



Manki Ho, Ph.D., DABT
Chr. Hansen A/S, part of Novonesis Group
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DENMARK

Re: GRAS Notice No. GRN 001257

Dear Dr. Ho:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001257. We received Chr. Hansen A/S, part of Novonesis Group (Chr. Hansen)'s notice on January 13, 2025, and filed it on June 27, 2025. Chr. Hansen submitted amendments to the notice on January 16, March 24, March 31, and April 2, 2026. Within these amendments, Chr. Hansen reduced the intended use level in non-exempt infant formula for term infants; and clarified the intended uses, manufacturing process, specifications, dietary exposure, and the narrative.

The subject of the notice is 2'-fucosyllactose (2'-FL) for use as an ingredient in the foods, including infant formula, at the maximum levels shown in Table 1. Chr. Hansen states that 2'-FL is not intended for use in products under the U.S. Department of Agriculture's jurisdiction. The notice informs us of Chr. Hansen's view that these uses of 2'-FL are GRAS through scientific procedures.

Table 1: Current and intended food categories and use levels for 2'-FL.

Food Categories	Maximum Use Levels (g/kg or g/L)
Non-exempt infant formula for term infants ¹	2.4
Formula intended for young children (>12 months) ²	2.4
Breads and baked goods ³	48
Carbonated beverages	1.2
Enhanced or fortified waters	1.2

¹ Chr. Hansen states that the use of 2'-FL in non-exempt infant formula is not restricted to any specific protein base (e.g., cow milk-based, soy-based).

² This use was concluded to be GRAS per GRN 001014. We evaluated this notice and responded in a letter dated July 15, 2022, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

³ The response letter for GRN 001051 listed this food category as breads and baked goods, gluten-free; however, we note that based on information provided in the dietary exposure assessment, this category included breads and baked goods, including gluten-free. We evaluated this notice and responded in a letter dated November 21, 2023, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

Food Categories	Maximum Use Levels (g/kg or g/L)
Sports and isotonic drinks ²	6
“Energy” drinks	6
Hot breakfast cereals, prepared	31
Ready-to-eat (RTE) cereals, puffed	80
RTE cereals, high fiber	40
RTE cereals, biscuit-type	40
Coffee and tea ⁴	10
Milk substitutes	1.2
Beverage whiteners (powdered)	600
Beverage whiteners (liquid)	80
Non-dairy yogurt	12
Frozen dairy-based desserts	17
Puddings, custards, and mousses	17
Fruit pie filling	14.1
Fruit filling/fruit preparations in bars, cookies, yogurt, cakes	30
Hot cereals for infants and young children, prepared (from dry instant) and ready-to-serve ²	12
Other foods for infants and young children: yogurt, fruits, vegetables, “toddler” meals, desserts	12
Other drinks for infants and young children: juice and yogurt drinks	10
Baby snacks: crackers, pretzels, cookies, and other dry snack items	57
Jams, jellies, preserves, and fruit butters	60
Meal replacement bars for general use	30
Cereal bars including snack, granola, and breakfast bars	30
Meal replacement bars for weight management	40
Meal replacement drinks (including nutritional drinks, smoothies) for general use, milk- and non-milk based	5
Meal replacement drinks for weight management, milk and non-milk based	12
Meal replacement beverages for children (e.g., pediatric nutritional drinks) ²	12
Unflavored pasteurized and sterilized milk	1.2
Buttermilk	1.2
Flavored and fermented milks	1.2
Yogurt	12
Fruit juices and nectars	1.2
Fruit-flavored drinks and ades	1.2
Vegetable juices and nectars	1.2

⁴ The category of coffee and tea includes ready-to-drink (e.g., bottled, flavored, presweetened) coffee and tea and powder mixes used to prepare coffee and tea. For the dietary exposure estimates, it is assumed that the intended uses of 2'-FL do not include plain brewed coffee or tea.

