



Maureen Dunn, ND
AIBMR Life Sciences, Inc.
1425 Broadway, Suite 458
Seattle, WA 98122

Re: GRAS Notice No. GRN 001093

Dear Dr. Dunn:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001093. We received the notice that you submitted on behalf of Ildong Bioscience Co., Ltd. (Ildong Bioscience) on May 12, 2022 and filed it on December 15, 2022. Ildong Bioscience submitted amendments on April 4, 2023, April 20, 2023, and May 1, 2023, that clarified the manufacturing process, specifications, dietary exposure, and provided additional safety information.

The subject of the notice is *Lacticaseibacillus rhamnosus* ATCC BAA-2836 (*L. rhamnosus* ATCC BAA-2836). It is intended to be used as an ingredient in conventional foods at levels up to 1.02×10^{11} colony forming units (CFU)/serving.¹ The notice informs us of Ildong Bioscience's view that these uses of *L. rhamnosus* ATCC BAA-2836 are GRAS through scientific procedures.

Ildong Bioscience describes *L. rhamnosus* ATCC BAA-2836 as a white to light yellow powder. Ildong Bioscience states that *L. rhamnosus* ATCC BAA-2836 is a non-motile, rod-shaped, facultative anaerobe and facultative heterofermentative bacterium. The strain was isolated from the feces of breast-fed infants and has been deposited in the American Type Culture Collection (ATCC) as ATCC BAA-2836. Ildong Bioscience conducted taxonomic analysis for the strain identity and discusses the results of phenotypic and genotypic characterization on antibiotic resistance, hemolysis, and a search of Virulence Factor Database for virulence factors. Ildong Bioscience states that *L. rhamnosus* ATCC BAA-2836 is non-pathogenic, non-toxicogenic, and does not produce biogenic amines.

Ildong Bioscience describes the manufacture of *L. rhamnosus* ATCC BAA-2836 by fermentation of a pure culture under controlled conditions. After fermentation, the *L. rhamnosus* ATCC BAA-2836 cells are separated from the medium and concentrated by

¹ Ildong Bioscience states that *L. rhamnosus* ATCC BAA-2836 is not intended for use in infant formula, products under the jurisdiction of the United States Department of Agriculture, foods for which standards of identity preclude its use, or in alcoholic beverages.

centrifugation, resuspended, and then lyophilized. Ildong Bioscience states that *L. rhamnosus* ATCC BAA-2836 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.

Ildong Bioscience provides specifications for *L. rhamnosus* ATCC BAA-2836 that include limits for total cell count ($\geq 4.5 \times 10^{11}$ CFU/g), microorganisms, including *Escherichia coli* (absent in 10 g), *Salmonella* serovars (absent in 10 g), *Staphylococcus aureus* (absent in 1 g), and heavy metals, including lead (< 0.1 mg/kg). Ildong Bioscience provides the results from the analyses of three non-consecutive batches to demonstrate that *L. rhamnosus* ATCC BAA-2836 can be manufactured to meet these specifications. Ildong Bioscience provides the results of stability studies and states that *L. rhamnosus* ATCC BAA-2836 is stable for 24 months at 5 °C and no humidity.

Ildong Bioscience estimates dietary exposure to *L. rhamnosus* ATCC BAA-2836 from the intended uses to be 1.02×10^{12} CFU/person (p)/d based on the maximum use level for *L. rhamnosus* ATCC BAA-2836, the average consumption of 20 servings of food/p/d in the U.S., and the assumption that 10 servings of food would contain *L. rhamnosus* ATCC BAA-2836.

Ildong Bioscience discusses data and information used to support the safety of *L. rhamnosus* ATCC BAA-2836, including a history of safe use of *L. rhamnosus* species in fermented foods, such as sausage, grains, fermented milk, and yogurt. Ildong Bioscience incorporates into their notice and provides summaries of the information pertaining to the safety of the *L. rhamnosus* strains discussed in GRNs 000281, 000288, and 001013.² Ildong Bioscience also summarizes published animal and human studies on *L. rhamnosus*. Ildong Bioscience states that no serious adverse events were reported in clinical trials using *L. rhamnosus* at levels up to 1×10^{11} CFU/d, and the toxicology studies did not show any adverse effects in rodents.

Based on the totality of the data and information, Ildong Bioscience concludes that *L. rhamnosus* ATCC BAA-2836 is GRAS for its intended use.

Standards of Identity

In the notice, Ildong Bioscience states its intention to use *L. rhamnosus* ATCC BAA-2836 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

² *L. rhamnosus* HN001 was the subject of GRNs 000281 and 000288. We evaluated these notices and responded letters dated August 31, 2009 and November 1, 2009, respectively, stating that we had no questions at the time regarding the notifier's GRAS conclusions.

L. rhamnosus DSM33156 was the subject of GRN 001013. We evaluated this notice and responded in a letter, dated December 15, 2021, stating that we had no questions at the time regarding the notifier's GRAS conclusion.

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* ATCC BAA-2836 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. rhamnosus* ATCC BAA-2836 requires labeling under the FD&C Act because the ingredient is grown in culture medium that contains a milk component.

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 Ildong Bioscience’s notice concluding that *L. rhamnosus* ATCC BAA-2836 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* ATCC BAA-2836. Accordingly, our response should not be construed to be a statement that foods containing *L. rhamnosus* ATCC BAA-2836, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Ildong Bioscience provided, as well as other information available to FDA, we have no questions at this time regarding Ildong Bioscience’s conclusion that *L. rhamnosus* ATCC BAA-2836 is GRAS under its intended conditions of use. This letter is not an affirmation that *L. rhamnosus* ATCC BAA-2836 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 001093 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

**Susan J.
Carlson -S**

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