Winnie Ng, Ph.D., DABT
Chr. Hansen, Inc.
9015 W Maple St.
Milwaukee, WI 53214

Re: GRAS Notice No. GRN 001089

Dear Dr. Ng:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001089. We received Chr. Hansen's notice on May 12, 2022, and filed it on November 8, 2022. Chr. Hansen submitted amendments to the notice on March 22, 2023, April 19, 2023, and May 8, 2023, including additional information regarding the manufacturing, specifications, dietary exposure, and safety of the ingredient.

The subject of the notice is *Lactobacillus gasseri* strain NCIMB 30370 for use as an ingredient in conventional foods[1] at levels up to 10^{11} colony forming units (CFU)/serving. The notice informs us of Chr. Hansen's view that these uses of *L. gasseri* NCIMB 30370 are GRAS through scientific procedures.

Chr. Hansen discusses the identity of *L. gasseri* NCIMB 30370 and describes it as an off-white to cream powder. Chr. Hansen states that *L. gasseri* NCIMB 30370 was first isolated from human breast milk. Chr. Hansen discusses the results of genomic analyses to confirm the strain's identity. Chr. Hansen states that the strain is not genetically modified and is deposited in the National Collection of Industrial, Food, and Marine Bacteria. Chr. Hansen discusses the results of phenotypic and genotypic characterization performed on *L. gasseri* NCIMB 30370 and concludes that no genes encoding antibiotic resistance, pathogenicity, or virulence factors were identified, and that the strain is non-pathogenic and non-toxigenic.

Chr. Hansen describes the manufacturing process for *L. gasseri* NCIMB 30370, stating that it is produced by industrial fermentation of a pure culture in a controlled, sterile environment. Chr. Hansen explains that after fermentation the *L. gasseri* NCIMB 30370 cells are concentrated by centrifugation, mixed with cryoprotectants, frozen into pellets, lyophilized, and milled to a powder. Chr. Hansen states that *L. gasseri* NCIMB 30370 is manufactured in accordance with current good manufacturing practices and that all processing aids used in the manufacture of *L. gasseri* NCIMB 30370 are safe and suitable for human consumption and are used in accordance with applicable U.S.

[1] Chr. Hansen states that *L. gasseri* NCIMB 30370 is not intended for use in infant formula or products under the jurisdiction of the United States Department of Agriculture.

regulations or are GRAS for their intended uses. Chr. Hansen states that no raw materials used in the manufacture of *L. gasseri* NCIMB 30370 are allergens or are derived from allergenic sources.

Chr. Hansen provides specifications for *L. gasseri* NCIMB 30370 that include a minimum amount of *L. gasseri* NCIMB 30370 (≥200 x 10^9 CFU/g); and limits for heavy metals, including lead (≤ 0.1 mg/kg); and other microorganisms, including *Salmonella* (negative/10 g) and *Enterococcus* (<100 CFU/g). Chr. Hansen provides the results of the analyses of three non-consecutive batches to demonstrate that *L. gasseri* NCIMB 30370 can be manufactured to meet these specifications. Chr. Hansen states that *L. gasseri* NCIMB 30370 is stable for at least 18 months from the date of manufacture when stored at or below 4 °C in the original packaging.

Chr. Hansen intends to use *L. gasseri* NCIMB 30370 at levels up to 10^{11} CFU/serving in conventional foods to ensure a minimum level of 1.0 x 10^9 CFU/serving throughout the shelf-life of the product. Chr. Hansen estimates the dietary exposure to *L. gasseri* NCIMB 30370 to be 2.0 x 10^{12} CFU/d based on the assumption that a healthy individual in the U.S. consumes 20 servings of food/d, and that all servings of food consumed would contain *L. gasseri* NCIMB at the maximum use level of 10^{11} CFU/serving.

Chr. Hansen discusses the safety of *L. gasseri* NCIMB 30370. In addition to noting the presence of *L. gasseri* NCIMB 30370 in human breast milk, Chr. Hansen discusses the results of published clinical studies in which adults were fed *L. gasseri* NCIMB 30370, and states that the microorganism was well tolerated with no adverse events reported. Chr. Hansen discusses an unpublished *in silico* analysis on *L. gasseri* NCIMB 30370's potential to produce biogenic amines and concludes that the genome does not contain genes that are involved in the synthesis of biogenic amines. Chr. Hansen states that no information contradicting their GRAS conclusion was identified when a comprehensive literature search was performed.

Based on the totality of the data and information, Chr. Hansen concludes that *L. gasseri* NCIMB 30370 is GRAS under the conditions of its intended use.

Standards of Identity

In the notice, Chr. Hansen states its intention to use *L. gasseri* NCIMB 30370 in several food categories, including foods for which standards of identity exist 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.*

gasseri NCIMB 30370 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 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 Chr. Hansen's notice concluding that *L. gasseri* NCIMB 30370 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. gasseri* NCIMB 30370. Accordingly, our response should not be construed to be a statement that foods containing *L. gasseri* NCIMB 30370, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Chr. Hansen provided, as well as other information available to FDA, we have no questions at this time regarding Chr. Hansen's conclusion that *L. gasseri* NCIMB 30370 is GRAS under its intended conditions of use. This letter is not an affirmation that *L. gasseri* NCIMB 30370 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 001089 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.06.20 17:52:41 -04'00'

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