Claire Kruger
Spherix Consulting Group, Inc.
751 Rockville Pike Unit 30-B
Rockville, MD 20852

Re: GRAS Notice No. GRN 001002

Dear Dr. Kruger,

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001002. We received the notice that you submitted on behalf of Morinaga Milk Industry Co., Ltd. (Morinaga) on April 29, 2021, and filed it on July 9, 2021. Morinaga submitted amendments to the notice on January 14, 2022, May, 23, 2022, and June 6, 2022 that clarified manufacturing, specifications, batch analysis data, intended uses, and intended use levels.

The subject of the notice is *Bifidobacterium breve* strain MCC1274 preparation (*B. breve* MCC1274) for use as an ingredient at a maximum level of 5 x 10^{10} colony forming units (CFU)/serving in the following conventional foods: baked goods, breakfast cereals, fruits (juices and nectars, ices, vegetable juices, frozen fruit, frozen juice bars), milk-based drinks and powders, yogurt, dairy product analogs, frozen dairy desserts, cheeses, condiments and spreads, nut and peanut spreads, gelatins and puddings, milk and non-milk meal replacements, soft and hard candies, and snack foods.[1] The notice informs us of Morinaga's view that these uses of *B. breve* MCC1274 are GRAS through scientific procedures.

Morinaga describes *B. breve* MCC1274 as a white to light brown powder. Morinaga states that *B. breve* MCC1274 is a Gram-positive, non-motile, non-spore forming, rod-shaped, anaerobic non-pathogenic and non-toxigenic bacterium. The strain was isolated from the feces of an infant in 2009 and is deposited with the National Institute of Technology and Evaluation (NITE) in Japan and is designated FERM BP-11175. Morinaga discusses the results of the phenotypic and genotypic characterization used to confirm the strain's identity. Morinaga states that *B. breve* MCC1274 does not carry any transposable elements that could be transferred to the commensal microbiome.

Morinaga describes the manufacture of *B. breve* MCC1274 by fermentation of a pure culture under controlled conditions. After fermentation is complete, the culture is cooled, concentrated via multiple centrifugation steps, and washed. The concentrated biomass is resuspended with a cryoprotectant composed of food-grade carbohydrates

[1] Morinaga states that *B. breve* MCC1274 is not intended for use in infant formula, infant and toddler foods, or in foods that fall under the purview of the U.S. Department of Agriculture.

and amino acids, freeze-dried, powdered, formulated with cornstarch, and sieved. The finished product is packed into air-tight aluminum bags. Morinaga states that *B. breve* MCC1274 is manufactured under current good manufacturing practices using food-grade raw materials. Morinaga notes that the fermentation medium does not contain any major food allergens.

Morinaga provides specifications for *B. breve* MCC1274 that include total anaerobic plate count (> 10^{11} CFU/g); heavy metals, including lead (< 0.5 mg/kg); and limits for other microorganisms, including yeast and mold (≤ 30 CFU/g), coliform bacteria (absent in 1 g), and *Salmonella* serovars (absent in 25 g). Morinaga provides results from three non-consecutive lots to demonstrate that the ingredient can be manufactured to conform with the provided specifications. Morinaga states that *B. breve* MCC1274 is stable for up to 3 years when stored below 10 °C.

Morinaga provides an estimate of dietary exposure to *B. breve* MCC1274 from the intended uses based on average daily food consumption data from the 2015-2016 National Health and Nutrition Examination Survey (NHANES). Morinaga estimates the mean and 90th percentile eaters-only dietary exposure to *B. breve* MCC1274 to be 5.68 x 10^{10} CFU/day and 1.05 x 10^{11} CFU/day, respectively, for the U.S. population aged 2 years and older.

Morinaga discusses data and information used to support the safety of *B. breve* MCC1274, including a history of safe use of *B. breve* strains in foods. Morinaga incorporates summaries of published literature from GRN 000268[2] to support the general safety of *Bifidobacteria*. Morinaga incorporates previous adverse case reports from GRN 000453[3] and states that there are no new published reports since the submission of this notice for review by FDA. Morinaga relies on published literature and reviews by other regulatory authorities to support the safe consumption of *B. breve* MCC1274. These include acute and subchronic studies, with no reports of toxicity or significant adverse effects. Additionally, Morinaga describes several published tolerance studies in which children and adults were fed *B. breve* MCC1274 at various levels and states that no adverse effects were noted.

Morinaga includes the report of a panel of individuals (Morinaga's GRAS panel). Based on its review, Morinaga's GRAS panel concluded that *B. breve* MCC1274 is safe under the conditions of its intended use.

Based on the totality of evidence, Morinaga concludes that *B. breve* MCC1274 is GRAS for its intended use.

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[2] *B. longum* BB536 was the subject of GRN 000268. We evaluated this notice and responded in a letter, dated July 8, 2009, stating that we had no questions at the time regarding the notifier's GRAS conclusion.
[3] *B. breve* M-16V was the subject of GRN 000453. We evaluated this notice and responded in a letter, dated July 25, 2017, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

Standards of Identity

In the notice, Morinaga states its intention to use *B. breve* MCC1274 in several food categories, including foods for which standards of identity exist, located in Title 21 of the Code of Federal Regulations (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 *B. breve* MCC1274 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.

Section 301(ll) of the Federal Food, Drug, and Cosmetic Act (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 Morinaga's notice concluding that *B. breve* MCC1274 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 *B. breve* MCC1274. Accordingly, our response should not be construed to be a statement that foods containing *B. breve* MCC1274, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Morinaga provided, as well as other information available to FDA, we have no questions at this time regarding Morinaga's conclusion that *B. breve* MCC1274 is GRAS under its intended conditions of use. This letter is not an affirmation that *B. breve* MCC1274 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 001002 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2022.07.22 17:58:19 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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