Mitzi Ng Clark
Keller and Heckman LLP
Three Embarcadero Center, Suite 1420
San Francisco, CA 94111

Re: GRAS Notice No. GRN 001158

Dear Ms. Clark:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001158. We received the notice that you submitted on behalf of Scott Laboratories, Inc. (Scott Labs) on July 20, 2023, and filed it on December 1, 2023. Scott Labs submitted amendments to the notice on November 9, 2023, March 8, 2024, and April 15, 2024, that clarified the manufacturing process, specifications, intended uses, dietary exposure, and safety information.

The subject of the notice is *Lactiplantibacillus plantarum* DSM 34613 for use at a maximum level of 1.5 x 10^8 colony forming units (CFU)/g in wine production to induce malolactic fermentation and to prevent the growth of microorganisms that could cause off flavors in the finished product.[1] The notice informs us of Scott Labs' view that these uses of *L. plantarum* DSM 34613 are GRAS through scientific procedures.

Scott Labs describes *L. plantarum* DSM 34613 as a white to beige colored powder and states that *L. plantarum* DSM 34613 is a non-pathogenic, non-toxigenic, Gram-positive, rod-shaped, non-spore forming bacterium. Scott Labs notes that the strain was isolated from an Italian red wine fermentation and has been deposited in the Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ) with the depository number DSM 34613. Scott Labs describes the taxonomic analysis for the identity of the strain. Scott Labs also discusses the results of *de novo* genomic sequence analyses and states that the strain is not genetically engineered. Scott Labs discusses the results of phenotypic and genotypic characterization performed on *L. plantarum* DSM 34613 and concludes that the strain neither carries antimicrobial resistance genes in its genome nor produces any virulence factors and biogenic amines.

Scott Labs describes the manufacture of *L. plantarum* DSM 34613 by fermentation of a pure culture under controlled conditions. After fermentation, the cells are separated from the fermentation medium and concentrated by centrifugation,

[1] Scott Labs states that *L. plantarum* DSM 34613 is not intended for use in infant formula, products under the jurisdiction of the United States Department of Agriculture, or in foods where standards of identity preclude its use.

freeze-dried, ground, and mixed with a maltodextrin to yield the final product. Scott Labs states that *L. plantarum* DSM 34613 is manufactured in accordance with good manufacturing practices and that all raw materials and processing aids used in the manufacture of *L. plantarum* DSM 34613 are permitted for their respective uses under U.S. regulations or are GRAS for their intended use. Scott Labs states that *L. plantarum* DSM 34613 is produced without the materials that account for the majority of human food allergens.

Scott Labs provides specifications for *L. plantarum* DSM 34613 that include total cell count (> 1 x 10^{11} CFU/g), dry matter (> 92 %) and limits for microorganisms, including *Escherichia coli* (absent in 1 g), *Salmonella* serovars (absent in 25 g), *Staphylococcus aureus* (absent in 1 g), and heavy metals, including lead (< 0.1 mg/kg). Scott Labs provides the results from the analyses of three non-consecutive batches to demonstrate that *L. plantarum* DSM 34613 can be manufactured to meet these specifications.

Scott Labs estimates an eaters-only dietary exposure to *L. plantarum* DSM 34613 using food consumption data from the 2015-2018 National Health and Nutrition Examination Survey (NHANES), the maximum use level of 1.5 x 10^{8} CFU/g in wine, and the total cell count of 1 x 10^{11} CFU/g to be 2.4 x 10^{10} CFU/person (p)/d (or 0.24 g/p/d) at the mean and 4.7 x 10^{10} CFU/p/d (0.47 g/p/d) at the 90th percentile for the U.S. population aged 21 years and older.

Scott Labs discusses data and information used to support the safety of *L. plantarum* DSM 34613, including a history of safe use of the *L. plantarum* species in fermented foods. Scott Labs incorporates into their notice and provides summaries of the information pertaining to the safety of the *L. plantarum* strains discussed in GRNs 000685, 000722, 000847, 000946, and 000953.[2] Scott Labs discusses opportunistic infection caused by certain *L. plantarum* strains and states that the infection is extremely rare, generally occurs in very ill or immunocompromised patients, and is not linked to its consumption in food or as a food ingredient. Scott Labs summarizes published animal and human studies on *L. plantarum* consumption and concludes that there are no indications of safety concerns.

Based on the totality of the data and information, Scott Labs concludes that *L. plantarum* DSM 34613 is GRAS for its intended use.

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

[2] *L. plantarum* strains 299v, Lp-115, ECGC13110402, DSM 33452 and individual or combined strains CECT 7527, CECT 7528, and CECT 7529 were the subjects of GRNs 000685, 000722, 000847, 000946, and 000953, respectively. We evaluated these notices and responded in letters dated October 31, 2017, February 16, 2018, September 30, 2019, February 5, 2021, and February 5, 2021, respectively, stating that we had no questions at the time regarding the notifiers' GRAS conclusions.

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. plantarum* DSM 34613 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 Scott Labs' notice concluding that *L. plantarum* DSM 34613 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. plantarum* DSM 34613. Accordingly, our response should not be construed to be a statement that foods containing *L. plantarum* DSM 34613, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Scott Labs provided, as well as other information available to FDA, we have no questions at this time regarding Scott Labs' conclusion that *L. plantarum* DSM 34613 is GRAS under its intended conditions of use. This letter is not an affirmation that *L. plantarum* DSM 34613 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 001158 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2024.05.08 17:30:50 -04'00'

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