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

Re: GRAS Notice No. GRN 001085

Dear Mr. Lassiter:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001085. We received the notice that you submitted on behalf of Cell Biotech Co. Ltd. (CBI) on May 12, 2022 and filed it on February 23, 2023. CBI submitted amendments to the notice on July 20, 2023, August 8, 2023, September 29, 2023, and October 6, 2023 discussing phenotypic characteristics, manufacturing, analytical methods, and dietary exposure.

The subject of the notice is *Lacticaseibacillus casei*[1] KCTC 12398BP for use as an ingredient at a level up to 10^9 colony forming units (CFU)/serving in liquid unflavored milk.[2] The notice informs us of CBI's view that this use of *L. casei* KCTC 12398BP is GRAS through scientific procedures.

CBI describes *L. casei* KCTC 12398BP as a light-brown powder and states that *L. casei* KCTC 12398BP is a non-pathogenic and non-toxigenic bacterium that can be described as Gram-positive, and non-spore forming. The strain was isolated from cheese and was deposited at the Korean Collection for Type Cultures (KCTC) with accession number KCTC 12398BP. CBI discusses the results of the phenotypic and genotypic characterization used to confirm the strain identity.

CBI describes the manufacture of *L. casei* KCTC 12398BP 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. casei* KCTC 12398BP is manufactured under current good manufacturing practices and

[1] We note that *Lactobacillus casei* was reclassified as *Lacticaseibacillus casei* as reported in Zheng, et al. (Ref. 1)

[2] CBI states that *L. casei* KCTC 12398BP is not intended for use in infant formula, food products intended for infants and young children, or in food products under the jurisdiction of the United States Department of Agriculture.

that all raw materials are food-grade and are used in accordance with existing U.S. authorizations.

CBI provides specifications for *L. casei* KCTC 12398BP 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 the results from the analyses of three non-consecutive batches to demonstrate that the ingredient can be manufactured to conform with the provided specifications.

CBI estimates an eaters-only dietary exposure to *L. case*i KCTC 12398BP from the intended uses 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 data and information used to support the safety of *L. casei*, including its safe use in fermented foods. CBI performed a literature search through May 2022 of *L. casei*, including *L. casei* KCTC 12398BP, with no serious adverse effects reported. CBI notes that *L. casei* was the subject of GRNs 000231, 000429, and 000736.[3] CBI also discusses the available data and information from animal studies supporting the safety of lactic acid bacteria in general and *L. casei* specifically. CBI discusses three human clinical studies that showed that human consumption of microorganisms is tolerated with no serious adverse effects. CBI states that the phenotypic characteristics of *L. plantarum* KCTC 10782BP do not pose a safety concern and it does not produce antibiotics. CBI concludes that based on the totality of the information, *L. casei* KCTC 12398BP is safe under the intended conditions of use.

Based on the data and information, CBI concludes that *L. casei* KCTC 12398BP is GRAS for its intended use.

Standards of Identity

In the notice, CBI states its intention to use *L. casei* KCTC 12398BP 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

[3] FDA evaluated these notices and responded in letters dated May 29, 2008, December 10, 2012, and April 11, 2018, respectively, and stated that we had no questions at the time regarding the notifier's GRAS conclusion.

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. casei* KCTC 12398BP 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. The Office of Food 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.

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. plantarum* KCTC 12398BP 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 the Office of Food Additive Safety. Questions related to food labeling in general should be directed to the ONFL in the Center for Food Safety and Applied Nutrition.

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. casei* KCTC 12398BP 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. casei* KCTC 12398BP. Accordingly, our response should not be construed to be a statement that foods containing *L. casei* CBT LC5, 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. casei* KCTC 12398BP is GRAS under its intended conditions of use. This letter is not an affirmation that *L. casei* KCTC 12398BP 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 001085 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.10.27 18:10:20 -04'00'

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

Reference

1. Zheng, J., et al. (2020). A taxonomic note on the genus Lactobacillus: Description of 23 novel genera, emended description of the genus Lactobacillus Beijerinck 1901, and union of Lactobacillaceae and Leuconostocaceae. International Journal of Systematic and Evolutionary Microbiology, 70(4), 1-77. doi: 10.1099/ijsem.0.004107