	Infant formula, powder, made with water, NFS (Similac Sensitive)
11710374	Infant formula, liquid concentrate, made with tap water (Similac Sensitive)
11710375	Infant formula, liquid concentrate, made with plain bottled water (Similac Sensitive)
11710376	Infant formula, liquid concentrate, made with baby water (Similac Sensitive)
11710377	Infant formula, powder, made with tap water (Similac Sensitive)
11710378	Infant formula, powder, made with plain bottled water (Similac Sensitive)
11710379	Infant formula, powder, made with baby water (Similac Sensitive)
11710380	Infant formula, NS as to form (Similac for Spit-Up)
11710381	Infant formula, ready-to-feed (Similac for Spit-Up)
11710383	Infant formula, powder, made with water, NFS (Similac for Spit-Up)
11710620	Infant formula, NS as to form (Enfamil Newborn)
11710621	Infant formula, ready-to-feed (Enfamil Newborn)
11710626	Infant formula, powder, made with water, NFS (Enfamil Newborn)
11710627	Infant formula, powder, made with tap water (Enfamil Newborn)
11710628	Infant formula, powder, made with plain bottled water (Enfamil Newborn)
11710629	Infant formula, powder, made with baby water (Enfamil Newborn)
11710630	Infant formula, NS as to form (Enfamil Infant)
11710631	Infant formula, ready-to-feed (Enfamil Infant)
11710632	Infant formula, liquid concentrate, made with water, NFS (Enfamil Infant)

11710633 Infant formula, liquid concentrate, made with tap water (Enfamil Infant)
11710634 Infant formula, liquid concentrate, made with plain bottled water (Enfamil Infant)
11710635 Infant formula, liquid concentrate, made with baby water (Enfamil Infant)
11710636 Infant formula, powder, made with water, NFS (Enfamil Infant)
11710637 Infant formula, powder, made with tap water (Enfamil Infant)
11710638 Infant formula, powder, made with plain bottled water (Enfamil Infant)
11710639 Infant formula, powder, made with baby water (Enfamil Infant)
11710660 Infant formula, NS as to form (Enfamil A.R.)
11710661 Infant formula, ready-to-feed (Enfamil A.R.)
11710663 Infant formula, powder, made with water, NFS (Enfamil A.R.)
11710664 Infant formula, powder, made with tap water (Enfamil A.R.)
11710668 Infant formula, powder, made with plain bottled water (Enfamil A.R.)
11710669 Infant formula, powder, made with baby water (Enfamil A.R.)
11710670 Infant formula, NS as to form (Enfamil Gentlease)
11710671 Infant formula, ready-to-feed (Enfamil Gentlease)
11710673 Infant formula, powder, made with water, NFS (Enfamil Gentlease)
11710677 Infant formula, powder, made with tap water (Enfamil Gentlease)
11710678 Infant formula, powder, made with plain bottled water (Enfamil Gentlease)
11710679 Infant formula, powder, made with baby water (Enfamil Gentlease)
11710910 Infant formula, NS as to form (Gerber Good Start Gentle)
11710911 Infant formula, ready-to-feed (Gerber Good Start Gentle)
11710912 Infant formula, liquid concentrate, made with water, NFS (Gerber Good Start Gentle)
11710913 Infant formula, powder, made with water, NFS (Gerber Good Start Gentle)
11710914 Infant formula, liquid concentrate, made with tap water (Gerber Good Start Gentle)
11710915 Infant formula, liquid concentrate, made with plain bottled water (Gerber Good Start Gentle)
11710916 Infant formula, liquid concentrate, made with baby water (Gerber Good Start Gentle)
11710917 Infant formula, powder, made with tap water (Gerber Good Start Gentle)
11710918 Infant formula, powder, made with plain bottled water (Gerber Good Start Gentle)
11710919 Infant formula, powder, made with baby water (Gerber Good Start Gentle)
11710920 Infant formula, NS as to form (Gerber Good Start Protect)
11710923 Infant formula, powder, made with water, NFS (Gerber Good Start Protect)
11710927 Infant formula, powder, made with tap water (Gerber Good Start Protect)
11710928 Infant formula, powder, made with plain bottled water (Gerber Good Start Protect)
11710929 Infant formula, powder, made with baby water (Gerber Good Start Protect)
11710960 Infant formula, NS as to form (Store Brand)
11710961 Infant formula, liquid concentrate, made with water, NFS (Store Brand)
11710962 Infant formula, powder, made with water, NFS (Store Brand)
11710963 Infant formula, ready-to-feed (Store Brand)
11710964 Infant formula, liquid concentrate, made with tap water (Store Brand)
11710965 Infant formula, liquid concentrate, made with plain bottled water (Store Brand)
11710966 Infant formula, liquid concentrate, made with baby water (Store Brand)
11710967 Infant formula, powder, made with tap water (Store Brand)
11710968 Infant formula, powder, made with plain bottled water (Store Brand)

11710969 Infant formula, powder, made with baby water (Store Brand)
11720310 Infant formula, NS as to form (Enfamil ProSobee)
11720311 Infant formula, ready-to-feed (Enfamil ProSobee)
11720312 Infant formula, liquid concentrate, made with water, NFS (Enfamil ProSobee)
11720313 Infant formula, powder, made with water, NFS (Enfamil ProSobee)
11720314 Infant formula, liquid concentrate, made with tap water (Enfamil ProSobee)
11720315 Infant formula, liquid concentrate, made with plain bottled water (Enfamil ProSobee)
11720316 Infant formula, liquid concentrate, made with baby water (Enfamil ProSobee)
11720317 Infant formula, powder, made with tap water (Enfamil ProSobee)
11720318 Infant formula, powder, made with plain bottled water (Enfamil ProSobee)
11720319 Infant formula, powder, made with baby water (Enfamil ProSobee)
11720410 Infant formula, NS as to form (Similac Isomil Soy)
11720411 Infant formula, ready-to-feed (Similac Isomil Soy)
11720412 Infant formula, liquid concentrate, made with water, NFS (Similac Isomil Soy)
11720413 Infant formula, powder, made with water, NFS (Similac Isomil Soy)
11720414 Infant formula, liquid concentrate, made with tap water (Similac Isomil Soy)
11720415 Infant formula, liquid concentrate, made with plain bottled water (Similac Isomil Soy)
11720416 Infant formula, liquid concentrate, made with baby water (Similac Isomil Soy)
11720417 Infant formula, powder, made with tap water (Similac Isomil Soy)
11720418 Infant formula, powder, made with plain bottled water (Similac Isomil Soy)
11720419 Infant formula, powder, made with baby water (Similac Isomil Soy)
11720610 Infant formula, NS as to form (Gerber Good Start Soy)
11720611 Infant formula, ready-to-feed (Gerber Good Start Soy)
11720612 Infant formula, liquid concentrate, made with water, NFS (Gerber Good Start Soy)
11720613 Infant formula, powder, made with water, NFS (Gerber Good Start Soy)
11720614 Infant formula, liquid concentrate, made with tap water (Gerber Good Start Soy)
11720615 Infant formula, liquid concentrate, made with plain bottled water (Gerber Good Start Soy)
11720616 Infant formula, liquid concentrate, made with baby water (Gerber Good Start Soy)
11720617 Infant formula, powder, made with tap water (Gerber Good Start Soy)
11720618 Infant formula, powder, made with plain bottled water (Gerber Good Start Soy)
11720619 Infant formula, powder, made with baby water (Gerber Good Start Soy)
11720800 Infant formula, NS as to form (Store Brand Soy)
11720801 Infant formula, ready-to-feed (Store brand Soy)
11720802 Infant formula, liquid concentrate, made with water, NFS (Store Brand Soy)
11720803 Infant formula, powder, made with water, NFS (Store Brand Soy)
11720807 Infant formula, powder, made with tap water (Store Brand Soy)
11720808 Infant formula, powder, made with plain bottled water (Store Brand Soy)
11720809 Infant formula, powder, made with baby water (Store Brand Soy)

Toddler formula

[2'-FL] = 0.24 g/100 g

11720430	Infant formula, NS as to form (Similac Expert Care for Diarrhea)
11720431	Infant formula, ready-to-feed (Similac Expert Care for Diarrhea)
11710480	Infant formula, NS as to form (Similac Go and Grow)
11710481	Infant formula, powder, made with water, NFS (Similac Go and Grow)
11710680	Infant formula, NS as to form (Enfamil Enfagrow Toddler Transitions)
11710681	Infant formula, ready-to-feed (Enfamil Enfragrow Toddler Transitions)
11710683	Infant formula, powder, made with water, NFS (Enfamil Enfragrow Toddler Transitions)
11710687	Infant formula, powder, made with tap water (Enfamil Enfagrow Toddler Transitions)
11710688	Infant formula, powder, made with plain bottled water (Enfamil Enfagrow Toddler Transitions)
11710689	Infant formula, powder, made with baby water (Enfamil Enfagrow Toddler Transitions)
11710690	Infant formula, NS as to form (Enfamil Enfagrow Toddler Transitions Gentlease)
11710693	Infant formula, powder, made with water, NFS (Enfamil Enfagrow Toddler Transitions Gentlease)
11710697	Infant formula, powder, made with tap water (Enfamil Enfagrow Toddler Transitions Gentlease)
11710698	Infant formula, powder, made with plain bottled water (Enfamil Enfagrow Toddler Transitions Gentlease)
11710699	Infant formula, powder, made with baby water (Enfamil Enfagrow Toddler Transitions Gentlease)
11710800	Infant formula, NS as to form (PediaSure)
11710801	Infant formula, ready-to-feed (PediaSure)
11710805	Infant formula, with fiber, NS as to form (PediaSure Fiber)
11710806	Infant formula, with fiber, ready-to-feed (PediaSure Fiber)
11710930	Infant formula, NS as to form (Gerber Graduates Gentle)
11710940	Infant formula, NS as to form (Gerber Graduates Protect)
11720320	Infant formula, NS as to form (Enfamil Enfagrow Toddler Transitions Soy)
11720323	Infant formula, powder, made with water, NFS (Enfamil Enfagrow Toddler Transitions Soy)
11720620	Infant formula, NS as to form (Gerber Graduates Soy)

Hypoallergenic infant formula

[2'-FL] = 0.24 g/100 g

11710050	Infant formula, NS as to form (Similac Expert Care Alimentum)
11710051	Infant formula, ready-to-feed (Similac Expert Care Alimentum)
11710053	Infant formula, powder, made with water, NFS (Similac Expert Care Alimentum)
11710054	Infant formula, powder, made with tap water (Similac Expert Care Alimentum)
11710055	Infant formula, powder, made with plain bottled water (Similac Expert Care Alimentum)
11710056	Infant formula, powder, made with baby water (Similac Expert Care Alimentum)
11740310	Infant formula, NS as to form (Enfamil Nutramigen)
11740311	Infant formula, ready-to-feed (Enfamil Nutramigen)
11740312	Infant formula, liquid concentrate, made with water, NFS (Enfamil Nutramigen)
11740313	Infant formula, powder, made with water, NFS (Enfamil Nutramigen)

