U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Juan Cristián Santa María
Tate & Lyle
5450 Prairie Stone Parkway
Hoffman Estates, IL 60192

Re: GRAS Notice No. GRN 001271

Dear Mr. Santa María:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001271. We received Tate & Lyle's notice on April 3, 2025, and filed it on September 12, 2025. Tate & Lyle submitted amendments to the notice on January 30, 2026, and March 12, 2026, that clarified the intended use, specifications, dietary exposure, and aspects of the safety narrative.

The subject of the notice is short-chain fructooligosaccharides (scFOS) for use as an ingredient in cow-milk based, non-exempt infant formula for term infants at a level, as consumed, up to 400 mg scFOS/100 mL formula for infants 0-6 months of age and up to 500 mg scFOS/100 mL formula for infants >6 months of age. The intended uses of scFOS also include as a bulking agent and ingredient in the same food categories and use levels as in GRN 001006[1] (Table 1). Tate & Lyle states that scFOS 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. The notice informs us of Tate & Lyle's view that these uses of scFOS are GRAS through scientific procedures.

Table 1: Intended food categories and use levels for scFOS

Food Categories	Maximum use level (%)
Acidophilus Milk	0.4
Analogs and substitutes for meat, poultry, or fish	1.2 to 6.7
Bars	15
Breakfast cereals	1.8 to 2.5
Beverages and juices	0.4
Cakes	1.8
Cheese	0.9 to 3.3

[1] Various fructooligosaccharides were the subjects of GRNs 000044, 000537, 000605, 000623, 000717, 000797, 000990, and 001006. We evaluated these notices and responded in letters dated November 22, 2000; February 6, 2015; March 17, 2016; August 1, 2016; February 13, 2018; November 15, 2018; October 8, 2021; and January 19, 2022, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

Cream	3.3 to 6.7
Confectionery	2.5
Cookies	3.3
Crackers	3.3 to 6.7
Dairy beverages	1.3 to 3.2
Dairy product analogs	1.3
Dessert toppings and fillings	3.3
Hard candy	6.7
Ice cream	1.5
Infant foods (0 to 12 Months)	0.4 to 3.6
Jams and jellies	5
Meal replacement shakes (milk- and non-milk based)	2.5
Milk, flavored and unflavored	0.4
Milk, evaporated and condensed	2.6 to 3.1
Muffins and quick bread	1.8 to 2.0
Sauces, gravies, and condiments	0.8 to 3.3
Snacks	3.3
Sorbet and sherbet	1.2
Soup	0.4
"Toddler" foods (12 to 24 months)	0.8 to 6.7
Yogurt	0.4

Tate & Lyle provides information on the identity and composition of scFOS. scFOS is described as a white to yellowish powder with a minimum content of 95% scFOS on a dry-matter (DM) basis. scFOS is composed of fructan oligosaccharides that are linear chains of fructose with β-(2-1) linkages with a terminal glucose residue. scFOS primarily consists of fructans with 2, 3, or 4 fructose residues that are referred to as 1-kestose, nystose, or fructofuranosylnystose, respectively.

Tate & Lyle describes the manufacturing process for scFOS, stating that scFOS is synthesized from sucrose using a β-fructofuranosidase. Tate & Lyle also describes the optional use of an immobilized fructosyltransferase or a liquid fructosyltransferase that are obtained from two strains of *Aspergillus oryzae*. Tate & Lyle states that the enzyme preparations are manufactured following current good manufacturing practices (GMP) using food-grade materials, and the enzymes conform to the specifications for enzyme preparations established by The Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2006) and the Food Chemicals Codex (FCC, 2025). The manufacture starts with dissolving sucrose in water and filtering to form a syrup, and then the syrup is subjected to either the liquid or immobilized enzyme preparation. The liquid enzyme preparation is combined with the syrup, and the reaction is allowed to proceed until the desired scFOS content is obtained. The enzyme is then deactivated with heat and the syrup filtered. Alternatively, the syrup is combined with the resin-immobilized enzyme preparation under continuous circulation in a column and the reaction is allowed to proceed until the desired scFOS content is obtained and the immobilized enzyme is removed by filtration. The resulting product after enzyme treatment is cooled and

subjected to purification steps using ion exchange resin, chromatography, and filtration. The product is then concentrated by evaporation, subjected to a heat treatment step, and then dried to obtain the final scFOS powder. Tate & Lyle states that scFOS is manufactured in accordance with GMP and that all raw materials, processing aids, and food contact materials used in the manufacture of scFOS are not major food allergens, are food grade, and are used in accordance with applicable federal regulations or have been concluded to be GRAS for their respective uses.

