U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Madhu Soni, Ph.D.
Soni & Associates Inc.,
749 46th Square
Vero Beach, FL 32968

Re: GRAS Notice No. GRN 001214

Dear Dr. Soni:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001214. We received the notice that you submitted on behalf of Unique Biotech Limited on August 15, 2024, and filed it on December 5, 2024. Unique Biotech Limited submitted amendments to the notice on December 12, 2024, February 7, 2025, February 26, 2025, March 21, 2025, and April 17, 2025 that clarified the intended uses, genome characterization, safety, allergen potential, specifications, and manufacturing process.

The subject of the notice is *Shouchella clausii* MTCC 5472[1] (*S. clausii* MTCC 5472) spore preparation for use as an ingredient at a level up to 2 x 10^9 colony forming units (CFU) per serving in baked goods and baking mixes, breakfast cereals, cheeses, non-alcoholic beverages and beverage bases, coffee and tea, milk and milk products, dairy product analogs, fats and oils, fruit juices, condiments and relishes, confections and frostings, frozen dairy desserts and mixes, fruit and water ices, gelatins, puddings and fillings, jams and jellies, grain products and pastas, hard candy and cough drops, soft candy, chewing gum, herbs, seeds, spices, seasonings, blends, extracts, and flavorings, nuts and nut products, plant protein products, processed fruits, processed vegetables and vegetable juices, snack foods, soups and soup mixes, sugar and sweet sauces, toppings, and syrups.[2] The notice informs us of Unique Biotech Limited's view that these uses of *S. clausii* MTCC 5472 spore preparation are GRAS through scientific procedures.

Unique Biotech Limited describes *S. clausii* MTCC 5472 spore preparation as a greyish white to light, brown-colored powder. Unique Biotech Limited states that *S. clausii* MTCC 5472 spore preparation is a non-pathogenic, non-toxigenic Gram-positive, motile, spore-forming, rod-shaped bacterium that was isolated from soil. The strain is deposited in the strain collection of the Indian Microbial Type Culture Collection (MTCC) and Gene Bank with an accession number of MTCC 5472. Unique Biotech Limited discusses the results of the phenotypic and genotypic characterization used to confirm the strain's identity.

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[1] We note that *Bacillus clausii* was reclassified as *Shouchella clausii* as reported in Patel and Gupta (Ref.1).

[2] Unique Biotech Limited states that *S. clausii* MTCC 5472 spore preparation is not intended for use in infant formula, foods intended for infants and toddlers, products under the jurisdiction of the United States Department of Agriculture, and in foods where standards of identity preclude its use.

Unique Biotech Limited describes the manufacture of *S. clausii* MTCC 5472 spore preparation by batch type fermentation of a pure culture under controlled conditions. After the required incubation period, the biomass is collected by centrifugation. The resulting spore biomass is a thick slurry that is spray-dried to yield a powder. The finished product (either a 25 x 10^9 or 1 x 10^{11} CFU/g preparation) is prepared from the concentrated product by diluting with food grade maltodextrin and/or microcrystalline cellulose powder (MCCP) and/or fructooligosaccharides (FOS). Unique Biotech Limited states that no components of the fermentation media are allergens or are derived from allergenic sources. Unique Biotech Limited states that the manufacturing process is monitored for contamination, and that *S. clausii* MTCC 5472 spore preparation is manufactured in accordance with current good manufacturing practices. Unique Biotech Limited states that all raw materials and processing aids are food-grade and are approved as a food additive or are GRAS for their intended use.

Unique Biotech Limited provides specifications for *S. clausii* MTCC 5472 spore preparation that include total viable spore count (≥1 x 10^{11} CFU/g); and limits for loss on drying (≤ 5%), heavy metals, including lead (≤ 0.05 mg/kg), and microorganisms, including yeast and mould (absent/g), total coliforms (≤ 50 CFU/g), *Escherichia coli* (absent in 1 g), *Salmonella* species (absent in 10 g), *Pseudomonas aeruginosa* (absent in 1 g), *Staphylococcus aureus* (absent in 1 g), and *Listeria monocytogenes* (absent in 25 g). Unique Biotech Limited provides the results from the analyses of three non-consecutive batches to demonstrate that the *S. clausii* MTCC 5472 spore preparation can be manufactured to conform with the provided specifications. Unique Biotech Limited states that *S. clausii* MTCC 5472 spore preparation is stable for 24 months at 25°C and 60% relative humidity.

