U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Kevin Gillies
Kevin O. Gillies Consulting Services, LLC
1759 Grape St.
Denver, CO 80220

Re: GRAS Notice No. GRN 001264

Dear Mr. Gillies:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001264. We received the notice that you submitted on behalf of Beijing Scitop Bio-Tech Co., Ltd. (Scitop Bio) on March 12, 2025, and filed it on July 18, 2025. Scitop Bio submitted amendments to the notice on September 22, 2025, November 19, 2025, and December 08, 2025, that clarified the manufacturing process, specifications, intended uses and safety information.

The subject of the notice is *Lacticaseibacillus rhamnosus* CGMCC18639 (*L. rhamnosus* CGMCC18639) for use as an ingredient in all conventional foods at levels up to $1x10^{11}$ colony forming units (CFU)/serving (excluding use in infant formula, alcoholic beverages, and products under the jurisdiction of the United States Department of Agriculture). The notice informs us of Scitop Bio's view that these uses of *L. rhamnosus* CGMCC18639 are GRAS through scientific procedures.

Scitop Bio describes *L. rhamnosus* CGMCC18639 as a white to yellow powder and states that *L. rhamnosus* CGMCC18639 is a non-pathogenic, non-toxigenic, Gram-positive, non-motile, non-spore-forming, rod-shaped bacterium. Scitop Bio notes that the strain is a human colostrum isolate and has been deposited in the China General Microbiological Culture Collection with the depository number CGMCC18639. Scitop Bio describes the taxonomic analysis for the identity of the strain. Scitop Bio also discusses the results of genomic analyses to confirm the strain's identity and states that the strain is not genetically engineered. Scitop Bio discusses the results of phenotypic and genotypic characterization performed on *L. rhamnosus* CGMCC18639 and states that *L. rhamnosus* CGMCC18639 has no genes for pathogenicity and virulence, and lacks antibiotic resistance characteristics.

Scitop Bio describes the manufacture of *L. rhamnosus* CGMCC18639 by fermentation of a pure culture under controlled conditions. After fermentation, the fermentate is subjected to two centrifugation steps. The washed bacterial cells are collected and mixed with a cryoprotectant, lyophilized and ground. Scitop Bio states that *L. rhamnosus* CGMCC18639 is manufactured in accordance with current good manufacturing practices and that all raw materials are food grade and are used in

accordance with applicable U.S. regulations, are GRAS for their intended use, or are the subject of an effective food contact notification. Scitop Bio states that the cultured *L. rhamnosus* CGMCC18639 does not contain any major allergens.

Scitop Bio provides specifications for *L. rhamnosus* CGMCC18639 that include viable cell count (≥ 5.0 x 10^{11} CFU/g), and limits for heavy metals, including lead (< 0.15 mg/kg), and microorganisms, including *Escherichia coli* (< 3 most probable number in 1 g), *Salmonella* spp. (not detected in 25 g), *Listeria monocytogenes* (not detected in 25 g), *Staphylococcus aureus* (not detected in 25 g), and *Cronobacter sakazakii* (not detected in 100 g). Scitop Bio provides the results from the analyses of three non-consecutive batches to demonstrate that *L. rhamnosus* CGMCC18639 can be manufactured to meet these specifications.

Scitop Bio estimates the dietary exposure to *L. rhamnosus* CGMCC18639 from the intended uses to be 1x10^{12} CFU/person (p)/day (d) based on the assumption that an individual consumes on average 20 servings of food/d and that 10 servings of food will contain *L. rhamnosus* CGMCC18639 at the maximum use level of 1.0 x 10^{11} CFU/serving. Scitop Bio states that the intended uses are substitutional to the current uses of other *L. rhamnosus* strains and therefore, an increase in dietary exposure to *L. rhamnosus* is not expected from the intended uses.

Scitop Bio discusses data and information used to support the safety of *L. rhamnosus* CGMCC18639, including a history of safe use of *L. rhamnosus* in fermented foods, such as fermented milk, meat and vegetables. Scitop Bio incorporates into their notice and provides summaries of the information pertaining to the safety of live *L. rhamnosus* in food discussed in GRNs 000288, 001013, 001084, 001093 and 001130.[1] Scitop Bio discusses the phylogenetic and 16s rRNA similarity between *L. rhamnosus* CGMCC18639 and other *L. rhamnosus* strains that were the subjects of previous GRNs. Scitop Bio also discusses opportunistic infection caused by certain *L. rhamnosus* strains and states that there is no concern for safety and the reported infections occur predominantly in individuals with compromised immune systems or other predisposing factors such as surgical implants. Scitop Bio summarizes published human feeding studies on *L. rhamnosus* CGMCC18639 and states that no adverse effects were observed at the test doses in these studies.

Based on the totality of the data and information, Scitop Bio concludes that *L. rhamnosus* CGMCC18639 is GRAS for its intended use.

[1] The L. rhamnosus strains HN001, DSM 33156, KCTC 12202BP, ATCC BAA-2836 and CGMCC 21225 are the subjects of GRNs 000288, 001013, 001084, 001093 and 001130, respectively. We evaluated these notices and responded in letters dated November 1, 2009, December 15, 2021, October 31, 2023, June 9, 2023, and September 28, 2023, respectively, stating that we had no questions at the time regarding the notifiers' GRAS conclusions.

Standards of Identity

In the notice, Scitop Bio states its intention to use *L. rhamnosus* CGMCC18639 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 *L. rhamnosus* CGMCC18639 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

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 Scitop Bio's notice concluding that *L. rhamnosus* CGMCC18639 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 *L. rhamnosus* CGMCC18639. Accordingly, our response should not be construed to be a statement that foods containing *L. rhamnosus* CGMCC18639, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Scitop Bio provided, as well as other information available to FDA, we have no questions at this time regarding Scitop Bio's conclusion that *L. rhamnosus* CGMCC18639 is GRAS under its intended conditions of use. This letter is not an affirmation that *L. rhamnosus* CGMCC18639 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 001264 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2025.12.09 17:25:23 -05'00'

Susan J. Carlson, Ph.D.
Director
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