



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

Re: GRAS Notice No. GRN 000760

Dear Ms. Gregoire:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000760. We received Chr. Hansen, Inc.'s (Hansen) notice on February 8, 2018, and filed it on April 13, 2018. Hansen submitted amendments to the notice on December 3 and December 5, 2018, that provided additional detail regarding the manufacturing process and additional information regarding dietary exposure, respectively.

The subject of the notice is *Lactobacillus curvatus* DSM 18775 for use as an antimicrobial spray on ready-to-eat meat and poultry products at a use level that will result in a final concentration between 6.4 and 7.4 log CFU per gram of the finished product. The notice informs us of Hansen's view that these uses of *L. curvatus* DSM 18775 are GRAS through scientific procedures.

Hansen states that *L. curvatus* is a species of the lactic acid bacteria (LAB) order; a broader grouping of bacteria characterized by the production of lactic acid as the major metabolic end product of carbohydrate metabolism. Hansen notes that *L. curvatus* and other LAB are native to environments such as plants, silage, meat, milk, and soil, and they are also found in the digestive tracts of humans and other animals. Hansen provides the results of phenotypic and genotypic analysis (16S ribosomal DNA) to confirm the strain identity.

Hansen describes the production of *L. curvatus* DSM 18775, noting that it is a pure culture, fermented under pH- and temperature-controlled conditions. Hansen states that when microbial growth ends, fermentation is stopped by cooling. The microbes are then concentrated and harvested by centrifugation. The final product is either frozen into pellets or freeze-dried as a powder. Hansen notes that all ingredients are safe and suitable for use in human food, and the production is conducted in accordance with current good manufacturing practices. Hansen notes that there are no allergens in the fermentation medium and none are present in the final product.

Hansen provides specifications for *L. curvatus* DSM 18775, including cell count (frozen: 4.0×10^{10} , freeze-dried: 3.2×10^{10}), pH, and limits for microorganisms, including *Bacillus cereus* (< 100 CFU/g), *Enterobacteriaceae* (< 10 CFU/g), Enterococci (<1000

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CFU/g), *Staphylococcus aureus* (<50 CFU/g), yeast and molds (<100 CFU/g), *Listeria monocytogenes* (absent in 25 g), and *Salmonella* spp. (absent in 25 g). Hansen provides analytical data for both forms of the product to demonstrate that the *L. curvatus* DSM 18775 products can meet the specifications.

Hansen discusses the dietary exposure to *L. curvatus* DSM 18775. Hansen intends for *L. curvatus* DSM 18775 to be applied at a level between 6.4 to 7.4 log CFU per gram, with a maximum possible concentration of 9 log CFU per gram at the end of the shelf life for the product. Based on a published estimate of the daily consumption of meat and poultry products where *L. curvatus* DSM 18775 would be added, and the maximum concentration of the organism resulting from the intended use, Hansen estimates a maximum intake of 1.3×10^{11} CFU per person per day.

Hansen discusses the safety of *L. curvatus* DSM 18775, citing published studies stating that the organism *L. curvatus* is present in humans and in nature and occurs widely as part of the endogenous food matrices of fermented foods. Hansen states that *L. curvatus* DSM 18775 is non-pathogenic and non-toxigenic and is unable to produce biogenic amines. Hansen also reports that *L. curvatus* DSM 18775 is susceptible to antimicrobial agents tested and thus would not pose a risk of transferring antibiotic resistance to other microorganisms. Hansen notes that *L. curvatus* is recognized by the European Food Safety Authority (EFSA) with a Qualified Presumption of Safety.

Hansen provides data from its own studies demonstrating the antimicrobial effects on *Listeria monocytogenes* when applied to ready-to-eat meat and poultry products.

Based on the totality of the data and information described above, Hansen concludes that *L. curvatus* DSM 18775 is GRAS for its intended use in food.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 000760 we coordinated with the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture. Under the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act, FSIS determines the efficacy and suitability of ingredients used in meat, poultry, and egg products, and prescribes safe conditions of use. Suitability relates to the ingredient's effectiveness in performing its intended technical effect and the assurance that the ingredient's use will not result in products that are adulterated or misleading for consumers.

FSIS has completed its evaluation and has no objection to the use of *L. curvatus* DSM 18775 as an antimicrobial spray on ready-to-eat meat and poultry products at a use level that will result in a final concentration between 6.4 and 7.4 log CFU per gram of the finished product. Regarding labeling, any establishment which uses this product is required to label the ingredient as "culture," "bacterial culture," "lactic acid bacterial culture," or "lactic acid starter culture" in the ingredients statement of the products in which it is used in.

FSIS requested that we advise you to seek regulatory guidance from its Risk, Innovations, and Management Staff (RIMS) about the use of *L. curvatus* DSM 18775 on ready to eat meat and poultry products. You should direct such an inquiry to Dr. Melanie Abley, Acting Director, RIMS, Office of Policy and Program Development, FSIS by email at Melanie.Abley@fsis.usda.gov.

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 Hansen's notice concluding that *L. curvatus* DSM 18775 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. curvatus* DSM 18775. Accordingly, our response should not be construed to be a statement that foods containing *L. curvatus* DSM 18775, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Hansen provided, as well as other information available to FDA, we have no questions at this time regarding Hansen's conclusion that *L. curvatus* DSM 18775 is GRAS under its intended conditions of use. This letter is not an affirmation that *L. curvatus* DSM 18775 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 000760 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

**Dennis M.
Keefe -S**

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Dennis M. Keefe, Ph.D.

Director

Office of Food Additive Safety
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cc: Melanie Abley, Ph.D.
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