



Dietrich Conze, Ph.D.
Spherix Consulting Group
751 Rockville Pike
Unit 30-B
Rockville, MD 20852

Re: GRAS Notice No. GRN 001076

Dear Dr. Conze:

The Food and Drug Administration (FDA, we) completed our evaluation of the supplement that you submitted on behalf of Vitalus Nutrition, Inc. (Vitalus) to GRN 001076. We received the supplement on July 31, 2024. The supplement addresses manufacturing the powder form of the subject of GRN 001076. Vitalus submitted information on November 19, 2024, and November 25, 2024, that clarified the intended uses, manufacturing, batch analyses, and estimated dietary exposure.

We previously responded to GRN 001076 on March 2, 2023. We stated that we had no questions at that time regarding Vitalus' conclusion that galacto-oligosaccharides (GOS) is GRAS for use as an ingredient in powdered, ready-to-feed, and concentrated liquid forms of cow milk-based, non-exempt infant formula for term infants at a maximum level of 7.8 g/L of infant formula, as consumed. GOS is also for use as an ingredient in milk and milk products; soups; coconut beverages; bakery products; ready-to-eat cereals; jams, jellies, and preserves; and non-alcoholic beverages at maximum levels ranging from 0.55 to 33.4%.¹ In the supplement dated July 31, 2024, Vitalus informed us of its view that GOS is GRAS, through scientific procedures, for use as an ingredient in the same food categories and at the same use levels as in GRN 001076.

In GRN 001076, Vitalus describes the manufacturing method and specifications for GOS in a syrup form. This supplement describes the manufacturing process and specifications for the powder form of GOS that is the subject of GRN 001076. Vitalus states that the difference in the manufacturing method for the GOS powder compared to the GOS syrup that was the subject of GRN 001076 is limited to further processing of the GOS syrup to yield GOS powder. In the manufacture of GOS powder, GOS syrup is further purified by size-exclusion chromatography to reduce the total glucose and galactose content. The resulting GOS syrup is then mixed with water and steam, filtered, spray-dried, and milled to yield GOS powder. Vitalus states that GOS is manufactured

¹ Vitalus states that GOS is not intended for use in products under the U.S. Department of Agriculture's jurisdiction or in foods for which standards of identity do not permit its addition.

under good manufacturing practices and all raw materials and processing aids are used in accordance with applicable U.S. regulations, are GRAS for the intended use, or are the subject of an effective food contact notification.

Vitalus provides specifications for GOS that include moisture ($\leq 5.5\%$), GOS content ($\geq 65\%$ on a dry matter (DM)), lactose ($\leq 28\%$ DM), glucose and galactose ($\leq 5.5\%$ DM; total), nitrogen ($\leq 0.032\%$), nitrate (≤ 50 mg/kg), nitrite (≤ 2 mg/kg), sulfated ash ($\leq 0.3\%$), arsenic (≤ 0.05 mg/kg), lead (0.05 mg/kg), cadmium (≤ 0.005 mg/kg), mercury (≤ 0.005 mg/kg), and limits for microorganisms, including *Cronobacter sakazakii* (negative in 25 g), *Salmonella* serovars (negative in 25 g), and *Listeria monocytogenes* (negative in 25 g). Vitalus provides the results from three non-consecutive batch analyses to demonstrate that GOS can be manufactured to meet these specifications. Vitalus states that GOS powder is stable for at least 8 months when stored under ambient conditions (18-25 °C) and is expected to be stable for up to 2 years.

Vitalus states that the intended uses of GOS powder are substitutional for the uses described in GRN 001076; therefore, the dietary exposure from the intended uses in this supplement is expected to remain the same.

Vitalus conducted an updated literature search through June 2024, and discussed new published toxicity, piglet, and clinical studies surrounding the safe use of GOS. Vitalus did not identify any data or information that would contradict its safety conclusion from GRN 001076.

Based on the totality of the data and information described above, Vitalus concludes that GOS is GRAS for its intended use.

Standards of Identity

In the notice, Vitalus states its intention to use GOS 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, & Cosmetic (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 GOS 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. 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. GOS may require labeling under the FD&C Act because it may contain protein derived from milk. Questions about petitions or notifications for exemptions from the food allergen labeling requirements should be directed to the Division of Food Ingredients in OPMAS. Questions related to food labeling in general should be directed to ONFL.

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 Vitalus’ GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing GOS to make the submission required by section 412. Infant formulas are the purview of the Office of Critical Foods in the Nutrition Center of Excellence.

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 Vitalus’ supplement concluding that GOS 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 GOS. Accordingly, our response should not be construed to be a statement that foods containing GOS, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Vitalus provided, as well as other information available to FDA, we have no questions at this time regarding Vitalus’ conclusion that GOS is GRAS under its intended conditions of use. This letter is not an affirmation that GOS 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 the supplement to GRN 001076 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

**Mical E.
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For Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Pre-Market Additive Safety
Office of Food Chemical Safety, Dietary
Supplements, and Innovation