



Stella Si
Anchor Center for Certification
No. 1295 Chuan Qiao Road, Building 2, Suite 302
Shanghai 201206
CHINA

Re: GRAS Notice No. GRN 001243

Dear Ms. Si:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001243. We received the notice that you submitted on behalf of Thankcome Biological Science and Technology Co., Ltd.'s (Thankcome) notice on December 23, 2024 and filed it on March 13, 2025. Thankcome submitted an amendment to the notice on June 17, 2025, that provided additional information regarding the intended use, manufacturing process, specifications, and the safety narrative.

The subject of the notice is *Heyndrickxia coagulans*¹ CCTCC M2017813 spore preparation for use as an ingredient at up to 2 x 10⁹ colony forming units (CFU)/serving in baked goods and baking mixes; non-alcoholic beverages and beverages bases; breakfast cereals; milk and milk products; dairy product alternatives; condiments and relishes; confections and frostings; frozen dairy desserts and mixes; fruit and water ices; jams and jellies; gelatins, puddings and fillings; grain products and pastas; hard candy and cough drops; soft candy; chewing gum; extracts, flavorings, herbs, seeds, spices, seasonings, blends; nuts and nut products; plant protein products; processed fruits; snack foods; soups and soup mixes; sugar; and sweet sauces, toppings, and syrups, (excluding use in infant formula and products under the jurisdiction of the United States Department of Agriculture). The notice informs us of Thankcome's view that these uses of *H. coagulans* CCTCC M2017813 spore preparation are GRAS through scientific procedures.

Thankcome describes *H. coagulans* CCTCC M2017813 spore preparation as a pale yellow to pale grey powder. Thankcome states that *H. coagulans* CCTCC M2017813 is a non-pathogenic, non-toxigenic, Gram-positive, spore-forming, motile, rod-shaped bacterium. The strain was isolated from homemade thick broad bean sauce in Sichuan Province, China and has been deposited in the China Center for Type Culture Collection (CCTCC), with deposit number M2017813. Thankcome discusses the results of

¹ Thankcome states that *Heyndrickxia coagulans* was formerly classified as *Bacillus coagulans*, as reported in Narsing Rao, M. P., Banerjee, A., Liu, G.-H., & Thamchaipenet, A. (2023). Genome-based reclassification of *Bacillus acidicola*, *Bacillus pervagus* and the genera *Heyndrickxia*, *Margalitia* and *Weizmannia*. *Int J Syst Evol Microbiol*, 73(7). <https://doi.org/10.1099/ijsem.0.005961>. The notice refers to this organism by its former name, *B. coagulans*.

phenotypic and genotypic characterization used to confirm the strain's identity. Thankcome states that the organism is not genetically modified and is free of transferable antibiotic resistant genes.

Thankcome describes the manufacture of *H. coagulans* CCTCC M2017813 spore preparation by batch or fed-batch fermentation of a pure culture under controlled conditions. After fermentation, the cells are separated from the fermentation medium and concentrated via centrifugation. The biomass is then freeze-dried, crushed, filtered, and may be formulated with maltodextrin. Thankcome states that *H. coagulans* CCTCC M2017813 spore preparation is manufactured under current good manufacturing practices using food-grade raw materials and that all processing aids used in the manufacturing process are used in accordance with applicable U.S. regulations, are GRAS for their respective uses, or are the subject of an effective food contact notification.

Thankcome provides specifications for *H. coagulans* CCTCC M2017813 spore preparation that include total viable spore count ($\geq 2 \times 10^{11}$ CFU/g), limits for moisture ($\leq 7\%$), heavy metals, including lead (< 0.3 mg/kg), and microorganisms, including *Enterobacteriaceae* (≤ 10 CFU/g), *Escherichia coli* (absent in 1 g), *Salmonella* species (absent in 25 g), *Staphylococcus aureus* (< 10 CFU/g), and *Listeria monocytogenes* (absent in 25 g). Thankcome provides results from the analyses of three non-consecutive batches to demonstrate that *H. coagulans* CCTCC M2017813 spore preparation can be manufactured to meet these specifications. Thankcome states that *H. coagulans* CCTCC M2017813 spore preparation is stable at 25°C and 40% relative humidity for 24 months.

