James T. Heimbach, Ph.D., F.A.C.N
JHeimbach, LLC
923 Water Street #66
Port Royal, VA 22535

Re: GRAS Notice No. GRN 000956

Dear Dr. Heimbach:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000956. We received Advanced Enzymes Technologies Ltd.'s (AET) notice on June 11, 2020 and filed it on January 15, 2021. AET submitted an amendment to the notice on June 17, 2021, that provided clarifications on the batch analyses for heavy metals and revised the heavy metals specifications. The notifier also supplied additional information on the manufacturing process and the test used to determine that there are no remaining vegetative cells.

The subject of the notice is *Bacillus subtilis* ATCC SD-7280[1] spore preparation for use as an ingredient at up to $6x10^9$ spores/serving in baked goods and baking mixes; breakfast cereals; beverages and beverage bases; coffee and tea; milk and milk products; dairy product analogs; fruit juices; condiments and relishes; confections and frostings; frozen dairy desserts and mixes; fruit and water ices; sports drinks; gelatins; jams and jellies; puddings and fillings; grain products and pastas; hard candy, soft candy, and chewing gum; extracts and flavorings; herbs, seeds, spices, seasonings, and blends; nuts and nut products; plant protein products; processed fruits, processed vegetables, and vegetable juices; snack foods; soups and soup mixes; sugar, sweet sauces, toppings, and syrups.[2] The notice informs us of AET's view that these uses of *B. subtilis* ATCC SD-7280 spore preparation are GRAS through scientific procedures.

AET describes *B. subtilis* ATCC SD-7280 spore preparation as a light brown to brown colored powder. AET states that *Bacillus* are Gram-positive, catalase-positive, spore-forming, motile rods. *B. subtilis* ATCC SD-7280 was isolated from soil and is deposited in the strain collection of the American Type Culture Collection (ATCC) in Manassas, Virginia, with the accession number SD-7280. AET discusses phenotypic and genotypic characteristics to confirm the strain's identity. AET states that *B. subtilis* ATCC SD-7280 is a non-pathogenic and non-toxigenic organism that does not contain any virulence genes and does not produce antibiotics or biogenic amines.

[1] AET uses an internal designation of *Bacillus subtilis* PLSSC; we are using the ATCC deposit designation to maintain our standard naming practice.
[2] AET states that *B. subtilis* ATCC SD-7280 spore preparation is not intended for use in infant formula, or in any products under the jurisdiction of the United States Department of Agriculture.

AET describes the manufacture of *B. subtilis* ATCC SD-7280 spore preparation as a batch-fed fermentation of a pure culture of vegetative cells under controlled conditions. Upon completion of growth, the vegetative cells are converted to spores in a process regulated by multiple parameters including nutrient availability, aeration, pH, and temperature to ensure that the spore formation is complete. The spores are separated from the fermentation medium by centrifugation, washed, and spray dried. The dried spores are further formulated with maltodextrin. AET states that no components of the fermentation medium are allergens or are derived from allergenic sources and that *B. subtilis* ATCC SD-7280 spore preparation is manufactured under current good manufacturing practices using food-grade raw materials.

AET provides specifications for *B. subtilis* ATCC SD-7280 spore preparation that include limits for lead (<0.3 mg/kg) and microorganisms, including *Salmonella* serovars (absent in 10 g), *Listeria monocytogenes* (absent in 25 g), *Staphylococci* spp. (absent in 1 g). AET provides the results from the analyses of three non-consecutive lots to demonstrate that the ingredient is manufactured to conform with the provided specifications. AET states that *B. subtilis* ATCC SD-7280 spore preparation real-time stability studies showed less than 10% loss of viable count in 12 months. AET states that the shelf-life of *B. subtilis* ATCC SD-7280 spore preparation is 2 years under real-time storage conditions.

AET states that according to a publication from the USDA Center for Nutrition Policy and Promotion (2000), adult males aged 51 and older consume the greatest number of servings of food per day, at approximately 18 servings. Based on this number of servings of food and the intended use level for *B. subtilis* ATCC SD-7280 spore preparation, AET estimates a maximum dietary exposure for the ingredient to be $1.1x10^{11}$ spores/day. AET indicates that the intended uses for *B. subtilis* ATCC SD-7280 spore preparation are the same as those for *B. subtilis* DE111 spore preparation, which was the subject of GRN 000831,[3] and therefore, the intended use of this ingredient would be an alternative strain and there would be no increase in the consumer dietary exposure to *B. subtilis*.

AET states that there is a history of safe use of *B. subtilis* in the manufacture of fermented foods, including fermented sausages, fermented vegetables, cereal products, and dairy products. AET relies on published literature to support the safety of oral consumption of *B. subtilis* spore preparation. AET states that there have been no human infections related to ingesting food products containing *B. subtilis* spores.

AET includes the report of a panel of individuals (AET's GRAS panel). Based on its review, AET's GRAS panel concluded that *B. subtilis* ATCC SD-7280 spore preparation is safe under the conditions of its intended use.

[3] *B. subtilis* DE111 spore preparation was the subject of GRN 000831. We evaluated this notice and responded in a letter dated August 13, 2019, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

Based on the evidence, AET concludes that *B. subtilis* ATCC SD-7280 spore preparation is GRAS for its intended use.

Standards of Identity

In the notice, AET states its intention to use *B. subtilis* ATCC SD-7280 spore preparation 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 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-7280 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 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, and 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 AET's notice concluding that *B. subtilis* ATCC SD-7280 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-7280 spore preparation. Accordingly, our response should not be construed to be a statement that foods containing *B. subtilis* ATCC SD-7280 spore preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that AET provided, as well as other information available to FDA, we have no questions at this time regarding AET's conclusion that *B. subtilis* ATCC SD-7280 spore preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *B. subtilis* ATCC SD-7280 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 000956 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2021.08.18 14:30:38 -04'00'

Susan Carlson, Ph.D.
Director
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