Tate & Lyle provides specifications for scFOS that include a minimum content of total scFOS (≥95% on a DM basis), pH (4 to 7 for a 30% solution), moisture (≤5%), ash (≤0.1%), arsenic (≤0.05 mg/kg), cadmium (≤0.1 mg/kg), lead (≤0.05 mg/kg), mercury (≤0.01 mg/kg), cereulide (<0.1 µg/kg), and microorganisms, including *Bacillus cereus* (≤10 colony forming units/g), *Salmonella* serovars (absent in 25 g), *Cronobacter sakazakii* (absent in 100 g), and *Listeria monocytogenes* (absent in 25 g). Tate & Lyle provides the results of six non-consecutive batch analyses (three batches produced using the liquid enzyme preparation and three batches produced using the immobilized enzyme preparation) to demonstrate that scFOS can be manufactured to meet these specifications.

Tate & Lyle discusses the results of stability studies conducted with scFOS stored at 10 to 30 °C and 45 to 70% relative humidity (RH) for up to 24 months and stored at 37 °C and 75% RH for up to 3 months. Tate & Lyle reports that the results of these studies demonstrate that scFOS is stable for up to at least 24 months under the intended conditions of storage and at least 3 months under accelerated conditions.

Tate & Lyle states that the intended uses are the same as in GRN 001006 and incorporates into the notice the dietary exposure estimates from GRN 001006 that are based on food consumption data from the 2015-2016 National Health and Nutrition Examination Survey. Tate & Lyle reports the mean and 90th percentile eaters-only dietary exposure to scFOS for the U.S. population aged 2 years and older to be 10 g/person (p)/d (0.16 g/kg body weight (bw)/d) and 18 g/p/d (0.33 g/kg bw/d), respectively, and the mean and 90th percentile eaters-only dietary exposure to scFOS for young children aged 1 to 2 years to be 10 g/p/d (0.8 g/kg bw/d) and 17 g/p/d (1.32 g/kg bw/d), respectively. Tate & Lyle concludes that the intended uses are substitutional for other sources of scFOS and does not expect the cumulative dietary exposure to scFOS to change.

Tate & Lyle incorporates into the notice the scFOS dietary exposure estimates from GRN 000990 for the intended use in infant formula. Based on the assumptions that infants aged 14 to 27 days have the highest energy intake per kg bw (141.3 kcal/kg bw/d in males and 138.9 kcal/kg bw/d in females at the 90th percentile) and that infant formula contains 67 kcal/100 mL, Tate & Lyle estimates the 90th percentile dietary exposure to scFOS to be 828 and 1,035 mg/kg bw/d, respectively, for the use levels of 400 mg/100 mL and 500 mg/100 mL. Tate & Lyle notes that as infants grow, the daily intake of infant formula decreases on a bw basis. Tate & Lyle notes that the dietary exposure estimates for infants are based on the assumption that infant formula is the sole source of nutrition and further concludes that the dietary exposure to scFOS from consuming

other foods containing scFOS would offset the infant formula consumption and not increase the overall dietary exposure to scFOS.

Tate & Lyle provides data and information to support the safety of scFOS discussed in previous GRNs and from a literature search that was conducted through January 2026. Tate & Lyle notes that scFOS is not absorbed intact but is instead fermented by intestinal microbiota in the colon. Tate & Lyle states that scFOS is chemically identical to other scFOS products on the market and provides analytical data to support this statement. Tate & Lyle references toxicological data from GRNs 000044, 000537, 000605, 000623, 000717, 000797, 000990, and 001006,[1] which are applicable to the safety of the subject of this notice. These data include *in vitro* genotoxicity studies, acute and subchronic oral toxicity studies, combined chronic oral toxicity and carcinogenicity studies, developmental and reproductive toxicity studies, and clinical studies on healthy infants, children, and adults in support of scFOS safety. Tate & Lyle notes that it is generally understood that adverse effects related to dietary scFOS are limited to gastrointestinal symptoms characteristic of consuming non-digestible fibers, such as abdominal discomfort.

Based on the totality of the data and information, Tate & Lyle concludes that scFOS is GRAS for its intended use.

Standards of Identity

In the notice, Tate & Lyle state its intention to use scFOS 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 scFOS 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 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.

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 Tate & Lyle's GRAS notice does not

alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing scFOS 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 Tate & Lyle's notice concluding that scFOS 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 scFOS. Accordingly, our response should not be construed to be a statement that foods containing scFOS, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Tate & Lyle provided, as well as other information available to FDA, we have no questions at this time regarding Tate & Lyle's conclusion that scFOS is GRAS under its intended conditions of use. This letter is not an affirmation that scFOS 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 001271 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

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