11740320 Infant formula, NS as to form (PurAmino)
11740323 Infant formula, powder, made with water, NFS (PurAmino)
11740400 Infant formula, NS as to form (Enfamil Pregestimil)
11740401 Infant formula, ready-to-feed (Enfamil Pregestimil)
11740403 Infant formula, powder, made with water, NFS (Enfamil Pregestimil)

Other baby foods for infants and young children
[2'-FL] = 1.2 g/100 g

11480010 Yogurt, whole milk, baby food
11480020 Yogurt, whole milk, baby food, with fruit and multigrain cereal puree, NFS
11480030 Yogurt, whole milk, baby food, with fruit and multigrain cereal puree, plus iron
11480040 Yogurt, whole milk, baby food, with fruit and multigrain cereal puree, plus DHA
20000070 Meat, baby food, NS as to type, NS as to strained or junior
20000090 Meat sticks, baby food, NS as to type of meat
21701000 Beef, baby food, NS as to strained or junior
21701010 Beef, baby food, strained
21701020 Beef, baby food, junior
22810010 Ham, baby food, strained
22820000 Meat stick, baby food
23410010 Lamb, baby food, strained
23420010 Veal, baby food, strained
24701000 Chicken, baby food, NS as to strained or junior
24701010 Chicken, baby food, strained
24701020 Chicken, baby food, junior
24703000 Turkey, baby food, NS as to strained or junior
24703010 Turkey, baby food, strained
24703020 Turkey, baby food, junior
24705010 Chicken stick, baby food
24706010 Turkey stick, baby food
27601000 Beef stew, baby food, toddler
27610100 Beef and egg noodles, baby food, NS as to strained or junior
27610110 Beef and egg noodles, baby food, strained
27610120 Beef and egg noodles, baby food, junior
27610710 Beef with vegetables, baby food, strained
27610730 Beef with vegetables, baby food, toddler
27640050 Chicken and rice dinner, baby food, strained
27640100 Chicken noodle dinner, baby food, NS as to strained or junior
27640110 Chicken noodle dinner, baby food, strained
27640120 Chicken noodle dinner, baby food, junior
27640810 Chicken, noodles, and vegetables, baby food, toddler
27641000 Chicken stew, baby food, toddler
27642100 Turkey, rice and vegetables, baby food, NS as to strained or junior

27642110 Turkey, rice and vegetables, baby food, strained
27642120 Turkey, rice and vegetables, baby food, junior
27642130 Turkey, rice, and vegetables, baby food, toddler
27644110 Chicken soup, baby food
58503000 Macaroni, tomatoes, and beef, baby food, NS as to strained or junior
58503010 Macaroni, tomatoes, and beef, baby food, strained
58503020 Macaroni, tomatoes, and beef, baby food, junior
58503050 Macaroni with beef and tomato sauce, baby food, toddler
58508000 Macaroni and cheese, baby food, strained
58508300 Macaroni and cheese, baby food, toddler
58509020 Spaghetti, tomato sauce, and beef, baby food, junior
58509100 Ravioli, cheese-filled, with tomato sauce, baby food, toddler
58509200 Macaroni with vegetables, baby food, strained
67100100 Fruit, baby food, NFS
67100200 Tropical fruit medley, baby food, strained
67100300 Apples, baby food, toddler
67101000 Apple-raspberry, baby food, NS as to strained or junior
67101010 Apple-raspberry, baby food, strained
67101020 Apple-raspberry, baby food, junior
67102000 Applesauce, baby food, NS as to strained or junior
67102010 Applesauce, baby food, strained
67102020 Applesauce, baby food, junior
67104000 Applesauce and apricots, baby food, NS as to strained or junior
67104010 Applesauce and apricots, baby food, strained
67104020 Applesauce and apricots, baby food, junior
67104030 Applesauce with bananas, baby food, NS as to strained or junior
67104040 Applesauce with bananas, baby food, strained
67104060 Applesauce with bananas, baby food, junior
67104070 Applesauce with cherries, baby food, strained
67104080 Applesauce with cherries, baby food, junior
67104090 Applesauce with cherries, baby food, NS as to strained or junior
67105030 Bananas, baby food, strained
67106010 Bananas with apples and pears, baby food, strained
67106030 Bananas with orange, baby food, strained
67106050 Banana with mixed berries, baby food, strained
67108000 Peaches, baby food, NS as to strained or junior
67108010 Peaches, baby food, strained
67108020 Peaches, baby food, junior
67108030 Peaches, baby food, toddler
67109000 Pears, baby food, NS as to strained or junior
67109010 Pears, baby food, strained
67109020 Pears, baby food, junior
67109030 Pears, baby food, toddler
67110000 Prunes, baby food, strained

67113000 Apples and pears, baby food, NS as to strained or junior
67113010 Apples and pears, baby food, strained
67113020 Apples and pears, baby food, junior
67114000 Pears and pineapple, baby food, NS as to strained or junior
67114010 Pears and pineapple, baby food, strained
67114020 Pears and pineapple, baby food, junior
67304000 Plums, baby food, NS as to strained or junior
67304010 Plums, baby food, strained
67304020 Plums, baby food, junior
67304030 Plums, bananas, and rice, baby food strained
67304500 Prunes with oatmeal, baby food, strained
67307000 Apricots, baby food, NS as to strained or junior
67307010 Apricots, baby food, strained
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
67309010 Bananas and pineapple, baby food, strained
67309020 Bananas and pineapple, baby food, junior
67309030 Bananas and strawberry, baby food, junior
67501000 Apples and chicken, baby food, strained
67501100 Apples with ham, baby food, strained
67600100 Apples and sweet potatoes, baby food, strained
76102010 Spinach, creamed, baby food, strained
76102030 Broccoli, carrots and cheese, baby food, junior
76201000 Carrots, baby food, NS as to strained or junior
76201010 Carrots, baby food, strained
76201020 Carrots, baby food, junior
76201030 Carrots, baby food, toddler
76202000 Carrots and peas, baby food, strained
76205000 Squash, baby food, NS as to strained or junior
76205010 Squash, baby food, strained
76205020 Squash, baby food, junior
76205030 Squash and corn, baby food, strained
76205060 Corn and sweet potatoes, baby food, strained
76209000 Sweet potatoes, baby food, NS as to strained or junior
76209010 Sweet potatoes, baby food, strained
76209020 Sweet potatoes, baby food, junior
76401000 Beans, green string, baby food, NS as to strained or junior
76401010 Beans, green string, baby food, strained
76401020 Beans, green string, baby food, junior
76401060 Beans, green string, baby food, toddler
76402000 Green beans and potatoes, baby food, strained
76403010 Beets, baby food, strained

76405000 Corn, creamed, baby food, NS as to strained or junior
76405010 Corn, creamed, baby food, strained
76405020 Corn, creamed, baby food, junior
76407000 Mixed vegetables, garden vegetables, baby food, NS as to strained or junior
76407010 Mixed vegetables, garden vegetables, baby food, strained
76407020 Mixed vegetables, garden vegetables, baby food, junior
76409000 Peas, baby food, NS as to strained or junior
76409010 Peas, baby food, strained
76409020 Peas, baby food, junior
76409030 Peas, baby food, toddler
76420000 Potatoes, baby food, toddler
76501000 Vegetables and rice, baby food, strained
76502000 Peas and brown rice, baby food
76602000 Carrots and beef, baby food, strained
76603000 Vegetable and beef, baby food, NS as to strained or junior
76603010 Vegetable and beef, baby food, strained
76603020 Vegetable and beef, baby food, junior
76604000 Broccoli and chicken, baby food, strained
76604500 Sweet potatoes and chicken, baby food, strained
76605000 Vegetable and chicken, baby food, NS as to strained or junior
76605010 Vegetable and chicken, baby food, strained
76605020 Vegetable and chicken, baby food, junior
76607100 Potatoes with cheese and broccoli, baby food, toddler
76611000 Vegetable and turkey, baby food, NS as to strained or junior
76611010 Vegetable and turkey, baby food, strained
76611020 Vegetable and turkey, baby food, junior

Hot cereals (dry and RTE)
[2'-FL] = 1.09 g/100 g

56210000 Cereal, nestum
57805090 Rice cereal with mixed fruits, baby food, dry, instant
57806050 Multigrain, whole grain cereal, baby food, dry, instant
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

Foods adjusted for being present in dried form
Reconstitution factor of 8.33
[2'-FL] = 9.08 g/100 g

57801000 Barley cereal, baby food, dry, instant
57803000 Mixed cereal, baby food, dry, instant
57804000 Oatmeal cereal, baby food, dry, instant
57805000 Rice cereal, baby food, dry, instant
57805080 Rice cereal with apples, baby food, dry, instant
57805100 Rice cereal with bananas, baby food, dry, instant
57805500 Brown rice cereal, baby food, dry, instant
57806000 Mixed cereal with bananas, baby food, dry, instant
57806100 Oatmeal cereal with bananas, baby food, dry, instant
57806200 Oatmeal cereal with fruit, baby food, dry, instant, toddler
57807010 Whole wheat cereal with apples, baby food, dry, instant

Other drinks for young children, including yogurt and juice beverages identified as "baby drinks"
[2'-FL] = 1 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 including fruit desserts, cobblers, yogurt/fruit combinations ("junior type desserts")
[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
67404000 Fruit dessert, baby food, NS as to strained or junior
67404010 Fruit dessert, baby food, strained
67404020 Fruit dessert, baby food, junior
67404050 Fruit Supreme dessert, baby food

67404070 Apple yogurt dessert, baby food, strained
67404110 Banana apple dessert, baby food, strained
67404300 Blueberry yogurt dessert, baby food, strained
67404500 Mixed fruit yogurt dessert, baby food, strained
67404550 Cherry cobbler, baby food, junior
67405000 Peach cobbler, baby food, NS as to strained or junior
67405010 Peach cobbler, baby food, strained
67405020 Peach cobbler, baby food, junior
67408010 Banana pudding, baby food, strained
67408500 Banana yogurt dessert, baby food, strained
67410000 Cherry vanilla pudding, baby food, strained
67412000 Dutch apple dessert, baby food, NS as to strained or junior
67412010 Dutch apple dessert, baby food, strained
67412020 Dutch apple dessert, baby food, junior
67413700 Peach yogurt dessert, baby food, strained
67414010 Pineapple dessert, baby food, strained
67414100 Mango dessert, baby food
67415000 Tutti-fruitti pudding, baby food, NS as to strained or junior
67415010 Tutti-fruitti pudding, baby food, strained
67415020 Tutti-fruitti pudding, baby food, junior
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
67100110 Fruit bar, with added vitamin C, baby food, toddler
67430000 Fruit flavored snack, baby food

