



Kevin O. Gillies
Kevin O. Gillies Consulting Services, LLC
1759 Grape St.
Denver, Colorado 80220

Re: GRAS Notice No. GRN 000872

Dear Mr. Gillies:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000872. We received the notice that you submitted on behalf of UAS Laboratories, LLC (UAS) on June 18, 2019 and filed it on September 3, 2019. UAS submitted an amendment to the notice on November 14, 2019 providing additional manufacturing specifications.

The subject of the notice is *Bifidobacterium animalis* subsp. *lactis* strain NCIMB 30334 (*B. animalis* NCIMB 30334) for use as an ingredient in foods generally (excluding infant formula and foods under the jurisdiction of the United States Department of Agriculture) at levels ranging from 10^9 to 10^{11} colony forming units (CFU)/serving. The notice informs us of UAS's view that these uses of *B. animalis* NCIMB 30334 are GRAS through scientific procedures.

UAS describes *B. animalis* NCIMB 30334 as an off-white to cream-colored powder. UAS states that *B. animalis* NCIMB 30334¹ is a Gram-positive, non-motile, non-spore forming, Y- or V-shaped bacterium, which is deposited in the strain collection of the National Collection of Industrial, Food and Marine Bacteria (NCIMB), Bucksburn Aberdeen, Scotland, UK. UAS discusses the results of phenotypic and genotypic characterization used to confirm the strain's identity. UAS states that *B. animalis* NCIMB 30334 is non-pathogenic and non-toxicogenic. Moreover, bifidobacteria occur naturally in food and in the digestive tract of humans and animals.

UAS describes the manufacture of *B. animalis* NCIMB 30334 by fermentation of a pure culture under controlled conditions. After fermentation, the medium is concentrated by centrifugation, cryoprotectants are added, and then frozen into pellets. The resulting pellets are lyophilized and milled to a powder. During production, the manufacturing process is monitored for contamination at three process control points, including the initial fermentation seed vial, the frozen pellet stage, and the final powdered product. UAS states that *B. animalis* NCIMB 30334 is manufactured with food-grade materials

¹ FDA notes that *B. animalis* subsp. *lactis* 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.

that comply with FDA regulations for such use under current good manufacturing practices. UAS states that no components of the manufacturing process are allergens or are derived from allergenic sources.

UAS provides specifications for *B. animalis* NCIMB 30334 that include a minimum of CFU (no less than 200 billion CFU/g) and limits for other microorganisms, including non-lactics (< 5,000 CFU/g), *Escherichia coli* (absent in 10 g), *Staphylococcus aureus* (absent in 10 g), *Salmonella* serovars (absent in 10 g), *Enterococcus* (< 100/g), *Listeria* species (absent in 25 g), *Enterobacteriaceae* (< 100 CFU/g), coliforms (< 100 CFU/g), and lead (< 1 ppm (mg/kg)), arsenic (< 1 ppm), cadmium (< 0.3 ppm) and mercury (< 0.05 ppm). UAS 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.

UAS intends to use *B. animalis* NCIMB 30334 in foods generally (excluding infant formula and foods under the jurisdiction of the United States Department of Agriculture) at levels from 10⁹ to 10¹¹ CFU/serving. UAS states that the use of *B. animalis* NCIMB 30334 will replace other *B. animalis* subsp. *lactis* strains already present in foods and therefore, the dietary exposure from the intended uses will not materially increase the dietary exposure to *B. animalis* subsp. *lactis*.

UAS states that the addition of *B. animalis* NCIMB 30334 is limited to foods that will sustain the live culture through the shelf-life of the product. The inclusion rate of the strain is limited by the upper limit of fermentation and drying technology to produce cell concentrates.

UAS discusses the long history of safe use of LAB in foods and how *B. animalis* subsp. *lactis* has been safely used in fermented foods. UAS cites publications that support the safe consumption of *B. animalis* subsp. *lactis*, including peer-reviewed scientific journals, governmental reviews, and product approvals. Additionally, UAS describes published clinical trials in which infants, children and adults were fed *B. animalis* NCIMB 30334 and states that no significant adverse effects on participants were noted in any of these studies.

Based on the totality of evidence, UAS concludes that *B. animalis* NCIMB 30334 is GRAS for its intended use.

Standards of Identity

In the notice, UAS states its intention to use *B. animalis* NCIMB 30334 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* NCIMB 30334 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(II) of the FD&C Act

Section 301(II) 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(II)(1)-(4) applies. In our evaluation of UAS's notice concluding that *B. animalis* NCIMB 30334 is GRAS under its intended conditions of use, we did not consider whether section 301(II) or any of its exemptions apply to foods containing *B. animalis* NCIMB 30334. Accordingly, our response should not be construed to be a statement that foods containing *B. animalis* NCIMB 30334, if introduced or delivered for introduction into interstate commerce, would not violate section 301(II).

Conclusions

Based on the information that UAS provided, as well as other information available to FDA, we have no questions at this time regarding UAS's conclusion that *B. animalis* NCIMB 30334 is GRAS under its intended conditions of use. This letter is not an affirmation that *B. animalis* NCIMB 30334 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 000872 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 16:01:01
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Susan Carlson, Ph.D.
Director
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