Fernando Schved, Ph.D.
Galam Ltd.
Kibbutz Maanit
M.P. Menashe
3785500, ISRAEL

Re: GRAS Notice No. GRN 000717

Dear Dr. Schved:

The Food and Drug Administration (FDA, we) completed our evaluation of Galam Ltd. (Galam)'s supplement to GRN 000717. We received the supplement on February 7, 2022. The supplement addresses additional uses for the subject of GRN 000717. Galam submitted clarifying information on April 12, 2022, June 12, 2022, July 15, 2022, November 25, 2022, and April 6, 2023.

We previously responded to GRN 000717 on February 13, 2018. We stated that we had no questions at that time regarding Galam's conclusion that short-chain fructo-oligosaccharides (scFOS) is GRAS for use at levels ranging from 0.4 to 6.7% as a bulking agent and as a general-purpose food ingredient in various food categories, including substitutes for meat, poultry, and fish; nutritional bars; breakfast cereals; beverages and juices; cakes; cheese; cream; confectionery; cookies; crackers; dessert toppings and fillings; hard candy; ice cream; infant foods; jams and jellies; milks (acidophilus; flavored and unflavored; evaporated and condensed); muffins and quick bread; sauces, gravies, and condiments; snacks; sorbet and sherbet; soups; toddler (12–24 months old) foods; and yogurt.

In the supplement dated February 3, 2022, Galam informs us of its view that the powdered form of scFOS is GRAS, through scientific procedures, for use as an ingredient in cow milk- and soy-based non-exempt infant formula, as consumed, at a level up to 4 g/L for term infants aged 0–6 months and at a level up to 5 g/L for term infants aged >6 months.

In the supplement, Galam states that the identity and method of manufacture of scFOS are the same as described in GRN 000717. Galam provides the following additional or updated specifications for scFOS: ash (≤0.15%), lead (≤0.1 mg/kg), arsenic (≤0.1 mg/kg), cadmium (≤0.1 mg/kg), total mercury (≤0.01 mg/kg), *Salmonella* serovars (not detected in 25 g), *Cronobacter sakazakii* (not detected in 10 g), *Listeria* sp. (not detected in 25 g), *Shigella* sp. (not detected in 25 g), *Staphylococcus aureus* (not detected in 10 g), *Enterobacteriaceae* (not detected in 10 g), and *Bacillus cereus* (≤50 colony forming units/g). Galam provides the results from the analyses of five non-consecutive batches to demonstrate that scFOS can be manufactured to meet these

specifications.

Galam estimates the dietary exposure to scFOS for infants aged 0–6 months based on published data on the 90th percentile daily energy intakes and a typical caloric density of infant formula (670 kcal/L as consumed). Galam states that the dietary exposure to scFOS is expected to be the highest for boys and girls aged 14–27 days and is estimated to be 844 and 829 mg/kg body weight (bw)/d, respectively, at the 90th percentile. Galam states that the actual total daily energy intake from infant formula in infants aged >6 months decreases compared to infants aged 0–6 months and concludes that the dietary exposure to scFOS for infants aged >6 months is expected to be lower than that for infants aged 14–27 days. Galam further notes that the intended uses of scFOS are substitutional for those described in GRNs 000537 and 000797[1] and therefore the dietary exposure to scFOS is not expected to change.

Galam discusses data and information supporting the safety of scFOS in infant formula and states that an updated literature search conducted through June 2021 did not identify any additional acute oral toxicity, repeated dose toxicity, carcinogenicity, reproductive or developmental toxicity, or genotoxicity studies. The article of commerce is compared to other scFOS ingredients previously concluded to be GRAS, and Galam states that the article of commerce is compositionally equivalent to scFOS described in GRN 000797. Therefore, Galam incorporates into the supplement and provides summaries of information discussed in GRN 000797, including studies in weaning animals including rats, mice, and piglets. Galam also discusses published studies in piglets and rats which were not summarized in previous GRAS notices for scFOS and states that that no adverse effects were reported in any of these studies. To further support the safe use in infant formula, Galam incorporates into the supplement published clinical studies from GRN 000797 in which scFOS was safely consumed by infants.

Based on the data and information presented in the supplement, Galam concludes that scFOS is GRAS for its intended use.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic 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 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 Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety did not consult with ONFL on this issue or

[1] scFOS is the subject of GRNs 000537 and 000797. We evaluated these notices and responded in letters dated February 6, 2015 and November 15, 2018, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

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 Galam's GRAS supplement 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 ONFL in the Center for Food Safety and Applied Nutrition.

Section 301(ll) 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 Galam's supplement 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 Galam provided, as well as other information available to FDA, we have no questions at this time regarding Galam'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 the supplement to GRN 000717 is accessible to the public at

www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.04.21 16:20:40 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition