

William Rowe
GRAS Associates, LLC
11810 Grand Park Avenue, Suite 500
North Bethesda, MD 20852

Re: GRAS Notice No. GRN 001231

Dear Mr. Rowe:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001231. We received the notice that you submitted on behalf of BIO-CAT Microbials, LLC (BIO-CAT) on November 18, 2024, and filed it on February 28, 2025. BIO-CAT submitted amendments to the notice on May 6, 2025 and June 4, 2025 that clarified the manufacturing process, specifications and safety information.

The subject of the notice is *Bacillus velezensis* PTA-127359 (*B. velezensis* PTA-127359) spore preparation for use as an ingredient in baked goods and baking mixes, non-alcoholic beverages and beverage bases (including carbonated and flavored waters, sports and nutritional drinks), breakfast cereals, cheese, chewing gum, coffee and tea, confections and frostings, dairy product analogs, frozen desserts (dairy, non-dairy and ices), gelatins, puddings and fillings, grain products and pastas, soft and hard candy, milk products, plant protein products, processed fruits and fruit juices, processed vegetables and vegetable juices, and snack foods at a maximum level of 2×10^9 colony forming units (CFU) per serving (excluding use in infant formula and products under the jurisdiction of the United States Department of Agriculture). The notice informs us of BIO-CAT's view that these uses of *B. velezensis* PTA-127359 spore preparation are GRAS through scientific procedures.

BIO-CAT describes *B. velezensis* PTA-127359 spore preparation as a light tan to dark tan colored powder and states that *B. velezensis* PTA-127359 is a non-pathogenic, non-toxigenic, Gram-positive, rod-shaped, spore forming, facultative aerobic bacterium. BIO-CAT notes that the strain was isolated from soil samples from Douglas County, WI and has been deposited in the American Type Culture Collection with the depository number PTA-127359. 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 engineered. BIO-CAT discusses published results of phenotypic and genotypic characterization performed on *B. velezensis* PTA-127359 and states that the strain lacks characteristics for pathogenicity and virulence, resistance to medically

relevant antibiotics, hemolytic activity, and biogenic amine activity that would negatively impact the human cells.

BIO-CAT describes the manufacture of *B. velezensis* PTA-127359 spore preparation by fermentation of a pure culture under controlled conditions. After fermentation, vegetative cells are killed by acid treatment. The spores are harvested by centrifugation, spray-dried, sifted, and mixed with maltodextrin to yield the final spore preparation. The concentrated spore preparation may also be optionally blended with maltodextrin prior to spray drying so that the total solids are at least 10%. BIO-CAT further states that other safe and suitable carriers or processing aids may be used as an alternative to maltodextrin. BIO-CAT states that *B. velezensis* PTA-127359 spore preparation is manufactured under current good manufacturing practices and that all raw materials are food grade and are used in accordance with an applicable U.S. regulation, are GRAS for their intended use, or are the subject of an effective food contact notification. BIO-CAT states that *B. velezensis* PTA-127359 spore preparation does not contain any major allergens.

BIO-CAT provides specifications for *B. velezensis* PTA-127359 spore preparation that include total cell count ($\geq 1.0 \times 10^{11}$ CFU/g), moisture content ($< 10\%$), limits for heavy metals, including lead (≤ 0.1 mg/kg) and microorganisms, including *Escherichia coli* (negative in 25 g), *Salmonella* spp. (negative in 25 g), *Listeria* spp. (negative in 25 g), and *Staphylococcus aureus* (< 10 CFU/g). BIO-CAT provides the results from the analyses of four non-consecutive batches to demonstrate that *B. velezensis* PTA-127359 spore preparation can be manufactured to meet these specifications. BIO-CAT states that *B. velezensis* PTA-127359 spore preparation is stable for up to 18 months at 30 °C, 65% relative humidity and 25 °C, 60% relative humidity.

BIO-CAT estimates the dietary exposure to *B. velezensis* PTA-127359 spore preparation from the intended uses to be 3.16×10^{10} CFU/person (p)/d based on the greatest number of servings of food/d for males aged 51 and older (15.8 servings of food/ d),¹⁴ and assuming that all the servings contain *B. velezensis* PTA-127359 spore preparation at the maximum use level of 2×10^9 CFU/serving.

BIO-CAT discusses data and information used to support the safety of *B. velezensis* PTA-127359 spore preparation, including a history of safe use of *B. velezensis* in fermented foods. BIO-CAT discusses the European Qualified Presumption of Safety (QPS) status of the *B. velezensis* species and the use of the species in animal feeds. BIO-CAT describes a published rat toxicity study with *B. velezensis* PTA-127359 and states that the no-observed-adverse-effect-level (NOAEL) for the oral administration of the microorganism was determined to be 10×10^{10} CFU/kg body weight/d, which supports the proposed use level. BIO-CAT also describes human clinical safety and tolerability studies with *B. velezensis* PTA-127359 and summarizes published toxicology and human studies for other *B. velezensis* strains. BIO-CAT states that no toxicity was reported in the animal studies and no adverse effects were noted in the human studies.

Based on the totality of the data and information, BIO-CAT concludes that *B. velezensis* PTA-127359 spore preparation is GRAS for its intended use.

Standards of Identity

In the notice, BIO-CAT states its intention to use *B. velezensis* PTA-127359 spore preparation 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. velezensis* PTA-127359 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 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 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 BIO-CAT's notice concluding that *B. velezensis* PTA-127359 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. velezensis* PTA-127359 spore preparation. Accordingly, our response should not be construed to be a statement that foods containing *B. velezensis* PTA-127359 spore preparation, 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. velezensis* PTA-127359 spore preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *B. velezensis* PTA-127359 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 21CFR 170.275(b)(2), the text of this letter responding to GRN 001231 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J.
Carlson -S
Date: 2025.07.11 15:42:03 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Pre-Market Additive Safety
Office of Food Chemical Safety, Dietary
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1. [^] BIO-CAT states that 15.8 servings is from grains, fruits, vegetables, milk, and other (fats, oils, sweets) food categories. Servings of meat were not included in the dietary exposure estimation because *B. velezensis* PTA-127359 is not intended for use in meat.