Jams and Jellies

Jellies and jams, fruit preserves, and fruit butters
[2'-FL] = 6 g/100 g

91401000 Jelly, all flavors

91402000	Jam, preserve, all flavors
91403000	Fruit butter, all flavors
91404000	Marmalade, all flavors
91405000	Jelly, sugar free, all flavors
91405500	Jelly, reduced sugar, all flavors
91406000	Jam, preserve, marmalade, sugar free, all flavors
91406500	Jam, preserve, marmalade, sweetened with fruit juice concentrates, all flavors
91406600	Jam, preserve, marmalade, reduced sugar, all flavors
91407100	Guava paste
91407120	Sweet potato paste
91407150	Bean paste, sweetened

Milk, Whole, and Skim

Unflavored pasteurized and sterilized milk
[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
11116000	Goat's milk, 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)

Mixed foods containing milk
Adjusted for milk content of 42.1 to 83.6%
[2'-FL] = 05 to 0.10 g/100 g

92101900	Coffee, Latte
92101901	Coffee, Latte, nonfat
92101903	Coffee, Latte, with non-dairy milk

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
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
92101950 Coffee, Cafe Mocha
92101955 Coffee, Cafe Mocha, nonfat
92101965 Coffee, Cafe Mocha, decaffeinated
92101970 Coffee, Cafe Mocha, decaffeinated, nonfat
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
92102500 Coffee, Iced Latte
92102501 Coffee, Iced Latte, nonfat
92102503 Coffee, Iced Latte, flavored
92102504 Coffee, Iced Latte, nonfat, flavored
92102510 Coffee, Iced Latte, decaffeinated
92102511 Coffee, Iced Latte, decaffeinated, nonfat
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
92161000 Coffee, Cappuccino
92161001 Coffee, Cappuccino, nonfat
92162000 Coffee, Cappuccino, decaffeinated
92162001 Coffee, Cappuccino, decaffeinated, nonfat

Foods adjusted for being present in dried form

Reconstitution factor of 11
[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)

Milk Products

Buttermilk
[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

Flavored milk
[2'-FL] = 0.12 g/100 g

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
11511300	Chocolate milk, ready to drink, fat free
11511400	Chocolate milk, ready to drink, low fat
11511550	Chocolate milk, ready to drink, reduced sugar, NS as to milk
11511600	Chocolate milk, ready to drink, low fat (Nesquik)
11511610	Chocolate milk, ready to drink, fat free (Nesquik)
11511700	Chocolate milk, ready to drink, low fat, no sugar added (Nesquik)
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
11513200	Chocolate milk, made from dry mix with low fat milk
11513300	Chocolate milk, made from dry mix with fat free milk
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
11513365	Chocolate milk, made from reduced sugar mix with low fat milk
11513370	Chocolate milk, made from reduced sugar mix with fat free milk

11513380 Chocolate milk, made from dry mix, NS as to type of milk (Nesquik)
11513381 Chocolate milk, made from dry mix with whole milk (Nesquik)
11513382 Chocolate milk, made from dry mix with reduced fat milk (Nesquik)
11513383 Chocolate milk, made from dry mix with low fat milk (Nesquik)
11513384 Chocolate milk, made from dry mix with fat free milk (Nesquik)
11513390 Chocolate milk, made from no sugar added dry mix, NS as to type of milk (Nesquik)
11513391 Chocolate milk, made from no sugar added dry mix with whole milk (Nesquik)
11513392 Chocolate milk, made from no sugar added dry mix with reduced fat milk (Nesquik)
11513393 Chocolate milk, made from no sugar added dry mix with low fat milk (Nesquik)
11513394 Chocolate milk, made from no sugar added dry mix with fat free milk (Nesquik)
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
11513600 Chocolate milk, made from syrup with low fat milk
11513700 Chocolate milk, made from syrup with fat free 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
11513803 Chocolate milk, made from light syrup with low fat milk
11513804 Chocolate milk, made from light syrup with fat free 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
11513853 Chocolate milk, made from sugar free syrup with low fat milk
11513854 Chocolate milk, made from sugar free syrup with fat free milk
11514100 Hot chocolate / Cocoa, made with dry mix and water
11514110 Hot chocolate / Cocoa, made with dry mix and whole milk
11514120 Hot chocolate / Cocoa, made with dry mix and reduced fat milk
11514130 Hot chocolate / Cocoa, made with dry mix and low fat milk
11514140 Hot chocolate / Cocoa, made with dry mix and fat free milk
11514310 Hot chocolate / Cocoa, made with no sugar added dry mix and water
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
11514340 Hot chocolate / Cocoa, made with no sugar added dry mix and low fat milk
11514350 Hot chocolate / Cocoa, made with no sugar added dry mix and fat free milk
11519040 Strawberry milk, NFS
11519050 Strawberry milk, whole
11519105 Strawberry milk, reduced fat
11519200 Strawberry milk, low fat
11519205 Strawberry milk, fat free
11519210 Strawberry milk, reduced sugar
11526000 Milk, malted
11531000 Eggnog
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 or Batido
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 Chocolate milk drink
92610030 Horchata beverage, made with milk
92611100 Oatmeal beverage with milk
92613510 Cornmeal beverage with chocolate milk

Foods adjusted for being present in dried form
Reconstitution factor of 10.6
[2'-FL] = 1.27 g/100 g

11830150 Cocoa powder, not reconstituted
11830160 Chocolate beverage powder, dry mix, not reconstituted
11830165 Chocolate beverage powder, light, dry mix, not reconstituted
11830260 Milk, malted, dry mix, not reconstituted
11830400 Strawberry beverage powder, dry mix, not reconstituted

Evaporated and condensed milk
[2'-FL] = 0.12 g/100 g

11210050 Milk, evaporated, NS as to fat content
11211050 Milk, evaporated, whole
11211400 Milk, evaporated, reduced fat (2%)
11212050 Milk, evaporated, fat free (skim)
11220000 Milk, condensed, sweetened

Milk-based meal replacement beverages for weight reduction
[2'-FL] = 0.5 g/100 g

95101000 Nutritional drink or shake, ready-to-drink (Boost)
95101010 Nutritional drink or shake, ready-to-drink (Boost Plus)
95102000 Nutritional drink or shake, ready-to-drink (Carnation Instant Breakfast)
95103000 Nutritional drink or shake, ready-to-drink (Ensure)
95103010 Nutritional drink or shake, ready-to-drink (Ensure Plus)
95104000 Nutritional drink or shake, ready-to-drink, sugar free (Glucerna)
95105000 Nutritional drink or shake, ready-to-drink (Kellogg's Special K Protein)
95106000 Nutritional drink or shake, ready-to-drink (Muscle Milk)
95106010 Nutritional drink or shake, ready-to-drink, light (Muscle Milk)

95110000 Nutritional drink or shake, ready-to-drink (Slim Fast)
95110010 Nutritional drink or shake, ready-to-drink, sugar free (Slim Fast)
95110020 Nutritional drink or shake, high protein, ready-to-drink (Slim Fast)
95120000 Nutritional drink or shake, ready-to-drink, NFS
95120010 Nutritional drink or shake, high protein, ready-to-drink, NFS
95120020 Nutritional drink or shake, high protein, light, ready-to-drink, NFS

Foods adjusted for being present in dried form
Reconstitution factor of 6 to 10
[2'-FL] = 3 to 5 g/100 g

95201000 Nutritional powder mix (Carnation Instant Breakfast)
95201010 Nutritional powder mix, sugar free (Carnation Instant Breakfast)
95202000 Nutritional powder mix (Muscle Milk)
95202010 Nutritional powder mix, light (Muscle Milk)
95210000 Nutritional powder mix (Slim Fast)
95210010 Nutritional powder mix, sugar free (Slim Fast)
95220000 Nutritional powder mix, NFS

Yogurt
[2'-FL] = 1.2 g/100 g

11400000 Yogurt, NFS
11400010 Yogurt, Greek, NS as to type of milk or flavor
11410000 Yogurt, NS as to type of milk or flavor
11411010 Yogurt, NS as to type of milk, plain
11411100 Yogurt, whole milk, plain
11411200 Yogurt, low fat milk, plain
11411300 Yogurt, nonfat milk, plain
11411390 Yogurt, Greek, NS as to type of milk, plain
11411400 Yogurt, Greek, whole milk, plain
11411410 Yogurt, Greek, low fat milk, plain
11411420 Yogurt, Greek, nonfat milk, plain
11430000 Yogurt, NS as to type of milk, fruit
11431000 Yogurt, whole milk, fruit
11432000 Yogurt, low fat milk, fruit
11433000 Yogurt, nonfat milk, fruit
11433990 Yogurt, Greek, NS as to type of milk, fruit
11434000 Yogurt, Greek, whole milk, fruit
11434010 Yogurt, Greek, low fat milk, fruit
11434020 Yogurt, Greek, nonfat milk, fruit
11434090 Yogurt, NS as to type of milk, flavors other than fruit
11434100 Yogurt, whole milk, flavors other than fruit
11434200 Yogurt, low fat milk, flavors other than fruit
11434300 Yogurt, nonfat milk, flavors other than fruit

11435000 Yogurt, Greek, NS as to type of milk, flavors other than fruit
11435010 Yogurt, Greek, whole milk, flavors other than fruit
11435020 Yogurt, Greek, low fat milk, flavors other than fruit
11435030 Yogurt, Greek, nonfat milk, flavors other than fruit
11435100 Yogurt, Greek, with oats
11436000 Yogurt, liquid
11446000 Yogurt parfait, low fat, with fruit

Processed Fruits and Fruit Juices

Fruit flavored drinks and ades
[2'-FL] = 0.12 g/100 g

42403010 Coconut water, unsweetened
42404010 Coconut water, sweetened
92432000 Fruit juice drink, citrus, carbonated
92433000 Fruit juice drink, noncitrus, carbonated
92510610 Fruit juice drink
92510650 Tamarind drink
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
92512050 Frozen daiquiri mix, from frozen concentrate, reconstituted
92512090 Pina Colada, nonalcoholic
92512110 Margarita mix, nonalcoholic
92513000 Slush frozen drink
92513010 Slush frozen drink, no sugar added
92530410 Fruit flavored drink, with high vitamin C
92530510 Cranberry juice drink, with high vitamin C
92530610 Fruit juice drink, with high vitamin C
92530950 Vegetable and fruit juice drink, with high vitamin C
92531030 Fruit juice drink (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
92550400 Vegetable and fruit juice drink, with high vitamin C, diet
92550405 Vegetable and fruit juice drink, with high vitamin C, 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 Fruit juice drink, reduced sugar (Sunny D)
92552030 Fruit juice drink (Capri Sun)
92582100 Fruit juice drink, with high vitamin C, plus added calcium
92582110 Fruit juice drink, added calcium (Sunny D)
92612010 Sugar cane beverage
92801000 Wine, nonalcoholic
92802000 Wine, light, nonalcoholic
92803000 Nonalcoholic malt beverage
92804000 Shirley Temple

Foods adjusted for being present in dried form
Reconstitution factor of 4 to 10.23
[2'-FL] = 0.48 to 1.23 g/100 g

