Amy Mozingo
GRAS Associates, LLC
11810 Grand Park Avenue, Suite 500
North Bethesda, MD 20852

Re: GRAS Notice No. GRN 001131

Dear Ms. Mozingo:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001131. We received the notice that GRAS Associates submitted on behalf of BIO-CAT Microbials, LLC (BIO-CAT) on February 13, 2023, and filed it on May 23, 2023. BIO-CAT submitted amendments on September 7, 2023, and September 21, 2023, that clarified the identity, manufacturing process, specifications, batch analyses, intended use, and safety information.

The subject of the notice is *Bacillus subtilis* ATCC PTA-127287 for use as an ingredient at a maximum level of 2 x 10^9 colony forming units (CFU)/serving in baked goods and baking mixes, non-alcoholic beverages and beverage bases, breakfast cereals, cheese, chewing gum, coffee and tea, confections and frostings, dairy product alternatives, frozen dairy desserts, fruit and water ices, gelatins, puddings and fillings, grain products and pastas, hard candy, milk products, plant protein products, processed fruits and fruit juices, processed vegetables and vegetable juices, snack foods and soft candy.[1] The notice informs us of BIO-CAT's view that these uses of *B. subtilis* ATCC PTA-127287 are GRAS through scientific procedures.

BIO-CAT describes *B. subtilis* ATCC PTA-127287 as a light tan to tan colored powder and states that *B. subtilis* ATCC PTA-127287 is a non-pathogenic, non-toxigenic, Gram-positive, spore forming, facultative bacterium. BIO-CAT notes that the strain was isolated from soil samples in Gallatin County, Montana, USA and has been deposited in the American Type Culture Collection (ATCC). BIO-CAT describes the taxonomic analysis for the identity of the strain. BIO-CAT also discusses the results of genomic analyses to confirm the strain identity and states that the strain is not genetically modified. BIO-CAT discusses the results of phenotypic and genotypic characterization performed on *B. subtilis* ATCC PTA-127287, and concludes that the strain does not produce hemolysin, *Bacillus* toxins, biogenic amines and mobile elements to transfer the identified streptomycin-resistance gene.

[1] BIO-CAT states that *B. subtilis* ATCC PTA-127287 is not intended for use in infant formula, alcoholic beverages, cough drops, or in products under the jurisdiction of the United States Department of Agriculture.

BIO-CAT describes the manufacture of *B. subtilis* ATCC PTA-127287 by fermentation of a pure culture under controlled conditions. After fermentation, the cells are separated from the fermentation medium and concentrated by centrifugation, blended with maltodextrin, spray dried, and blended with additional maltodextrin to yield the final product. BIO-CAT states that *B. subtilis* ATCC PTA-127287 is manufactured under current good manufacturing practices using food-grade raw materials. BIO-CAT confirms that all materials used in the manufacture of *B. subtilis* ATCC PTA-127287 are permitted for their respective uses under a current U.S. regulation, are the subject of an effective food contact notification, or are GRAS for their intended use. BIO-CAT states that the fermentation medium is allergen-free, and that no allergen is used for fermentation of other products in shared equipment.

BIO-CAT provides specifications for *B. subtilis* ATCC PTA-127287 that include total cell count (≥1.0 x 10^{11} CFU/g), moisture (<10%) and limits for microorganisms, including *Escherichia coli* (negative in 25 g), *Salmonella* serovars (negative in 25 g), *Listeria* spp. (negative in 25 g), *Staphylococcus aureus* (<10 CFU/g), and heavy metals, including lead (≤0.3 mg/kg). BIO-CAT provides the results from the analyses of four non-consecutive batches to demonstrate that *B. subtilis* ATCC PTA-127287 can be manufactured to meet these specifications. BIO-CAT provides the results of stability studies and states that *B. subtilis* ATCC PTA-127287 is stable for 18 months at 30°C/65% Relative Humidity (RH) and at 25°C/60% RH.

BIO-CAT states that males 51 years and older consume the greatest number of servings of food/day(d) at an estimated 18.2 servings. BIO-CAT estimates the dietary exposure to *B. subtilis* ATCC PTA-127287 from the intended uses based on the assumption that all the servings contain *B. subtilis* ATCC PTA-127287 at the maximum use level of 2 x 10^9 CFU/serving. Therefore, BIO-CAT states that the maximum dietary exposure to *B. subtilis* ATCC PTA-127287 is 3.64 x 10^{10} CFU/d.

BIO-CAT discusses data and information used to support the safety of *B. subtilis* ATCC PTA-127287, including a history of safe use of the *B. subtilis* species in fermented food products. BIO-CAT incorporates into their notice and provides summaries of the information pertaining to the safety of the *B. subtilis* strains discussed in GRNs 000831, 000905, 000955, 000956, and 000969.[2] BIO-CAT discusses opportunistic infection caused by certain *B. subtilis* strains and states that the infection cases were strain-specific and there was no evidence for pathogenic potential of *B. subtilis* to healthy humans in general. BIO-CAT summarizes published animal and human studies on *B. subtilis*. BIO-CAT states that either no adverse effects were reported, or the adverse effects were unrelated to the consumption of the *B. subtilis* strains according to

[2] *B. subtilis* strains DE111, DSM32444, BS-MB40 PTA-122264, ATCC SD-7280 and ATCC SD-7780 were the subjects of GRNs 000831, 000905, 000955, 000956, and 000969, respectively. We evaluated these notices and responded in letters dated August 13, 2019, June 8, 2020, March 26, 2021, August 18, 2021, and October 6, 2021, respectively, stating that we had no questions at the time regarding the notifiers' GRAS conclusions.

the published clinical studies.

Based on the totality of the data and information, BIO-CAT concludes that *B. subtilis* ATCC PTA-127287 is GRAS for its intended use.

Standards of Identity

In the notice, BIO-CAT states its intention to use *B. subtilis* ATCC PTA-127287 in several food categories, including foods for which standards of identity 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 PTA-127287 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 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 BIO-CAT's notice concluding that *B. subtilis* ATCC PTA-127287 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 PTA-127287. Accordingly, our response should not be construed to be a statement that foods containing *B. subtilis* ATCC PTA-127287, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that BIO-CAT provided, as well as other information available to FDA, we have no questions at this time regarding BIO-CAT's

conclusion that *B. subtilis* ATCC PTA-127287 is GRAS under its intended conditions of use. This letter is not an affirmation that *B. subtilis* ATCC PTA-127287 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 001131 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.10.20 16:46:12 -04'00'

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