



Amy Clewell, ND, DABT
AIBMR Life Sciences, Inc.
1425 Broadway, Suite 458
Seattle, WA 98122

Re: GRAS Notice No. GRN 000969

Dear Dr. Clewell:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000969. We received the notice that you submitted on behalf of Danisco USA, Inc. (Danisco) on September 16, 2020 and filed it on January 8, 2021. We received amendments to the notice on May 7, 2021, September 1, 2021, and September 27, 2021 that clarified analytical methods, provided stability test data, clarified intended uses and dietary exposure, drying method, and withdrew uses in alcoholic beverages.

The subject of the notice is *Bacillus subtilis* strain ATCC SD-7780¹ spore preparation (*B. subtilis* ATCC SD-7780 spore preparation) for use as an ingredient in foods generally² at up to 1×10^{10} colony forming units (CFU)/serving. The notice informs us of Danisco's view that these uses of *B. subtilis* ATCC SD-7780 spore preparation are GRAS through scientific procedures.

Danisco describes *B. subtilis* ATCC SD-7780 spore preparation as a white to cream-colored powder. Danisco states that *B. subtilis* ATCC SD-7780 is a Gram-positive, rod-shaped, endospore-forming bacterium, which is deposited in the strain collection of ATCC. Danisco discusses the results of phenotypic and genotypic characterizations used to confirm the strain's identity.

Danisco describes the manufacture of *B. subtilis* ATCC SD-7780 spore preparation by fermentation of a pure culture under controlled conditions. After fermentation, the bacterial spores are concentrated by centrifugation and spray-dried to produce a granular powder preparation, which is heat treated to kill any vegetative cells present. Danisco states that *B. subtilis* ATCC SD-7780 spore preparation is manufactured with food-grade materials under current good manufacturing practices. Danisco states that *B. subtilis* ATCC SD-7780 spore preparation does not contain any major allergens.

¹ Danisco refers to *B. subtilis* ATCC SD-7780 as "Bss-19." Danisco states that the strain is also known as BS7711 and is designated internally as DGCC12972 within the DuPont Global Culture Collection.

² Danisco states that *B. subtilis* "Bss-19" spore preparation is not intended for use in infant formulas, products under the jurisdiction of the US Department of Agriculture, or alcoholic beverages.

Danisco provides specifications for *B. subtilis* ATCC SD-7780 spore preparation that include viable spore count ($\geq 2.25 \times 10^{11}$ CFU/g) and limits for lead (< 0.5 mg/kg) and microorganisms, including coliforms (< 10 CFU/g) and *Escherichia coli* (< 10 CFU/g). Danisco provides the results of three non-consecutive batch analyses to demonstrate that *B. subtilis* ATCC SD-7780 spore preparation can be manufactured to meet the specifications. Additionally, Danisco provides the results of stability testing to demonstrate that *B. subtilis* ATCC SD-7780 spore preparation is stable for up to two years.

Danisco estimates dietary exposure to *B. subtilis* ATCC SD-7780 spore preparation from the intended uses at up to 1×10^{10} CFU/serving. Danisco states that the intended uses may be in part substitutional for uses of other *B. subtilis* strains (including those described in GRNs 000831³ and 000905⁴). Danisco estimates the highest dietary exposure to be 2.78×10^{11} CFU/day for the adult male population based on the highest reported mean number of servings of food consumed per day.

Danisco discusses the safety of *B. subtilis* and *B. subtilis* ATCC SD-7780 to support the safety of consumption of *B. subtilis* ATCC SD-7780 spore preparation. Danisco discusses the history of consumption of *B. subtilis* and published literature demonstrating that it is found in soil and has been isolated from the human gastrointestinal tract. Danisco states that *B. subtilis* is non-pathogenic and non-toxicogenic. Danisco discusses the results of published human and toxicological studies demonstrating that *B. subtilis* strains are well tolerated and do not induce toxicity, as well as an unpublished acute oral toxicity study in rats demonstrating that *B. subtilis* ATCC SD-7780 does not induce toxicity. Danisco states that *B. subtilis* ATCC SD-7780 is non-pathogenic and non-toxicogenic. Danisco discusses the results of unpublished studies demonstrating that *B. subtilis* ATCC SD-7780 spore preparation is susceptible to antibiotics and lacks antibiotic resistance genes. Danisco discusses published reports of opportunistic infections in immunocompromised individuals and states that these do not present a safety concern for *B. subtilis* ATCC SD-7780 spore preparation. Additionally, Danisco notes that the European Food Safety Authority concluded that *B. subtilis* met Qualified Presumption of Safety status in 2007 and has maintained this status.

Based on the totality of evidence, Danisco concludes that *B. subtilis* ATCC SD-7780 spore preparation is GRAS for its intended use.

Standards of Identity

In the notice, Danisco states its intention to use *B. subtilis* ATCC SD-7780 spore preparation in several food categories, including foods for which standards of identity

³ GRN 000831 describes uses of *B. subtilis* DE1111 spore preparation. We evaluated GRN 000831 and responded in a letter dated October 7, 2019, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

⁴ GRN 000905 describes uses of *B. subtilis* strain DSM 32444 spore preparation. We evaluated GRN 000905 and responded in a letter dated June 8, 2020 stating that we had no questions at the time regarding the notifier's GRAS conclusion.

exist, located in Title 21 of the Code of Federal Regulations. 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 *B. subtilis* ATCC SD-7780 spore preparation 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 (OFAS) 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 Federal Food Drug & Cosmetic Act (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 *B. subtilis* ATCC SD-7780 spore preparation 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 *B. subtilis* ATCC SD-7780 spore preparation. Accordingly, our response should not be construed to be a statement that foods containing *B. subtilis* ATCC SD-7780 spore preparation, 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 *B. subtilis* ATCC SD-7780 spore preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *B. subtilis* ATCC SD-7780 spore preparation 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 000969 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J.
Carlson -S

Digitally signed by Susan J.
Carlson -S
Date: 2021.10.06 17:00:54
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Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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