92511000 Lemonade, frozen concentrate, not reconstituted
92512040 Frozen daiquiri mix, frozen concentrate, not reconstituted
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

Fruit juices and nectars
[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
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%
64104610 Blueberry juice
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%
64134015 Fruit smoothie, with whole fruit, no dairy
64134020 Fruit smoothie, with whole fruit, no dairy, added protein
64134025 Fruit smoothie, with whole fruit, non-dairy
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, nectar
75200700 Aloe vera juice drink
78101000 Vegetable and fruit juice, 100% juice, with high vitamin C
78101100 Fruit and vegetable smoothie, with dairy
78101110 Fruit and vegetable smoothie, added protein
78101115 Fruit and vegetable smoothie, non-dairy
78101118 Fruit and vegetable smoothie, non-dairy, added protein
78101120 Fruit and vegetable smoothie, bottled
78101125 Fruit and vegetable smoothie, no dairy
95342000 Fruit juice, acai blend

Foods adjusted for being present in dried form
Reconstitution factor of 4
[2'-FL] = 0.48 g/100 g

61210720 Orange juice, 100%, frozen, not reconstituted

Canned fruit
[2'-FL] = 1.7 g/100 g

61101200 Grapefruit, canned
61122300 Orange, canned, NFS
61122320 Orange, canned, juice pack
61122330 Orange, canned, in syrup
63103110 Apricot, canned
63115110 Cherries, canned
63119110 Fig, canned
63129030 Mango, canned
63133100 Papaya, canned
63135110 Peach, canned, NFS
63135140 Peach, canned, in syrup
63135170 Peach, canned, juice pack
63137110 Pear, canned, NFS
63137140 Pear, canned, in syrup
63137170 Pear, canned, juice pack
63141110 Pineapple, canned, NFS
63141140 Pineapple, canned, in syrup
63141170 Pineapple, canned, juice pack
63143110 Plum, canned
63147110 Rhubarb
63203110 Bluberries, canned
63207110 Cranberry sauce
63223110 Strawberries, canned
63311110 Fruit cocktail, canned, NFS
63311140 Fruit cocktail, canned, in syrup
63311170 Fruit cocktail, canned, juice pack

Fruit-based desserts
[2'-FL] = 1.7 g/100 g

63301010 Ambrosia
63401010 Apple salad with dressing
63401060 Apple, candied
63401070 Fruit, chocolate covered
63402950 Fruit salad, excluding citrus fruits, with salad dressing or mayonnaise
63402960 Fruit salad, excluding citrus fruits, with whipped cream

63402970 Fruit salad, excluding citrus fruits, with nondairy whipped topping
63402980 Fruit salad, excluding citrus fruits, with marshmallows
63402990 Fruit salad, including citrus fruits, with pudding
63403000 Fruit salad, excluding citrus fruits, with pudding
63403010 Fruit salad, including citrus fruits, with salad dressing or mayonnaise
63403020 Fruit salad, including citrus fruit, with whipped cream
63403030 Fruit salad, including citrus fruits, with nondairy whipped topping
63403040 Fruit salad, including citrus fruits, with marshmallows

Processed Vegetables and Vegetable Juices

Vegetable juices and nectars
[2'-FL] = 0.12 g/100 g

73105000 Beet juice
73105010 Carrot juice, 100%
74301100 Tomato juice, 100%
74301150 Tomato juice, 100%, low sodium
74302000 Tomato juice cocktail
74303000 Tomato and vegetable juice, 100%
74303100 Tomato and vegetable juice, 100%, low sodium
75132000 Mixed vegetable juice
75132100 Celery juice
78101130 Vegetable smoothie

Sugar Substitutes

Table-top sweeteners
[2'-FL] = 30 g/100 g

91106010 Sugar substitute and sugar blend
91107000 Sugar substitute, sucralose, powder
91108000 Sugar substitute, stevia, powder
91108010 Sugar substitute, stevia, liquid
91108020 Sugar substitute, monk fruit, powder
91200000 Sugar substitute, powder, NFS
91200005 Sugar substitute, liquid, NFS
91200040 Sugar substitute, saccharin, powder
91200110 Sugar substitute, saccharin, liquid
91201010 Sugar substitute, aspartame, powder
91302020 Agave liquid sweetener

Sweet Sauces, Toppings, and Syrups

Syrups used to flavor milk beverages
[2'-FL] = 0.7 g/100 g

91301130 Strawberry drink syrup

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March 22, 2023

Dr. Ellen Anderson
Regulatory Review Scientist
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

Dear Dr. Anderson,

Re: GRAS Notice No. GRN 001051

In response to your Amendment_Follw-up of March 1, 2023, below are our responses to your request for additional information regarding GRN 001051. FDA's questions are italicized text and our responses are in plain text.

We hope the responses to your questions are satisfactory. We are looking forward to your completed evaluation. If you have any further questions or need clarification, please reach out to me at saori.akizuki@kyowa-kirin.co.jp.

Yours sincerely,

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Response to Questions from U.S. FDA – GRAS Notice No. GRN 001051 – 2'-Fucosyllactose (2'-FL)

OVERVIEW

Kyowa Hakko Bio Co., Ltd. ("Kyowa") presents the following responses to the United States (U.S.) Food and Drug Administration's (FDA's) letter dated 01 March 2023, pertaining to questions from the Agency on the Generally Recognized as Safe (GRAS) uses of 2'-fucosyllactose (2'-FL) described in GRAS Notice No. GRN 001051.

RESPONSES

Question 1

Based on our review of GRN 001051 and the October amendment, we recommend that Kyowa requests we cease our evaluation, unless Kyowa chooses to amend GRN 001051 to reflect the following:

1. *Limit the intended uses of your 2'-FL to substitutional uses for other sources of 2'-FL. In an amendment, Kyowa could cite existing uses and a cumulative estimate of dietary exposure from a recent GRAS notice that has received a "no questions" letter from FDA. Additional uses of the ingredient and any increases in dietary exposure may be addressed in a new submission provided that sufficient generally available and accepted data and information to support the safety of the expanded uses of 2'-FL exist.*

Response 1

In accordance with the FDA's recommendation, Kyowa would like to revise their intended uses to align with those that have previously been concluded to be Generally Recognized as Safe (GRAS) and notified to the Agency without questions (GRN 546, GRN 571, GRN 650, GRN 735, GRN 749, GRN 852, GRN 897, and GRN 1014 - U.S. FDA, 2015a,b, 2016, 2018a,b, 2019, 2020, 2022a). Therefore, the intended use of Kyowa's 2'-FL will be substitutional to other sources of 2'-FL that are currently available on the U.S. market.

Kyowa's intended uses are summarized in an updated food use table below (Table 1) and align with the existing uses previously concluded to be GRAS and notified to the Agency without questions, as outlined in GRN 1014 – U.S. FDA, 2022a.[1]

[1] GRAS Notice 1014, 2'-Fucosyllactose in Selected Conventional Foods and Enteral Tube Feeding Formulas (fda.gov).

Table 1 Summary of the Individual Proposed Food Uses and Use Levels for 2'-FL in the United States

Food Category (21 CFR §170.3 – U.S. FDA, 2022b)	Food Uses[a]	Use Levels (g/L or g/kg)
Baked goods and baking mixes	Breads and baked goods, gluten-free	48
Beverages and beverage bases	Carbonated beverages	1.2
	Enhanced, fortified, and flavored waters (incl. carbonated waters)	1.2
	Sports, isotonic, and energy drinks	6
	Oral electrolyte solution	1.2[b]
Breakfast cereals	Hot breakfast cereals (*e.g.*, oatmeal, grits), instant and RTE	31
	RTE breakfast cereals	
	Puffed cereals	80
	High-fiber cereals	40
	Biscuit-type cereals	40
Coffee and tea	Coffee	10
	Tea	10
Dairy product analogs	Milk imitates	1.2
	Beverage whiteners	600
	Non-dairy yogurt	12
Frozen dairy desserts and mixes	Frozen desserts	17
Gelatins, puddings, and fillings	Dairy-based puddings, custards, and mousses	17
	Fruit pie filling	14.1
	"Fruit prep" such as fruit filling in bars, cookies, yogurt, and cakes	30
Grain products and pastas	Snack/breakfast bars	30
Infant and toddler foods	Term infant formula	2.4
	Toddler formula	2.4
	Cereals (dry and RTE)	12
	Yogurt	10
	Drinks for young children, incl. juice beverages identified as "baby drinks"	1.2
	Baby snacks including crackers, pretzels, cookies, and other snack items	57
Jams and jellies	Jellies and jams, fruit preserves, and fruit butters	60
Meal replacement products	Meal replacement bars for weight loss	40
	Milk-based meal replacement beverages for weight reduction for adults and formulas for pregnant women	12
	Non-milk-based meal replacement drinks for weight reduction for adults and formulas for pregnant women	12
	Milk-based meal replacement beverages for children	12
Milk, whole, and skim	Unflavored pasteurized and sterilized milk	12
Milk products	Buttermilk	1.2
	Flavored milk	1.2
	Yogurt	1.2
Processed fruits and fruit juices	Fruit flavored drinks and ades	1.2
	Fruit juices and nectars	1.2
Processed vegetables and vegetable juices	Vegetable juices and nectars	1.2
Sugar substitutes	Table-top sweeteners	1.2

Table 1 Summary of the Individual Proposed Food Uses and Use Levels for 2'-FL in the United States

Food Category (21 CFR §170.3 – U.S. FDA, 2022b)	Food Uses[a]	Use Levels (g/L or g/kg)
Sweet sauces, toppings, and syrups	Syrups	7
Foods for special dietary uses	Oral nutritional supplements and enteral tube feeding	20

2'-FL = 2'-fucosyllactose; CFR = *Code of Federal Regulations*; incl. = including; RTE = ready-to-eat.
[a] 2'-FL is only intended for use in unstandardized products. It will not be used in standardized products where the standards of identity, as established under 21 CFR §130 to 169 (U.S. FDA, 2022b), do not permit its addition.
[b] Excluded from exposure assessment as products are solely intended for short term use.

Dietary exposure to the existing uses concluded to be GRAS and notified to the Agency without questions has recently been estimated in a cumulative assessment in GRN 1014[1] using data from the 2015-2016 National Health and Nutrition Examination Survey (NHANES) (USDA, 2019; CDC, 2020a,b; U.S. FDA, 2022a). Kyowa's 2'-FL will be substitutional to other sources of 2'-FL that are currently available on the U.S. market; no additional exposure assessment was conducted, as it was concluded that the intake estimates from the cumulative dietary exposure assessment in GRN 1014 are representative of the dietary exposure from Kyowa's intended uses, which include all uses previously concluded to be GRAS and notified to the Agency without questions. The "consumer-only" exposure estimates reported in GRN 1014,[1] which consider all uses of 2'-FL concluded to be GRAS and notified to the Agency without questions, are summarized below (U.S. FDA, 2022a).

