U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Evangelia C. Pelonis
Keller and Heckman LLP
1001 G Street, NW
Washington, DC 20001

Re: GRAS Notice No. GRN 001006

Dear Ms. Pelonis:

The Food and Drug Administration (FDA, we) completed our evaluation of the supplement that you submitted on behalf of Ingredion, Inc. (Ingredion) to GRN 001006. We received the supplement on September 9, 2024. The supplement addresses a change in the enzyme used during the manufacturing process and minor changes in the specifications for the subject of GRN 001006. Ingredion submitted clarifying information on November 8, 2024, regarding the specifications.

We previously responded to GRN 001006 on January 19, 2022. We stated that we had no questions at that time regarding Ingredion's conclusion that short-chain fructooligosaccharides (scFOS) is GRAS for the intended use as a bulking agent and an 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); cultured dairy beverages; dairy product analogs; muffins and quick bread; sauces, gravies, and condiments; snacks; sorbet and sherbet; soups; foods for young children (12-24 months old); yogurt; drinkable yogurt; and meal replacement shakes at levels ranging from 0.4% to 15%.[1]

In the supplement dated August 29, 2024, Ingredion informs us of a change in the β-fructofuranosidase enzyme used to manufacture scFOS. GRN 001006 described the use of an enzyme derived from *Aspergillus fijiensis*. According to the supplement, the new β-fructofuranosidase enzyme that Ingredion intends to use is produced by a strain of *Trichoderma reesei* expressing a gene for invertase from *Aspergillus niger* and is the subject of GRN 001173.[2] In the supplement, Ingredion states that the new enzyme acts in the same manner as the original enzyme described in GRN 001006. In the supplement, Ingredion notes minor changes to the specifications for scFOS (e.g.,

[1] Ingredion states that scFOS is not intended for use in foods under the jurisdiction of the United States Department of Agriculture. Ingredion states that GRN 000537 addresses the use of scFOS in infant formula.

[2] We evaluated GRN 001173 and responded in a letter dated August 15, 2024, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

reduced limits for arsenic) and provides results from the analyses of three non-consecutive batches of each form of scFOS (powder and liquid) to demonstrate that scFOS can be manufactured to conform with the specifications. Ingredion states there is no change to the intended use of scFOS described in GRN 001006, and therefore, no change in the dietary exposure to scFOS. Additionally, Ingredion conducted an updated review of the scientific literature in August 2024 and concludes that the safety of scFOS continues to be confirmed.

Based on the available data and information, Ingredion concludes that scFOS is GRAS under the intended conditions of use.

Standards of Identity

In the supplement, Ingredion states 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, 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 Nutrition Center of Excellence. 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.

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 Ingredion'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 Ingredion provided, as well as other information available to FDA, we have no questions at this time regarding Ingredion'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 001006 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2025.01.30 11:01:51 -05'00'

Susan J. Carlson, Ph.D.
Director
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