Emily Gregoire
Chr. Hansen, Inc.
9015 West Maple St.
Milwaukee, WI 53214

Re: GRAS Notice No. GRN 000856

Dear Ms. Gregoire:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000856. We received the notice that you submitted on behalf of Chr. Hansen A/S (Chr. Hansen) on April 16, 2019, and filed it on June 25, 2019. Chr. Hansen submitted an amendment to the notice on November 15, 2019, providing additional manufacturing specifications.

The subject of the notice is *Bifidobacterium animalis* subsp. *lactis* strain DSM 15954 (*B. animalis* DSM 15954) for use as an ingredient in milk and dairy products such as yogurt and other fermented milk products; dairy alternatives (plant-based (oat, soy, almond, coconut, pea, etc.) fermented milk and yogurt products); beverages such as juice and protein shakes; shelf-stable products such as bars (granola, protein, meal replacement bars), confectionery (gummy candy, hard candy, soft chew candy, chewing gum, coatings); and breakfast cereals (ready-to-eat (RTE) and hot) at levels up to 5×10^{11} colony forming units (CFU)/serving. The notice informs us of Chr. Hansen's view that these uses of *B. animalis* DSM 15954 are GRAS through scientific procedures.

Chr. Hansen describes *B. animalis* DSM 15954 as a white to light-beige powder. Chr. Hansen states that *B. animalis* DSM 15954[1] is a Gram-positive, non-motile, non-spore forming, rod or Y-shaped bacterium, which is deposited in the strain collection of the Deutsche Sammlung von Mikroorganismen (DSM). Chr. Hansen discusses the results of phenotypic and genotypic characterization used to confirm the strain's identity. Chr. Hansen states that *B. animalis* DSM 15954 is non-pathogenic and non-toxigenic. Moreover, *B. animalis* has been used for many years in fermented foods.

Chr. Hansen describes the manufacture of *B. animalis* DSM 15954 by fermentation of a pure culture under controlled conditions. After fermentation, the fermentation broth containing the bacterial culture is concentrated by centrifugation. Following this, cryoprotectants are added to the concentrated bacterial culture and frozen into pellets. The resulting pellets are lyophilized and then ground into a powder. During production,

[1] FDA notes that *B. animalis* is a member of the lactic acid bacteria (LAB) classification, a group characterized by the production of lactic acid as the major metabolic end-product of carbohydrate metabolism and other physiological traits.

the production environment and product facing areas are tested weekly for the presence of pathogenic microorganisms and indicator organisms. Furthermore, Chr. Hansen states that all batches are tested for the presence of pathogenic microorganisms and cross-contaminants. Chr. Hansen explains that *B. animalis* DSM 15954 is manufactured with food-grade materials that comply with FDA regulations for such use under current good manufacturing practices. Chr. Hansen states that milk is used during fermentation for some forms of the final powdered product, and that these forms contain traces of milk protein. However, Chr. Hansen explains that the presence of allergens is dependent upon the intended use of the final product, and that some forms of *B. animalis* DSM 15954 are dairy-free and contain no allergens in either the fermentation media or finished product.

Chr. Hansen provides specifications for *B. animalis* DSM 15954 that include a minimum CFU (no less than 1×10^{11} CFU/g) and limits for other microorganisms, including non-lactics (< 500 CFU/g), yeast and molds (< 10 CFU/g), Enterococci (< 100 CFU/g), *Enterobacteriaceae* (< 10 CFU/g), coagulase-positive *Staphylococcus* (< 10 CFU/g), *Salmonella* serovars (absent in 25 g) and *Listeria monocytogenes* (absent in 25 g). Chr. Hansen provides the results of the batch analyses for three non-consecutive lots to demonstrate that the ingredient can be manufactured to conform with the provided specifications.

Chr. Hansen intends to use *B. animalis* DSM 15954 in as an ingredient in milk and dairy products such as yogurt and other fermented milk products; dairy alternatives (plant-based (oat, soy, almond, coconut, pea, etc.) fermented milk and yogurt products); beverages such as juice and protein shakes; shelf-stable products such as bars (granola, protein, meal replacement bars), confectionery (gummy candy, hard candy, soft chew candy, chewing gum, coatings); and breakfast cereals (RTE and hot) at levels up to 5×10^{11} CFU/serving. Chr. Hansen states that the dietary exposure to *B. animalis* DSM 15954 is likely to be less than 10^{11} CFU/day, based on the assumption that the average consumption of a healthy individual is approximately 20 servings of all combined food per day.

Chr. Hansen states that the addition of *B. animalis* DSM 15954 is limited to foods that will sustain the live culture through the shelf-life of the product.

Chr. Hansen states that bifidobacteria are widely consumed in fermented foods and describes the long history of safe use of *B. animalis* subsp. *lactis* in fermented foods. Chr. Hansen explains that bifidobacteria may cause opportunistic infections in immunocompromised patients, however, this is not relevant under the intended conditions of use. Chr. Hansen cites publications in peer-reviewed scientific journals that support the safe consumption of *B. animalis* DSM 15954. Additionally, Chr. Hansen describes published clinical trials in which infants, children and adults were fed *B. animalis* DSM 15954 and states that no significant adverse effects on participants were noted in any of these studies.

Based on the totality of evidence, Chr. Hansen concludes that *B. animalis* DSM 15954 is GRAS for its intended use.

Standards of Identity

In the notice, Chr. Hansen states its intention to use *B. animalis* DSM 15954 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 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 *B. animalis* DSM 15954 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 eight foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, and soybeans) or a food ingredient that contains protein derived from one of those foods. *B. animalis* DSM 15954 produced using milk during fermentation requires labeling under the FD&C Act because it contains protein derived from milk.

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 *B. animalis* DSM 15954 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. animalis* DSM 15954. Accordingly, our response should not be construed to be a statement that foods containing *B. animalis* DSM 15954, 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 *B. animalis* DSM 15954 is GRAS under its intended conditions of use. This letter is not an affirmation that *B. animalis* DSM 15954 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 000856 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2019.12.09 11:44:47 -05'00'

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