The mean and 90th percentile consumer-only intakes in the total population (ages 2 years and up) were 2.50 g/day (0.037 g/kg body weight/day) and 5.16 g/day (0.077 g/kg body weight/day), respectively. On an absolute basis, the highest mean and 90th percentile intakes were reported in adults, at up to 2.90 g/day and 5.93 g/day, respectively. On a body weight basis, the highest mean and 90th percentile intakes were reported in toddlers (13 months-2 years), at up to 0.108 g/kg body weight/day and 0.233 g/kg body weight/day, respectively.

These intakes are not anticipated to change, as Kyowa's 2'-FL would be substitutional to current sources of 2'-FL on the U.S. market.

Question 2

2. *Reduce the specification for "unidentified carbohydrate peaks" and propose a specification of ≥ 92% of specified carbohydrates, where the specified carbohydrates include 2'-FL, D-lactose, DFL, and L-fucose, in accordance with FCC 13.*

Response 2

Kyowa agrees to revise the specification for 2'-FL. Kyowa will remove the specification for unidentified carbohydrate peaks and will increase the limit for 2'-FL to ≥92%, which will meet the specification for 2'-FL in the *Food Chemicals Codex* (FCC, 2023). Kyowa provides an updated Table 2.3.1-1 (specifications) below. The revised specification parameters appear in red text. Kyowa requests to remove Lot D from GRN 001051, as it does not meet the updated specifications in Table 2.3.1-1 and will therefore not be sold.

Table 2.3.1-1 Physical and Chemical Specifications for 2'-FL

Specification Parameter	Specification	Method
Organoleptic		
Appearance	Powder	Visual observation
Color	White to off-white	General Notice, JP[a]
Physicochemical		
Identification	RT of standard ± 3%	HPLC-PAD (internal method)
Purity	≥92% dwb	HPLC-PAD (internal method)
Water	≤9.0 w/w%	JP 2.48[a]
Ash	≤0.5 w/w%	JP 2.44[a]
Residual protein	≤100 mg/kg (0.01%)	Bradford method
pH (25˚C, 5% solution)	4.0 to 9.0	JP 2.54[a]
Other Carbohydrates		
D-lactose	≤5 (dwb%)	HPLC-PAD (internal method)
L-fucose	≤1 (dwb%)	HPLC-PAD (internal method)
D-glucose and D-galactose	≤1 (dwb%)	HPLC-PAD (internal method)
Fucosylgalactose	≤3 (dwb%)	HPLC-PAD (internal method)
Difucosyllactose	≤3 (dwb%)	HPLC-PAD (internal method)
Heavy Metals		
Arsenic	≤0.1 mg/kg	USP 233[b]
Cadmium	≤0.1 mg/kg	USP 233[b]
Lead	≤0.1 mg/kg	USP 233[b]
Mercury	≤0.1 mg/kg	USP 233[b]
Iron	≤10 mg/kg	USP 233[b]

2'-FL = 2'-fucosyllactose; dwb = dry weight basis; HPLC-PAD = high-performance liquid chromatography with pulsed amperometric detection; JP = *Japanese Pharmacopoeia*; RT = retention time; USP = *United States Pharmacopoeia*.
[a] Method is consistent with the compendial method specified in 17th edition of the *Japanese Pharmacopeia* (2016).
[b] Method is consistent with the compendial method specified in the *United States Pharmacopeia* 35th revision (2011).

Question 3

If Kyowa agrees to address the changes outlined above and have us continue review of an amended GRN 001051, we request that you also address the following:

3. *Please provide revised heavy metal limits that, at a minimum, are consistent with the FCC 13 monograph for 2'-FL.*

    - *In question 10b, we noted that the specified limits (each ≤ 0.2 mg/kg) for arsenic, cadmium, lead, and mercury are higher compared to the levels reflected in the results of the batch analyses (each ≤ 0.05 mg/kg (LOQ)). We recommended that specifications for these heavy metals be reduced to reflect the batch analyses. In the October amendment, you responded that Kyowa prefers to maintain the current specified limits because they "…are comparable to limits for other 2'-FL ingredients concluded to be GRAS and notified to the FDA without questions…" In view of FDA's recent "Closer to Zero" initiative focusing on reducing dietary exposure to arsenic, lead, cadmium, and mercury from foods consumed by infants and young children, we would anticipate acceptable limits for heavy*

metals to be reduced over time. We also note that, in the FCC 13 monograph for 2'-FL, the limit for lead is ≤0.1 mg/kg, a level that is below the 0.2 mg/kg value cited in GRN 001051 and earlier GRNs. We request that specifications for ingredients, particularly those consumed by infants and young children, are as low as possible and reflect results of batch analyses for an ingredient produced in accordance with current GMPs.

Response 3

Kyowa recognizes the FDA's recent "Closer to Zero" initiative (U.S. FDA, 2023). In support of this initiative, Kyowa proposes new specification limits for arsenic, lead, cadmium, and mercury of 0.1 mg/kg (each individually).

For clarity, Kyowa provides an updated Table 2.3.1-1 (specifications) in the response to FDA's question 2 above. Corrected information appears in red text.

Question 4

4. *For the administrative record, please provide a statement that the intended uses of 2'-FL do not include foods with standards of identity where the standards do not permit addition of the ingredient.*

    - *In response to question 3a subparts i and ii, Kyowa states the following: "All other varieties of bread, rolls, and buns with standards of identity must conform to the requirements prescribed under Part 136.110. It is expected that the addition of 2'-FL to bread products with standards of identity would comply with 21 CFR 136.110(c)(18) since its addition would not change the identity or the physical and nutritional characteristic of the bread product." We note, for your awareness, that food standards of identity are the purview of the Office of Nutrition and Food Labeling (ONFL).*

Response 4

Kyowa confirms that 2'-FL is solely intended for use in unstandardized products. 2'-FL will not be used in any foods whereby the standards of identity, as established under 21 CFR §130 to 169, do not permit its addition (U.S. FDA, 2022b).

Question 5

5. *For the administrative record, please provide a statement that all methods of analysis are validated for the uses described in the notice.*

    - *In response to question 10a, Kyowa notes, regarding the method for heavy metals based on USP 233, that "dietary supplement ingredients are legally defined as food ingredients in the U.S. and there is no scientific basis to infer that a method validated for use on a dietary supplement ingredient would not be similarly suitable for a high-purity food ingredient." We note that USP has both USP-NF dietary supplement standards and FCC dietary supplement standards.[2] When available, we defer to FCC standards, recognizing that there may be different forms of the ingredient intended for use as a dietary supplement versus as a food ingredient, and that the methods of manufacture and limits for impurities may be different. As noted in USP-NF 2232 Elemental Contaminants in*

Dietary Supplements (Official as of December 1, 2014), "Specific monographs may provide different limits for articles that need to be consumed in large quantities." We also typically look for the methods cited to be current. We note for example, the FCC 13 monograph for 2'-FL would be applicable to your ingredient. While it may be that the limits and associated methodology between USP-NF 2232 and the 2'-FL FCC 13 monograph are similar, rather than requesting a comparative discussion to support as much, we request a brief statement for the record that the methods are validated and fit for purpose.

[2] *Legal Recognition – Standards Categories | USP : https://www.usp.org/about/legal-recognition/standard-categories#food-ingredients*

Response 5

Kyowa confirms that all analytical methods are validated and fit for purpose.

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Table of CFR Sections Referenced (Title 21—Food and Drugs)

Part	Section §	Section Title
130—Food Standards: General; 131—Milk and cream; 133—Cheese and related cheese products; 135—Frozen desserts; 136—Bakery products; 137—Cereal flours and related products ; 139—Macaroni and noddle products; 145—Canned fruits; 146—Canned fruit juices; 150—Fruit butters, jellies, preserves, and related products; 152—Fruit pies; 155—Canned vegetables; 156—Vegetable juices; 158—Frozen vegetables; 160—Eggs and egg products; 161—Fish and shellfish; 163—Cacao products; 164—Tree nut and peanut products; 165—Beverages; 166—Margarine; 168—Sweeteners and table sirups; 169—Food dressings and flavorings	130—169	[full section]
170—Food additives	170.3	Definitions

U.S. FDA (2023). *Closer to Zero: Reducing Childhood Exposure to Contaminants from Foods*. Silver Spring (MD): U.S. Food and Drug Administration (U.S. FDA), Center for Food Safety and Applied Nutrition (CFSAN). Available at: https://www.fda.gov/media/147324/downloadhttps://www.fda.gov/food/environmental-contaminants-food/closer-zero-reducing-childhood-exposure-contaminants-foods [03/03/2023].

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September 23, 2023

Dr. Ellen Anderson
Regulatory Review Scientist
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Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

Dear Dr. Anderson,

Re: GRAS Notice No. GRN 001051

In response to your email of August 11, 2023, below are our responses to your request for additional information regarding GRN 001051. FDA's questions are italicized text and our responses are in plain text.

We hope the responses to your questions are satisfactory. We are looking forward to your completed evaluation. If you have any further questions or need clarification, please reach out to me at saori.akizuki@kyowa-kirin.co.jp.

Yours sincerely,

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Response to Questions from U.S. FDA – GRAS Notice No. GRN 001051 – 2'-Fucosyllactose (2'-FL)

OVERVIEW

Kyowa Hakko Bio Co., Ltd. ("Kyowa") presents the following responses to the United States (U.S.) Food and Drug Administration's (FDA's) letter dated 10 August 2023, pertaining to questions from the Agency on the Generally Recognized as Safe (GRAS) uses of 2'-fucosyllactose (2'-FL) described in GRAS Notice No. GRN 001051.

RESPONSES

Question 1

1. *Use of 2'-FL in oral electrolyte solutions (OES) in GRN 001014 as an existing use is in error. Although use in OES was proposed as a new use in GRN 001014, in the April 26, 2022, amendment to GRN 001014, the intended use of 2'-FL in OES was removed from the scope of that notice. Please confirm that OES are not among the intended uses in GRN 001051.*

Response 1

Kyowa confirms that OES are not within the intended uses in GRN 001051.

Question 2

2. *The maximum use level of 2'-FL in baby yogurt is listed as 10 g/kg in the March 2023 amendment. Please confirm that the intended use of 2'-FL in yogurt and other baby foods for infants and young children is at levels up to 12 g/kg and that the intended uses do not include foods under the jurisdiction of USDA.*

Response 2

Kyowa confirms that the intended use of 2'-FL in yogurt and other baby foods for infants and young children is up to 12 g/kg and that the intended uses do not include foods under the jurisdiction of the USDA.

Question 3

3. *The maximum use level of 2'-FL in drinks for young children is given as 1.2 g/L in the March 2023 amendment. Please confirm that the intended use of 2'-FL in other drinks for infants and young children (including juice and yogurt drinks but not "toddler formula") is at levels up to 10 g/L.*

Response 3

Kyowa confirms that the intended use of 2'-FL in other drinks for infants and young children (including juice and yogurt drinks but not "toddler formula") is at levels up to 10 g/L.