Unique Biotech Limited estimates the dietary exposure to *S. clausii* MTCC 5472 spore preparation from the intended uses to be 3.6 x 10^{10} CFU/d based upon 18.2 servings of food a day in the United States and presuming that all servings of food contain *S. clausii* MTCC 5472 spore preparation at the maximum use level of 2 x 10^9 CFU/serving. Unique Biotech Limited states that the uses of *S. clausii* MTCC 5472 spore preparation are identical to those in GRN 000971[3] and the use of *S. clausii* MTCC 5472 spore preparation is as an alternative strain to that in GRN 000971. Therefore, there would not be an increase in the cumulative dietary exposure to *S. clausii* from the intended use.

Unique Biotech Limited discusses data and information used to support the safety of *S. clausii* MTCC 5472. Unique Biotech Limited incorporates into their notice and provides a summary of the information pertaining to the safety of the *S. clausii* strain discussed in GRN 000971. Unique Biotech Limited conducted a genome analysis of *S. clausii* MTCC 5472 to determine the presence of genes for production of biogenic amines and concludes that the strain lacks genes for biogenic amines that pose safety concern. Unique Biotech Limited notes that *S. clausii* MTCC 5472 is capable of producing the bacteriocin Clausin and states that this characteristic does not pose a safety concern. Unique Biotech Limited further states that *S. clausii* MTCC 5472 exhibits antibiotic

[3] *B. clausii* MCC 0538 was the subject of GRN 000971. We evaluated this notice and responded in a letter dated March 3, 2022, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

resistance to clindamycin, erythromycin, and chloramphenicol, and they confirmed through sequencing that all three antibiotic resistant genes are located intrinsically and are not transferrable. Unique Biotech Limited summarizes and discusses acute and chronic studies in which no reports of toxicity or significant adverse effects associated with *S. clausii* MTCC 5472 spore preparation were reported. Unique Biotech Limited describes the history of safe consumption of *Shouchella* spp. in human food and notes that the European Food Safety Authority granted Qualified Presumption of Safety (QPS) status for *B. clausii* in 2008 and has renewed its status annually since then. Unique Biotech Limited performed a literature search through May 2024 and summarizes peer-reviewed scientific journals and governmental reviews, concluding that the publications support the safe consumption of *S. clausii*. Unique Biotech Limited states that *S. clausii* has been safely consumed by humans for decades and that the reports of infection associated with *S. clausii* appear coincidental and opportunistic in immunocompromised populations. Additionally, Unique Biotech Limited describes published human tolerance studies in which children and adults were fed *S. clausii* and states that no significant adverse effects were noted in any of these studies.

Based on the totality of evidence, Unique Biotech Limited concludes that *S. clausii* MTCC 5472 spore preparation is GRAS for its intended use.

Standards of Identity

In the notice, Unique Biotech Limited states its intention to use *S. clausii* MTCC 5472 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 Federal Food, Drug, 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 *S. clausii* MTCC 5472 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 (OPMAS) 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 Unique Biotech Limited's notice concluding that *S. clausii* MTCC 5472 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 *S. clausii* MTCC 5472 spore preparation. Accordingly, our response should not be construed to be a statement that foods containing *S. clausii* MTCC 5472 spore preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Unique Biotech Limited provided, as well as other information available to FDA, we have no questions at this time regarding Unique Biotech Limited's conclusion that *S. clausii* MTCC 5472 spore preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *S. clausii* MTCC 5472 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 001214 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2025.05.07 18:33:59 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Pre-Market Additive Safety
Office of Food Chemical Safety, Dietary Supplements, and Innovation
Human Foods Program

Reference

1. Patel, S., and Gupta, R. S. (2020). A phylogenomic and comparative genomic framework for resolving the polyphyly of the genus *Bacillus*: Proposal for six new genera of *Bacillus* species, *Peribacillus* gen. nov., *Cytobacillus* gen. nov., *Mesobacillus* gen. nov., *Neobacillus* gen. nov., *Metabacillus* gen. nov. and *Alkalihalobacillus* gen. nov. International Journal of Systematic and Evolutionary Microbiology, 70(1), 406-438. doi: 10.1099/ijsem.0.00