Thankcome states that the intended uses of *H. coagulans* CCTCC M2017813 spore preparation are the same as those in GRN 000399,² and the use of *H. coagulans* CCTCC M2017813 spore preparation is an alternative strain that would result in no increase in the dietary exposure. Therefore, Thankcome states that the dietary exposure of 3.64×10^{10} CFU/d is the same as in GRN 000399.

Thankcome discusses data and information to support the safety of *H. coagulans* CCTCC M2017813 spore preparation in food, including a history of safe use of *H. coagulans* in various fermented foods. Thankcome incorporates safety information discussed in GRN 000526³ and GRN 000949⁴. Thankcome provides data to demonstrate that *H. coagulans* CCTCC M2017813 shows genetic homology to the subjects of these notices and considers the safety information applicable to the notified ingredient. Additionally, Thankcome performed a literature search to identify studies published through October 2024 that were not included in the referenced GRNs.

² *H. coagulans* GBI-30, 6086 spores was the subject of GRN 000399. We evaluated this notice and responded in a letter dated July 31, 2012, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

³ *H. coagulans* Unique IS2 spore preparation was the subject of GRN 000526. We evaluated this notice and responded in a letter dated March 23, 2015, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

⁴ *H. coagulans* DSM 17654 spore preparation was the subject of GRN 000949. We evaluated this notice and responded in a letter dated January 7, 2021, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

Thankcome summarizes toxicological, genotoxicity, and human clinical studies, concluding that the publications support the safe consumption of *H. coagulans* CCTCC M2017813 spore preparation and that no treatment-related adverse effects were identified. Thankcome states that several strains of *H. coagulans* have been safely consumed as part of the human diet and that cases of bacteremia associated with this organism occur rarely and are primarily in immunocompromised populations.

Based on the data and information summarized above, Thankcome concludes that *H. coagulans* CCTCC M2017813 spore preparation is GRAS for its intended use.

Standards of Identity

In the notice, Thankcome states its intention to use *H. coagulans* CCTCC M2017813 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 *H. coagulans* CCTCC M2017813 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 (NCE). 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.

Allergen Labeling

The FD&C Act requires that the label of a food that is or contains an ingredient that contains a “major food allergen” declare the allergen’s presence (section 403(w)). The FD&C Act defines a “major food allergen” as one of nine foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, soybeans, and sesame) or a food ingredient that contains protein derived from one of those foods. *H. coagulans* CCTCC M2017813 spore preparation may require labeling under the FD&C Act because it may contain protein derived from soy or wheat. Questions about petitions or notifications for exemptions from the food allergen labeling requirements should be directed to the Division of Food Ingredients in the OPMAS. Questions related to food labeling in general should be directed to ONFL in NCE.

Section 301(l) of the FD&C Act

Section 301(l) 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(l)(1)-(4) applies. In our evaluation of Thankcome's notice concluding that *H. coagulans* CCTCC M2017813 spore preparation is GRAS under its intended conditions of use, we did not consider whether section 301(l) or any of its exemptions apply to foods containing *H. coagulans* CCTCC M2017813 spore preparation. Accordingly, our response should not be construed to be a statement that foods containing *H. coagulans* CCTCC M2017813 spore preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(l).

Conclusions

Based on the information that Thankcome provided, as well as other information available to FDA, we have no questions at this time regarding Thankcome's conclusion that *H. coagulans* CCTCC M2017813 spore preparation is GRAS under its intended conditions of use. This letter is not an affirmation that *H. coagulans* CCTCC M2017813 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 001243 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson

-S


Digitally signed by Susan J.
Carlson -S
Date: 2025.08.21 17:29:04
-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