Question 4

4. *There are existing uses of 2'-FL in meal replacements for general use (not weight reduction or management per se) that are not included in the March 2023 amendment. Please confirm that the maximum intended use levels of 2'-FL in meal replacement drinks (general use) and meal replacement bars (general use) are 5 g/L and 30 g/kg, respectively.*

Response 4

Kyowa confirms that the maximum use levels of 2'-FL in meal replacement drinks (general use) and meal replacement bars (general use) are 5 g/L and 30 g/kg, respectively.

Question 5

5. *The maximum use level for 2'-FL in unflavored pasteurized and sterilized milk is reversed with that for yogurt in the March 2023 amendment. Please confirm that the maximum use levels for 2'-FL in unflavored pasteurized and sterilized milk and for yogurt are 1.2 g/L and 12 g/kg, respectively.*

Response 5

Kyowa confirms that the maximum use levels for 2'-FL in unflavored pasteurized and sterilized milk and for yogurt are 1.2 g/L and 12 g/kg, respectively.

Question 6

6. *For table-top sweeteners, the use level in GRN 000546 is given as 0.12 g per 4-g serving of powder; by calculation this use level is 300 g/kg. Please confirm the maximum intended use level of 300 g 2'-FL per kg sweetener.*

Response 6

Kyowa confirms that the maximum intended use level for table-top sweeteners is up to 300 g/kg, based on alignment with the use level included in the GRN 000546 response letter (U.S. FDA, 2015a).

Question 7

7. *Oral and enteral tube feeding uses for individuals ≥11 years of age were included among the intended uses in GRNs 000897 and 001014. Although GRN 001014 does not identify an age range in its intended uses table, the notifier described the use level as identical to that of GRN 000897 in its January 24, 2023, amendment. Please confirm that the intended use of 2'-FL at levels up to 20 g/L in oral nutritional supplements and enteral tube feeding are for individuals ≥11 years of age.*

Table 1: *Intended food categories and maximum use levels for 2'-FL in previous GRNs (000546, 000571, 000650, 000735, 000749, 000852, 000897, 001014, 001060), GRN 001051 (March 2023 amendment), and cumulative maximum use levels of 2'-FL.*

Food Categories	***Previous GRNs: range of maximum use levels***	***GRN 001051: use levels stated in March 2023 amendment***	***Cumulative maximum use levels through GRN 001060***
Baked goods and baking mixes (g/kg)			
Breads and baked goods, gluten-free	*24-48*	*48*	*48*
Beverages and beverage bases (g/L)			
Carbonated beverages	*1.2*	*1.2*	*1.2*
Enhanced or fortified waters[a]	*1.2*	*1.2*	*1.2*
Sports, isotonic, and energy drinks[b]	*0.8-6.0*	*6.0*	*6.0*
Breakfast cereals (g/kg)			
Hot breakfast cereals, prepared	*4.8-31*	*31*	*31*
Ready to eat (RTE) breakfast cereals, puffed	*80*	*80*	*80*
RTE breakfast cereals, high fiber	*30-40*	*40*	*40*
RTE breakfast cereals, biscuit-type	*20-40*	*40*	*40*
Coffee and tea (g/L)[c]			
Coffee	*1.2-10*	*10*	*10*
Tea	*5-10*	*10*	*10*
Dairy product analogs (g/kg or g/L)			
Imitation milk	*1.2*	*1.2*	*1.2*
Beverage whiteners (powdered)[d]	*600*	*600*	*600*
Non-dairy yogurt	*5.3-12*	*12*	*12*
Frozen dairy desserts and mixes (g/kg)			
Frozen dairy-based desserts	*17*	*17*	*17*
Gelatins, Puddings and Fillings (g/kg)			
Puddings, custards, and mousses	*17*	*17*	*17*
Fruit pie filling	*14.1*	*14.1*	*14.1*
Fruit filling/fruit prep in bars, cookies, yogurt, cakes	*30*	*30*	*30*
Grain products and pastas (g/kg)			
Cereal bars incl. snack, granola, & breakfast bars[e]	*12-30*	*30*	*30*
Foods for infants and young children through 3 years of age (g/kg or g/L)			
Non-exempt infant formula for term infants	*2.0-2.4*	*2.4*	*2.4*
Exempt infant formula for term infants: hydrolyzed and amino acid-based formulas	*2.0-2.4*	*2.4*	*2.4*
Formula-type drinks for young children (incl. "toddler formula")	*2.0-2.4*	*2.4*	*2.4*
Hot cereals for infants and young children, prepared (from dry instant) and ready to serve	*10.9-12*	*12*	*12*
Other baby foods for infants and young children (incl. yogurt, fruits, vegetables, toddler meals & desserts)[f]	*10.9-12*	*10*	*12*

Table 1: *Intended food categories and maximum use levels for 2'-FL in previous GRNs (000546, 000571, 000650, 000735, 000749, 000852, 000897, 001014, 001060), GRN 001051 (March 2023 amendment), and cumulative maximum use levels of 2'-FL.*

Food Categories	***Previous GRNs: range of maximum use levels***	***GRN 001051: use levels stated in March 2023 amendment***	***Cumulative maximum use levels through GRN 001060***
Other drinks for infants and young children (incl. juice and yogurt drinks)	*1.2-10*	*1.2*	*10*
Baby snacks (crackers, pretzels, cookies, and other dry snack items)	*12-57*	*57*	*57*
Jams and jellies (g/kg)			
Jams, jellies, preserves, and fruit butters	*60*	*60*	*60*
Meal replacement drinks (g/L) and bars (g/kg)			
Meal replacement bars for weight management	*40*	*40*	*40*
Meal replacement bars, general use	*12-30*	*--*	*30*
Meal replacement drinks for weight management, milk and non-milk based	*1.2-12*	*12*	*12*
Meal replacement drinks, general use (incl. dairy and non-dairy nutritional drinks and smoothies)	*1.2-5*	*--*	*5*
Meal replacement drinks for children (e.g., pediatric drinks such as Pediasure®)[g]	*2.4-12*	*12*	*12*
Milk (whole and skim) and Milk products (g/L)			
Unflavored pasteurized and sterilized milk	*1.2*	*12*	*1.2*
Buttermilk	*1.2*	*1.2*	*1.2*
Flavored and fermented milks	*1.2*	*1.2*	*1.2*
Yogurt	*5.3-12*	*1.2*	*12*
Processed fruits and vegetables (g/L)			
Fruit-flavored drinks and ades	*1.2*	*1.2*	*1.2*
Fruit juices and nectars	*1.2*	*1.2*	*1.2*
Vegetable juices and nectars	*1.2*	*1.2*	*1.2*
Sugar substitutes, Syrups (g/kg or g/L)			
Table-top sweeteners	*300*	*1.2*	*300*
Syrups used to flavor milk beverages	*7*	*7*	*7*
Other nutritional drinks (g/L)[h]			
Nutritional drinks for pregnant women	*6-12*	*12*	*12*
Oral and enteral tube feeding formulas for ages ≥11 years	*20*	*20 (age not specified)*	*20*
Uses removed from previous notices			
Oral electrolyte solutions	*~~1.2~~*	*1.2*	*No uses*

Table 1: *Intended food categories and maximum use levels for 2'-FL in previous GRNs (000546, 000571, 000650, 000735, 000749, 000852, 000897, 001014, 001060), GRN 001051 (March 2023 amendment), and cumulative maximum use levels of 2'-FL.*

Food Categories	***Previous GRNs: range of maximum use levels***	***GRN 001051: use levels stated in March 2023 amendment***	***Cumulative maximum use levels through GRN 001060***

[a] The terms "flavored and enhanced water" has been previously used by notifiers; however, given that other categories of beverages (e.g., carbonated beverages, sports drinks) are also flavored, FDA uses the What We Eat in America (WWEIA) food category "Enhanced or fortified waters" to identify NHANES food codes for flavored/enhanced waters that may also contain vitamins, minerals, and some electrolytes, but a lower concentration of electrolytes than "sports drinks". Examples of enhanced and fortified waters include waters represented by the 94xxxxxxx NHANES food codes excluding 94300100 bottled water for babies (plain, unsweetened) and bottled water with a standard of identity (21 CFR Part 165.110).

[b] The category "sports, isotonic, and energy drinks" includes both "diet sport and energy drinks" and "sport and energy drinks" WWEIA food categories. Sport and energy drinks are represented by food codes 9531xxxx, 9532xxx, and 95341000 in the 2015-2016 and 2017-2018 NHANES. Foods codes 95330100 "fluid replacement, electrolyte solution" (e.g., Pedialyte) and 95330500 "fluid replacement, 5% glucose in water" are grouped in "sport and energy drinks" by the WWEIA classification system; however, FDA does not consider oral rehydration solutions to be sport or energy drinks and does not include these categories in its estimates of dietary exposure for sport and energy drinks.

[c] The category of coffee and tea is presumed to include ready to drink (e.g., bottled, flavored) coffees and teas and powder mixes used to prepare coffee and tea. Given the separate intended uses of 2'-FL in milk, imitation milk, beverage whiteners, and table-top sweeteners, for estimates of dietary exposure it is assumed that the intended uses of 2'-FL do not include use in plain brewed coffee or tea.

[d] Given the use level in beverage whiteners is based on the reference amount customarily consumed per eating occasion (21 CFR 101.12) or RACC of 2 g for "cream or cream substitutes, powder". Given the RACC of 15 g for liquid cream substitutes, for estimates of dietary exposure, it may be assumed that the use level of 2'-FL in liquid cream substitutes is reduced by a factor of 15/2 or 7.5 so that the use level is 80 g/kg.

[e] Although cereal bars and meal replacement bars (general use) are listed separately in the table, for practical purposes they may be combined given the similarity of many foods within these categories and the identical maximum use level.

[f] Uses of 2'-FL in infant and toddler foods do not include meat and poultry foods under the purview of USDA.

[g] Although Pediasure has been included as an example of both "infant meal replacement products" (GRNs 000735, 000852, 000932) and "milk-based meal replacement beverages for children" (GRN 001014), Pediasure is not an infant formula and is intended for children ages 2-13 as a meal supplement or, under medical supervision, as a sole source of nutrition. (https://pediasure.com/nutrition-questions-answers).

[h] Although meal replacement products (general and weight management) are also categorized as "nutritional beverages" and powders, intended uses in these foods are listed separately from nutritional beverages for pregnant women and products for tube feeding.

Response 7

Kyowa confirms that the intended uses of 2'-FL at levels up to 20 g/L in oral nutritional supplements and enteral tube feeding are for individuals ≥11 years of age.