Food Categories	Maximum Use Levels (g/kg or g/L)
Sugar substitutes: table-top sweeteners	300
Syrups used to flavor milk beverages	7
Nutritional drinks for pregnant women	12
Oral and enteral tube feeding formulas for ages ≥ 11 years ²	20

Chr. Hansen provides information on the identity and composition of 2'-FL. Chr. Hansen describes 2'-FL as a white to ivory powder containing a minimum of 90% 2'-FL (dry weight basis (DW)). Chr. Hansen states that 2'-FL is a fucosylated, neutral trisaccharide composed of L-fucose, D-galactose, and D-glucose. The chemical name for 2'-FL is α -L-fucopyranosyl-(1 \rightarrow 2)- β -D-galactopyranosyl-(1 \rightarrow 4)-D-glucopyranoside and the CAS registry number is 41263-94-9. Chr. Hansen states that 2'-FL is chemically and structurally identical to the 2'-FL obtained from human milk, as confirmed using liquid chromatography-tandem mass spectrometry and nuclear magnetic resonance spectroscopy. Chr. Hansen states that 2'-FL is the same as the subject of GRNs 000571, 000929, and 001014.⁵

Chr. Hansen describes the production organism used in the manufacturing process for 2'-FL. The production strain, *Escherichia coli* DSM 33609, was constructed through genetic engineering of *E. coli* BL21 (DE3) for production of 2'-FL, as described in GRNs 000571, 000929, and 001014.⁵ Chr. Hansen states that the production strain is non-pathogenic and non-toxicogenic.

Chr. Hansen states that the manufacturing process for 2'-FL is the same as described in GRNs 000571, 000929, and 001014⁵ and incorporates that information into GRN 001257. Chr. Hansen notes that cobalt chloride is not used in the production of 2'-FL described in GRN 001257. Chr. Hansen describes a two-stage manufacturing process, including fermentation and purification. In the first stage, fermentation is performed using *E. coli* DSM 33609 in a minimal medium containing D-lactose under controlled conditions. After fermentation is complete, the medium is separated from the production organism by filtration. The filtrate containing 2'-FL undergoes a series of purification steps, including filtration, ion exchange, electrodialysis, and concentration. The purified 2'-FL concentrate is filtered and spray dried to produce the final 2'-FL powder. Chr. Hansen states that 2'-FL is manufactured according to current good manufacturing practices, and that all raw materials and processing aids are food-grade and are used in accordance with applicable U.S. regulations, are GRAS for their intended uses, or are the subject of an effective food contact notification.

Chr. Hansen provides specifications for 2'-FL, which include the minimum content of 2'-FL ($\geq 90\%$ DW) and limits for carbohydrates (expressed as area %), including D-lactose ($\leq 5\%$), 3-fucosyl-D-lactose ($\leq 5\%$), 3,2'-difucosyl-D-lactose ($\leq 5\%$), 2-fucosyl-D-

⁵ 2'-FL is the subject of GRNs 000571, 000929, and 001014. We evaluated these notices and responded in letters dated November 6, 2015, February 26, 2021, July 15, 2022, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

galactose ($\leq 3\%$), D-glucose ($\leq 3\%$), D-galactose ($\leq 3\%$), and L-fucose ($\leq 3\%$). Additional specifications include ash ($\leq 0.5\%$), moisture ($\leq 9\%$), protein ($\leq 100\ \mu\text{g/g}$), heavy metals, including lead ($\leq 0.02\ \text{mg/kg}$), cereulide ($< 0.2\ \mu\text{g/kg}$) and microorganisms, including *Salmonella* serovars (absent in 25 g), *Listeria monocytogenes* (absent in 25 g) and *Cronobacter* spp. (absent in 10 g). Chr. Hansen provides the results from the analyses of three non-consecutive batches for cereulide and five non-consecutive batches for the remaining parameters to demonstrate that 2'-FL can be manufactured to meet the specifications. Chr. Hansen states that 2'-FL is stable for at least 2 years when stored under ambient conditions.

Chr. Hansen states that the intended uses of 2'-FL are substitutional for those described in GRN 001051 and incorporates into GRN 001257 the dietary exposure estimates from GRN 001051.³ Using food consumption data from the 2017-2018 National Health and Nutrition Examination Survey (NHANES), Chr. Hansen estimates an eaters-only dietary exposure to 2'-FL to be 2.4 g/person (p)/d (360 mg/kg body weight (bw)/d) at the mean and 4.4 g/p/d (578 mg/kg bw/d) at the 90th percentile for infants aged 0-6 months, and 4.3 g/p/d (474 mg/kg bw/d) at the mean and 7.7 g/p/d (812 mg/kg bw/d) at the 90th percentile for infants aged 7-12 months. For children aged 1-2 years, the estimated eaters-only dietary exposure to 2'-FL is 2.9 g/p/d (237 mg/kg bw/d) and 5.7 g/p/d (477 mg/kg bw/d) at the mean and 90th percentile, respectively. For the U.S. population aged 2 years and older, the eaters-only dietary exposure to 2'-FL is 4.2 g/p/d (65 mg/kg bw/d) and 9.1 g/p/d (146 mg/kg bw/d) at the mean and 90th percentile, respectively. Chr. Hansen notes that the intended uses are substitutional for the current uses of other sources of 2'-FL, and an increase in the cumulative dietary exposure to 2'-FL is not expected.

