Miriam Carnovale
Danisco USA, Inc. (A Wholly Owned Subsidiary of International Flavors and Fragrances, Inc.)
3329 Agriculture Drive
Madison, WI 53716

Re: GRAS Notice No. GRN 001229

Dear Ms. Carnovale:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001229. We received Danisco USA, Inc. (A Wholly Owned Subsidiary of International Flavors and Fragrances, Inc.) (Danisco)'s notice on October 21, 2024 and filed it on February 28, 2025. Danisco submitted amendments to the notice on April 25, 2025, May 15 and 20, 2025, and June 11 and 12, 2025 providing clarifying information about the microorganism, manufacturing method, intended use, specifications, including revised heavy metal specifications, and dietary exposure.

The subject of the notice is *Levilactobacillus brevis* ATCC SD-7285 (*L. brevis* ATCC SD-7285) for use as an ingredient in yogurt and other dairy products, soy products, beverages, chewing gum, confectionary snacks, snack/meal bars and ready-to-eat cereals at a level up to 5×10^{10} colony forming units (CFU)/serving. Danisco states that *L. brevis* ATCC SD-7285 is not intended for use in infant formula, food products intended for infants, alcoholic beverages, food products under the jurisdiction of the United States Department of Agriculture, or in foods for which standards of identity preclude its use. The notice informs us of Danisco's view that these uses of *L. brevis* ATCC SD-7285 are GRAS through scientific procedures.

Danisco describes *L. brevis* ATCC SD-7285 as an off-white powder and states that *L. brevis* ATCC SD-7285 is a non-pathogenic, non-toxigenic, Gram-positive, non-spore forming bacterium. The strain was isolated from a human fecal sample collected in Ireland and deposited in the strain collection of the American Type Culture Collection (ATCC) as SD-7285. Danisco discusses the results of the phenotypic and genotypic characterization used to confirm the strain's identity.

Danisco describes the manufacture of *L. brevis* ATCC SD-7285 by fermentation of a pure culture under controlled conditions. After fermentation, the bacterial cells are concentrated by centrifugation and cryoprotectants are added. The mixture is then pelletized in liquid nitrogen, freeze-dried, milled, blended and packaged. Danisco states that *L. brevis* ATCC SD-7285 is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids used in the manufacturing process are food-grade and are used in accordance with applicable U.S.

regulations, are GRAS for their intended use, or are the subject of an effective food contact notification. Danisco states that the raw materials used in the manufacturing process are not derived from major allergens and *L. brevis* ATCC SD-7285 does not contain any major allergens.

Danisco provides specifications for *L. brevis* ATCC SD-7285 that include viable cell count (≥ 4.25×10^{11} CFU/g); limits for heavy metals, including lead (≤ 0.1 mg/kg); and microorganisms, including non-lactic cell count (< 5000 CFU/g), coliforms (< 10 CFU/g), *Salmonella* serovars (absent in 40 g), and *Listeria monocytogenes* (absent in 25 g). Danisco provides the results from the analyses of three non-consecutive batches to demonstrate that the ingredient can be manufactured to conform with the provided specifications. Danisco states that *L. brevis* ATCC SD-7285 is stable for at least 1 year when stored in the original sealed package at or below 4 °C.

Danisco estimates the dietary exposure to *L. brevis* ATCC SD-7285 from the intended uses to be 5×10^{11} CFU/person/day based on the assumption that an individual consumes an average of 20 servings of food/day in the US and half of those servings contain *L. brevis* ATCC SD-7285 at the maximum level of 5×10^{10} CFU/serving.

Danisco discusses data and information used to support the safety of *L. brevis* ATCC SD-7285, including a history of safe use of the *L. brevis* species in fermented foods. Danisco states that the genome sequence of *L. brevis* ATCC SD-7285 has been determined and discusses the results of unpublished bioinformatic analyses that did not identify any safety concerns, including lack of genes encoding mobilizable antibiotic resistance elements or capacity to produce biogenic amines. Danisco also summarizes unpublished toxicological studies on *L. brevis* ATCC SD-7285 and published human studies on *L. brevis* and concludes that there are no indications of safety concerns. Danisco states that *L. brevis* meets the Qualified Presumption of Safety (QPS) status by the European Food Safety Authority.

Based on the totality of the data and information, Danisco concludes that *L. brevis* ATCC SD-7285 is GRAS for its intended use.

Standards of Identity

In the notice, Danisco states its intention to use *L. brevis* ATCC SD-7285 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 *L.*

brevis ATCC SD-7285 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 Danisco's notice concluding that *L. brevis* ATCC SD-7285 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 *L. brevis* ATCC SD-7285. Accordingly, our response should not be construed to be a statement that foods containing *L. brevis* ATCC SD-7285, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Danisco provided, as well as other information available to FDA, we have no questions at this time regarding Danisco's conclusion that *L. brevis* ATCC SD-7285 is GRAS under its intended conditions of use. This letter is not an affirmation that *L. brevis* ATCC SD-7285 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 001229 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2025.08.15 17:52:34 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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