Question 8

8. *In the March 2023 amendment, Kyowa cites the estimate of dietary exposure provided in GRN 001014. We note that the cumulative estimates of dietary exposure in GRN 001014 appear to not include use of 2'-FL in infant formula. Therefore, we felt it was necessary to establish a benchmark cumulative estimate of dietary exposure to 2'-FL going forward. We determined the cumulative estimates of dietary exposure for 2'-FL using the maximum use levels reported in all previously submitted GRAS notices (000546, 000571, 000650, 000735, 000749, 000852, 000897, 001014, 001060). We note that our cumulative estimate of dietary exposure for 2'-FL is similar to that reported in GRN 001060. For completeness of the record for GRN 001051, we recommend that you estimate dietary exposure using recent NHANES food consumption data and the maximum use levels included in the preceding table or, alternatively, cite a cumulative estimate of dietary exposure for 2'-FL from a recent GRAS notice that includes infant formula. If you choose to cite the estimate of dietary exposure from GRN 001060, please be aware that the cumulative use table provided in GRN 001060 (Table 7, November 18, 2022, amendment) appears to have inadvertently omitted some foods listed in GRN 000546 (e.g., coffee, tea, gluten-free bread) and your exposure discussion should address the effect of these foods on the estimated cumulative dietary exposure.*

Response 8

In accordance with the FDA's recommendation, Kyowa has conducted a cumulative exposure assessment for 2'-FL using the food uses and use levels outlined by the Agency in Table 1 of their follow up questions (see above). These uses and use levels align with the existing uses previously concluded to be GRAS and notified to the Agency without questions, as outlined in GRNs 000546, 000571, 000650, 000735, 000749, 000852, 000897, 000929, 001014, 001034, and 001060 (U.S. FDA 2015a,b, 2016, 2018a,b, 2019, 2020, 2021, 2022a,b, 2023). These uses and use levels also represent Kyowa's intended uses and use levels, as Kyowa's intended uses and use levels for 2'-FL in the U.S. are those that have been previously concluded to be GRAS and notified to the Agency without questions. The use of Kyowa's 2'-FL will be substitutional to other sources of 2'-FL that are currently available on the U.S. market. Kyowa's proposed uses used for the cumulative assessment are summarized in an updated food use table below (Table 2). The percent contribution of each food use to the intake estimates in the general population are also summarized in Table 2.

Table 2 Summary of Individual Food Uses and Use levels Notified as GRAS [a] for 2'-Fucosyllactose in the United States

Food Category (21 CFR §170.3) (U.S. FDA, 2022c)	Proposed Food Use[b]	Maximum Use Level (g/kg or g/L)[c]	General Population Contribution Percentage[d]
Baked Goods and Baking Mixes	Breads and baked goods, gluten-free	48.0	0.1 to 1.4
Beverages and Beverage Bases	Non-milk meal replacement, for weight management[e]	12.0	0.0 to 0.6
	Non-milk meal replacement and nutritional beverages, for general use (including smoothies)[e]	5.0	0.2 to 1.5
	Carbonated beverages	1.2	0.6 to 7.4
	Sports, isotonic, and energy drinks	6.0	1.3 to 12.9
	Enhanced or fortified waters	1.2	0.1 to 0.5

Table 2 Summary of Individual Food Uses and Use levels Notified as GRAS [a] for 2'-Fucosyllactose in the United States

Food Category (21 CFR §170.3) (U.S. FDA, 2022c)	Proposed Food Use[b]	Maximum Use Level (g/kg or g/L)[c]	General Population Contribution Percentage[d]
Breakfast Cereals	Hot cereals	31.0	7.9 to 29.2
	RTE cereals	80.0 (puffed) 40.0 (high fiber) 40.0 (biscuit type)	0.9 to 5.4 5.6 to 19.2 1.0 to 2.7
Coffee and Tea	Coffee	10	0.2 to 8.4
	Tea	10	0.2 to 7.9
Dairy Product Analogs	Imitation milk	1.2	0.1 to 0.7
	Non-dairy yogurts	12.0	<0.1
	Beverage whitener	600[f]	0.8 to 26.1
Frozen Dairy Desserts and Mixes	Frozen dairy-based desserts (including ice creams and frozen yogurts, frozen novelties)	17.0	2.2 to 19.1
Gelatins, Puddings, and Fillings	Puddings, custards, and mousses	17.0	0.3 to 1.2
	Fruit pie filling	14.1	0.1 to 0.5
	Fruit filling/fruit prep in bars, cookies, yogurt, and cakes	30.0	0.1 to 0.6
Grain Products and Pastas	Meal replacement bars, for weight management	40.0	0.1 to 2.1
	Cereal bars including snack, granola, breakfast, and nutrition bars (including meal replacement bars for general use)[g]	30.0	1.0 to 3.3
Infant and Toddler Foods	Non-exempt term infant formulas	2.4	22.0 to 63.8
	Exempt term infant formulas for food allergies (*i.e.*, extensively hydrolyzed formula and amino acid–based formula)	2.4	2.3 to 3.9
	Toddler formulas[h]	2.4	1.7 to 2.4
	Hot cereals for infants and young children	12.0	12.3 to 20.9
	Other baby foods for infants and young children	12.0	14.5 to 28.2
	Other drinks for young children	10.0	0.6 to 1.3
	Baby snacks (crackers, pretzels, cookies, and snack items)	57.0	1.4 to 5.6
Jams and Jellies	Jellies and jams, fruit preserves, and fruit butters	60.0	0.3 to 2.5
Milk, Whole and Skim	Unflavored pasteurized and sterilized milk (all acidophilus or fortified milks; whole milk, reduced-fat milk, low-fat milk, non-fat milk; including powdered milks, reconstituted)	1.2[i]	2.2 to 12.5
Milk Products	Buttermilk	1.2	<0.1
	Flavored milk and fermented milks	1.2	0.2 to 3.0
	Milk-based meal replacement, for weight management[e]	12.0	0.2 to 5.2
	Milk-based meal replacement and nutritional beverages, for general use (including smoothies)[e]	5.0	0.5 to 1.3
	Yogurt	12.0[j]	1.7 to 10.1
	Meal replacement drinks for children (*e.g.*, Pediasure)	12.0	0 to 3.4
	Formula and nutritional drinks intended for pregnant women (-9 to 0 months)[k]	12.0	NA
Processed Fruits and Fruit Juices	Fruit drinks and ades	1.2	1.4 to 3.8
	Fruit juices and nectars	1.2	1.0 to 4.9

Table 2 Summary of Individual Food Uses and Use levels Notified as GRAS [a] for 2'-Fucosyllactose in the United States

Food Category (21 CFR §170.3) (U.S. FDA, 2022c)	Proposed Food Use[b]	Maximum Use Level (g/kg or g/L)[c]	General Population Contribution Percentage[d]
Processed Vegetables and Vegetable Juices	Vegetable juices and nectars	1.2	0.0 to 0.2
Sugar Substitutes	Table-top sweeteners	300	0.0 to 2.4
Sweet Sauces, Toppings, and Syrups	Syrups used to flavor milk beverages	7.0	<0.1
Foods for Special Dietary Use	Oral nutritional supplements and enteral tube feeding (>11 years)[l]	20.0	NA

2'-FL = 2'-fucosyllactose; CFR = *Code of Federal Regulations*; FDA = Food and Drug Administration; GRAS = Generally Recognized as Safe; GRN = GRAS Notice; NA = not available; NHANES = National Health and Nutrition Examination Survey; RACC = Reference Amounts Customarily Consumed Per Eating Occasion; RTE = ready-to-eat; U.S. = United States.

[a] Food uses that have been previously notified as GRAS to the U.S. FDA and received a "no questions" letter, as detailed in GRNs 000546, 000571, 000650, 000735, 000749, 000852, 000897, 000929, 001014, 001034, and 001060.

[b] 2'-FL is intended for use in unstandardized products where standards of identity, as established under 21 CFR §130 to 169, do not permit its addition in standardized products (U.S. FDA, 2022d).

[c] Use level expressed on a 2'-FL basis in the final food, as consumed.

[d] Relative contribution (%) is provided as a range for each of the general population groups (ages ≥1 years), with the exception of the infant and toddler foods which present the range of contribution percentage for the two infant population groups <12 months of age.

[e] Includes ready-to-drink and powder forms.

[f] The use level in beverage whiteners is based on the reference amount customarily consumed per eating occasion (21 CFR 101.12) or RACC of 2 g for "cream or cream substitutes, powder." Given the RACC of 15 g for liquid cream substitutes, for estimates of dietary exposure, it may be assumed that the use level of 2'-FL in liquid cream substitutes is reduced by a factor of 15/2 or 7.5 so that the use level is 80 g/kg.

[g] Cereal bars and meal replacement bars (general use) have been combined given the similarity of many foods within these categories and the identical maximum use level.

[h] Formula products targeted toward young children (>12 months of age).

[i] It should be noted that in GRN 001014, this use level was erroneously reported as 12 g/L rather than 1.2 g/L.

[j] It should be noted that in GRN 001014, this use level was erroneously reported as 1.2 g/L rather than 12 g/L.

[k] Food codes for formula intended for pregnant women were not available in the 2017-2018 NHANES (USDA, 2022; CDC, 2023a,b). This intended use is excluded from the calculation of estimated daily intakes due to absence of consumption data.

[l] Foods for special dietary use are assessed separately from the intended food uses of 2'-FL in conventional foods, as they are intended for supplying a particular dietary need and/or supplementing the intake of a dietary component. Intake of 2'-FL from foods for special dietary use is, therefore, not expected to be cumulative to other dietary sources.

Estimates for the total cumulative intake of 2'-FL on both an absolute (g/day) and body weight (mg/kg body weight/day) basis from all food uses and use levels concluded to be GRAS and notified to the Agency without questions (GRNs 000546, 000571, 000650, 000735, 000749, 000852, 000897, 000929, 001014, 001034, and 001060) in the U.S are summarized in Table 3 below.

Table 3 Summary of the Estimated Cumulative Daily Intake of 2'-Fucosyllactose from Proposed Food Uses in the United States by Population Group (2017-2018 NHANES Data) (USDA, 2022; CDC, 2023a,b)

Population Group	Age Group	Consumer-only Intake					
		Percentage of Population (%)	n	Absolute Basis (g/day)		Body Weight Basis (mg/kg bw/day)	
				Mean	90th Percentile	Mean	90th Percentile
Infants	0 to 6 m	75.3	133	2.4	4.4	360	578
	7 to <12 m	100	124	4.3	7.7	474	812
Toddlers	1 to 2 y	99.9	306	2.9	5.7	237	477
Children	3 to 11 y	99.5	992	2.7	5.0	103	191
Female teenagers	12 to 19 y	98.0	439	3.0	6.4	50	103
Male teenagers	12 to 19 y	98.8	430	3.4	6.6	52	102
Female adults of childbearing age	16 to 49 y	96.7	1,182	4.0	8.5	56	119
Female adults	20 to 64 y	96.4	1,588	4.3	9.3	59	135
Male adults	20 to 64 y	97.1	1,393	4.6	10.3	53	122
Elderly	65 y and older	97.6	1,041	5.2	11.0	67	148
Total population	2 y and older	97.4	6,036	4.2	9.1	65	146

bw = body weight; n = sample size; m = months; NHANES = National Health and Nutrition Examination Survey; y = years.