Chr. Hansen provides data and information supporting the safety of 2'-FL for these substitutional intended uses, ensuring consistency with food uses that have already been evaluated. Chr. Hansen states that 2'-FL from GRN 001257 is chemically and structurally identical to the 2'-FL present in human milk, and concludes that the absorption, distribution, metabolism and excretion of Chr. Hansen's 2'-FL is expected to be the same as that found in human milk. Chr. Hansen also incorporates safety data from these previous GRAS notices (i.e., GRNs 000546, 000650, 000735, 000749, 000852, 000897, 000932, 001014, 001051, 001060, and 001091)⁶ to support the safe use of 2'-FL into GRN 001257. Chr. Hansen summarizes the published safety studies discussed in previous notices, which demonstrate no toxicologically significant adverse effects at the current use levels, confirming the safety of consumption levels previously evaluated. Following an updated search of the published literature through December 2025, Chr. Hansen did not identify any studies which contradict their GRAS conclusion.

Based on the totality of data and information included in their notice, Chr. Hansen

⁶ The subject of GRNs 000546, 000650, 000735, 000749, 000852, 000897, 000932, 001014, 001051, 001060, and 001091 is 2'-fucosyllactose (2'-FL; referred to as 2'-O-fucosyllactose in earlier GRNs). We evaluated these notices and responded in letters dated September 16, 2015, November 23, 2016, April 6, 2018, April 23, 2018, November 15, 2019, June 12, 2020, February 18, 2021, July 15, 2022, November 21, 2023, April 4, 2023, and December 1, 2023, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

concludes that 2'-FL is GRAS for its intended uses.

Standards of Identity

In the notice, Chr. Hansen states its intention to use 2'-FL in several food categories, including foods for which standards of identity exist located in Title 21 of the CFR. We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic FD&C Act (FD&C Act), a food is misbranded if its labeling is false or misleading in any way. Section 403(r) of the FD&C Act lays out the statutory framework for labeling claims characterizing a nutrient level in a food or the relationship of a nutrient to a disease or health-related condition (also referred to as nutrient content claims and health claims). If products containing 2'-FL bear any nutrient content or health claims on the label or in labeling, such claims are subject to the applicable requirements and are under the purview of the Office of Nutrition and Food Labeling (ONFL) in the Nutrition Center of Excellence (NCE). The Office of Pre-Market Additive Safety (OPMAS) did not consult with ONFL on this issue or evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

Allergen Labeling

The FD&C Act requires that the label of a food that is or contains an ingredient that contains a “major food allergen” declare the allergen’s presence (section 403(w)). The FD&C Act defines a “major food allergen” as one of nine foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, soybeans, and sesame) or a food ingredient that contains protein derived from one of those foods. 2'-FL derived from lactose requires labeling under the FD&C Act because it contains protein derived from milk.

Intended Use in Infant Formulas

Under section 412 of the FD&C Act, a manufacturer of a new infant formula must make a submission to FDA providing required assurances about the formula at least 90 days before the formula is marketed. Our response to Chr. Hansen’s GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing 2'-FL to make the submission required by section 412. Infant formulas are the purview of the Office of Critical Foods in NCE.

Section 301(ll) of the FD&C Act

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health

Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In our evaluation of Chr. Hansen’s notice concluding that 2’-FL is GRAS under its intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing 2’-FL. Accordingly, our response should not be construed to be a statement that foods containing 2’-FL, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Chr. Hansen provided, as well as other information available to FDA, we have no questions at this time regarding Chr. Hansen’s conclusion that 2’-FL is GRAS under its intended conditions of use. This letter is not an affirmation that 2’-FL is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to GRN 001257 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

**SUSAN J.
CARLSON -S**

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