Jim Lassiter
REJIMUS, Inc.
600 W. Santa Ana Blvd.
Suite 1100
Santa Ana, CA 92701

Re: GRAS Notice No. GRN 001084

Dear Mr. Lassiter:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001084. We received the notice that you submitted on behalf of Cell Biotech Co. Ltd. (CBI) on May 12, 2022, and filed it on December 2, 2022. CBI submitted amendments to the notice on October 6, 2023, October 12, 2023, and October 20, 2023, that provided additional information regarding the microorganism, manufacturing process, specifications, including revised heavy metal specifications, results from additional batch analyses, dietary exposure estimates, and an updated literature search.

The subject of the notice is *Lactobacillus rhamnosus* KCTC 12202BP for use as an ingredient at a level up to 10^9 colony forming units (CFU) per serving in liquid unflavored milk.[1] The notice informs us of CBI's view that this use of *L. rhamnosus* KCTC 12202BP is GRAS through scientific procedures.

CBI describes *L. rhamnosus* KCTC 12202BP as a light brown powder. CBI states that *L. rhamnosus* KCTC 12202BP is a Gram-positive, rod-shaped, non-spore forming bacterium. The strain was originally isolated from cheese and is deposited in the Korean Collection for Type Cultures (KCTC). CBI discusses the results of genotypic and phenotypic analyses performed on *L. rhamnosus* KCTC 12202BP to confirm the strain identity and concludes that the strain is non-pathogenic and non-toxigenic.

CBI describes the manufacture of *L. rhamnosus* KCTC 12202BP by fermentation of a pure culture under controlled conditions. After fermentation, the bacterial culture and the fermentation media are separated by centrifugation. Following this, coating ingredients are added to water, mixed, sterilized with saturated steam, and blended with the concentrated bacterial culture and corn starch. The resulting product is quick-frozen, freeze dried, milled, and blended with corn starch to ensure a standardized cell count. CBI states that the manufacturing process is monitored for contamination, and that *L. rhamnosus* KCTC 12202BP is manufactured under current good manufacturing practices and that all raw materials are food-grade and are used in accordance with

[1] CBI states that *L. rhamnosus* KCTC 12202BP is not intended for use in infant formula, food products intended for infants and young children, or in foods that fall under the purview of the U.S. Department of Agriculture.

existing U.S. authorizations.

CBI provides specifications for *L. rhamnosus* KCTC 12202BP that include viable cell count (≥10^{11} CFU/g); limits for heavy metals, including lead (≤ 0.01 mg/kg); and microorganisms, including coliforms (absent in 10 g), yeast and mold (≤ 10 CFU/g), *Escherichia coli* (absent in 1 g), *Staphylococcus aureus* (absent in 25 g), *Salmonella* serovars (absent in 25 g), and *Listeria monocytogenes* (absent in 25 g). CBI provides results from the analyses of three non-consecutive batches to demonstrate that *L. rhamnosus* KCTC 12202BP can be manufactured to meet these specifications.

CBI estimates an eaters-only dietary exposure to *L. rhamnosus* KCTC 12202BP from the intended use in liquid, unflavored milk to be 8.94 x 10^8 CFU/person (p)/d at the mean and 1.85 x 10^9 CFU/p/d at the 90th percentile for the U.S. population aged 2 years or older based on food consumption data from the 2017-2018 National Health and Nutrition Examination Survey (NHANES).

CBI discusses publicly available data and information to support the safety of *L. rhamnosus* KCTC 12202BP, including history of consumption of *L. rhamnosus* and other lactic acid bacteria in food. CBI concludes that the phenotypic characteristics of *L. rhamnosus* KCTC 12202BP do not pose a safety concern (i.e., production of antimicrobials, production of secondary metabolites, antibiotic resistance). CBI performed a literature search through October 2023 and summarizes published literature and governmental evaluations that support the safe consumption of *L. rhamnosus*, including *L. rhamnosus* KCTC 12202BP, with no serious adverse effects reported. CBI notes that bacteremia cases caused by lactobacilli, including *L. rhamnosus*, have been reported but notes that these cases occurred mainly in immunocompromised patients or those with underlying medical conditions.

Based on the totality of evidence and information summarized above, CBI concludes that *L. rhamnosus* KCTC 12202BP is GRAS for its intended use.

Standards of Identity

In the notice, CBI states its intention to use *L. rhamnosus* KCTC 12202BP in a food category 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, and 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 *L. rhamnosus* KCTC 12202BP 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 (CFSAN). 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.

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. *L. rhamnosus* KCTC 12202BP may require labeling under the FD&C Act because it may contain protein derived from soy. Questions about petitions or notifications for exemptions from the food allergen labeling requirements should be directed to the Division of Food Ingredients in OFAS. Questions related to food labeling in general should be directed to ONFL in CFSAN.

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 CBI's notice concluding that *L. rhamnosus* KCTC 12202BP 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* KCTC 12202BP. Accordingly, our response should not be construed to be a statement that foods containing *L. rhamnosus* KCTC 12202BP, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that CBI provided, as well as other information available to FDA, we have no questions at this time regarding CBI's conclusion that *L. rhamnosus* KCTC 12202BP is GRAS under its intended conditions of use. This letter is not an affirmation that *L. rhamnosus* KCTC 12202BP 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 001084 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.10.31 14:10:18 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
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