The mean and 90th percentile consumer-only intakes in the total population (ages 2 years and older) were 4.2 g/day (65 mg/kg body weight/day) and 9.1 g/day (146 mg/kg body weight/day), respectively. On an absolute basis, the highest mean and 90th percentile intakes were reported in the elderly, at up to 5.2 and 11.0 g/day, respectively. On a body weight basis, the highest mean and 90th percentile intakes were reported in infants (7 to 12 months), at up to 474 and 812 mg/kg body weight/day, respectively.

The Agency noted that their cumulative estimate of dietary exposure for 2'-FL was similar to that reported in GRN 001060. Kyowa has thus compared their cumulative estimate of dietary exposure for 2'-FL to that reported in GRN 001060 (see Table 4 below). Similar to the Agency's comparison, when Kyowa's cumulative estimates were compared to GRN 001060, the intake estimates in toddlers, children, and male and female teenagers were comparable to those reported in GRN 001060. In the adult and elderly populations, Kyowa's estimated intakes were slightly higher than those reported in GRN 001060; however, this is likely due to the inclusion of the categories that the Agency noted as previously omitted from the cumulative dietary estimates in GRN 001060 (*i.e.*, gluten-free breads and baked goods, coffee, tea, beverage whiteners, meal replacement drinks for children [*e.g.*, Pediasure], and tabletop sweeteners). For example, in the adult and elderly population groups, the top contributors of these omitted categories were beverage whiteners (13.6 to 26.1%), coffee (7.0 to 8.4%), and tea (5.4 to 7.9%), accounting for approximately 30% of intake estimates in these population groups in the current cumulative assessment. Furthermore, use levels for high-fiber and biscuit type ready-to-eat breakfast cereals, which are also relatively significant contributors to intakes, were incorrectly reported in GRN 001060 at lower use levels than have been concluded to be GRAS. In the current cumulative assessment, the correct use levels were used, which likely contributed to the higher cumulative intake estimates in the adult and elderly population groups. In the infant population groups (0 to 6 months and 7 to <12 months), Kyowa's estimated cumulative intakes were slightly higher than those reported in GRN 001060. These slight increases could have resulted from the food use meal replacement drinks for children (*e.g.*, Pediasure)—which has been concluded to be GRAS at a use level of 12 g/L in GRN 001014, but was not included in GRN 001060—as well as the correction of the use levels for

high-fiber and biscuit type ready-to-eat breakfast cereals in the current cumulative assessment compared to GRN 001060. Despite the slight increases in the cumulative intake estimates in some population groups in the current assessment compared to GRN 001060, the use of Kyowa's 2'-FL will be substitutional to other sources of 2'-FL available on the U.S. market, and the use of Kyowa's 2'-FL will not increase dietary intakes.

Table 4 Comparison of the 2'-Fucosyllactose Intake Estimates for Kyowa's Cumulative Assessment and GRN 001060 in the United States by Population Group (2017-2018 NHANES Data) (USDA, 2022; CDC, 2023a,b)

Population Group	Age Group	Consumer-only Intake on Body Weight Basis (mg/kg bw/day)			
		Kyowa's Cumulative Assessment		GRN 001060	
		Mean	90th Percentile	Mean	90th Percentile
Infants	0 to 6 m	360	578	328	499
	7 to <12 m	474	812	401	678
Toddlers	1 to 2 y	237	477	230	469
Children	3 to 11 y	103	191	104	205
Female teenagers	12 to 19 y	50	103	43	91
Male teenagers	12 to 19 y	52	102	45	87
Female adults of childbearing age	16 to 49 y	56	119	36	81
Female adults	20 to 64 y	59	135	36	79
Male adults	20 to 64 y	53	122	39	89
Elderly	65 y and older	67	148	46	102
Total population	2 y and older	65	146	50	112

bw = body weight; GRAS = Generally Recognized as Safe; GRN = GRAS Notice; m = months; NHANES = National Health and Nutrition Examination Survey; y = years.

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November 15, 2023

Dr. Ellen Anderson
Regulatory Review Scientist
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Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

Dear Dr. Anderson,

Re: GRAS Notice No. GRN 001051

In response to your Amendment_Follow-up of October 26, 2023, below are our responses to your request for additional information regarding GRN 001051. FDA's questions are italicized text and our responses are in plain text.

We hope the responses to your questions are satisfactory. We are looking forward to your completed evaluation. If you have any further questions or need clarification, please reach out to me at saori.akizuki@kyowa-kirin.co.jp.

Yours sincerely,

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Response to Questions from U.S. FDA – GRAS Notice No. GRN 001051 – 2'-Fucosyllactose

OVERVIEW

Kyowa Hakko Bio Co., Ltd. ("Kyowa") presents the following responses to the United States (U.S.) Food and Drug Administration's (FDA's) letter dated 26 October 2023, pertaining to the Agency's request for clarification of the intended uses for Generally Recognized as Safe (GRAS) Notice No. GRN 001051 and purity of 2'-fucosyllactose (2'-FL).

RESPONSES

Question 1

1. *We note that in a letter to you dated August 10, 2023, we provided a table of intended food categories and maximum use levels for 2'-FL in previous GRNs (000546, 000571, 000650, 000735, 000749, 000852, 000897, 001014, 001060), GRN 001051 (March 2023 amendment), and cumulative maximum use levels of 2'-FL. Our intention was to capture the intended uses in the notice as well as background uses from previous GRNs, including distinguishing that uses in term infant formula included both exempt and non-exempt infant formula. In having the table serve dual purposes, we realize that we may have confused the infant formula categories considered substitutional in the context of GRN 001051. The table we provided also included use of 2'-FL in exempt hypoallergenic infant formula for term infants, which was previously notified in GRNs 000929 and 001034. However, since the uses in hypoallergenic infant formulas for term infants, based on the initial GRN 001051 and previous responses from Kyowa, were clearly not a component of GRN 001051, we should have made clear that this particular use was being included in the table for its contribution to the background consumption of 2'-FL only and not representative of a substitutional use in the context of GRN 001051. We realize that further explanation about this particular use should have been included in the table that we provided, and we apologize for the oversight and any confusion this may have caused.*

   We recommend that you omit the category of hydrolyzed and amino acid-based exempt infant formulas from the scope of GRN 001051 so that we may issue a response letter for the other uses that are supported in the safety narrative of GRN 001051. *We would not ask Kyowa to update the cumulative estimate of dietary exposure provided in the September 23, 2023 amendment since it addressed all existing background uses. We recommend that after receipt of FDA's response to GRN 001051, you may submit the use of 2'-FL in exempt infant formula for cow's milk allergic infants as either a supplement to GRN 001051 or as a new notice, with supporting information that specifically addresses any intended use in hypoallergenic infant formula. Because this intended use impacts a vulnerable population of infant consumers with cow's milk allergy, we expect GRAS notices for this intended use to include a robust safety narrative that specifically addresses the allergenicity of the notified substance and its safe use in infants with a cow's milk allergy.*

Response 1

Kyowa agrees to omit the category of hydrolyzed and amino acid-based exempt infant formulas from the scope of GRN 001051.

Question 2

2. *We note that, while you state in the March 22, 2023 amendment that you would meet the specification for 2'-FL in the FCC monograph, it appears that you have a stricter limit for total 2'-FL, but do not have a specification for "Sum 2'FL+L-fucose+ D-lactose+3,2'-difucosyl-D-lactose." Please confirm that this was your intent. We note that, if your specification for 2'-FL were ≥ 82%, we would also look for you to include the specification for "Sum 2'FL+L-fucose+ D-lactose+3,2'-difucosyl-D-lactose." While it is certainly acceptable to exceed the purity specifications in FCC 13, we wanted to confirm that this was your intent. For ease of reference, we summarized the specification limits provided in the FCC monograph and your two amendments to GRN 001051 in the table below.*

Specification	FCC 13 limit	GRN 001051 limit amendment 1 (October 20, 2022)	GRN 001051 limit amendment 2 (March 22, 2023)
2′-FL	Not less than (NLT) 82% anhydrous or dry matter (DM) basis	NLT 82% DM basis	"≥92%, which will meet the specification for 2′-FL" in FCC (2023)
Sum 2′FL+L-fucose+ D-lactose+3,2′-difucosyl- D-lactose	NLT 92%	Not specified (NS)	NS
"Sum of other carbohydrates" 100% minus sum quantified carbohydrates (%w/w DM of 2′FL, D-lactose, L-fucose, D-glucose, D-galactose, fucosylgalactose, difucosyllactose) and ash (%w/w DM)	NS	NMT 10% DW	Removed specification
D-lactose	Not more than (NMT) 8.0% DW	NMT 5.0% DW	NMT 5.0% DW
3,2′-Difucosyl-D-lactose	NMT 7.0% DW	NMT 3.0% DW	NMT 3.0% DW
L-fucose	NMT 3.0% DW	NMT 1.0% DW	NMT 1.0% DW

2′-Fucosyl-D-lactulose	NMT 2.0% DW	NS	NS
D-glucose and D-galactose	NS	NMT 1.0% DW	NMT 1.0% DW
Fucosylgalactose	NS	NMT 3% DW	NMT 3% DW

Response 2

Kyowa confirms that the purity limits established for 2'-FL in the 22 March 2023 amendment for GRN 001051 were intended. The analytical results from Lots A to F of Kyowa's 2'-FL ingredient demonstrate that the content of L-fucose (~0.1 w/w%), D-lactose (2.1 to 3.1 w/w%), and difucosyllactose (0.5 to 1.4 w/w%) in Kyowa's 2'-FL ingredient is low. Since the content of these other carbohydrates is low, it would be the 2'-FL content that would primarily contribute to the 92% representing the "*Sum 2'FL+L-fucose+ D-lactose+3,2'-difucosyl-D-lactose*." Therefore, rather than set a limit of not less than (NLT) 92% for the "*Sum 2'FL+L-fucose+ D-lactose+3,2'-difucosyl-D-lactose*," Kyowa would prefer to increase the purity limit for 2'-FL to ≥92%. If Kyowa sets a limit of ≥92% 2'-FL, then Kyowa would also meet the FCC's specification limit of NLT 92% for the "*Sum 2'FL+L-fucose+ D-lactose+3,2'-difucosyl-D-lactose*" by default, without the need to establish a parameter for "*Sum 2'FL+L-fucose+ D-lactose+3,2'-difucosyl-D-lactose*" for their 2'-FL ingredient.

Question 3

3. *It is not clear if you consider the term "difucosyllactose" to be a synonym for "3,2'-Difucosyl-D-lactose." If you do not consider the two terms to be synonyms, please provide the full chemical name and a CAS number for "difucosyllactose."*

Response 3

Kyowa considers the term "difucosyllactose" to be a synonym for "3,2'-Difucosyl-D-lactose." This is based on the structure and the International Union of Pure and Applied Chemistry (IUPAC) condensed name for "difucosyllactose" (CAS RN: 34852-43-2) (GSRS, 2023; PubChem, 2023).

REFERENCES

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