U.S. FOOD & DRUG ADMINISTRATION
Human Foods Program

Marie-Eve Boyte
NutraPharma Consulting Services Inc.
32 Therese
Sainte-Anne-des-Plaines, J5N 4B3
CANADA

Re: GRAS Notice No. GRN 001245

Dear Ms. Boyte:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001245. We received NORDWISE BioTech OÜ (NORDWISE)'s GRAS notice on November 28, 2023, and filed it on March 21, 2025. NORDWISE submitted amendments to the notice on May 23, 2025, June 17, 2025, July 1, 2025, July 9, 2025, and July 14, 2025, that clarified the manufacturing process, specifications, intended uses, stability, dietary exposure, and safety information.

The subject of the notice is *Lactiplantibacillus plantarum* DSM 21379 (*L. plantarum* DSM 21379) for use as an ingredient in conventional foods at levels up to 5 x 10^9 colony forming units (CFU)/serving (excluding use in infant formula, infant foods, alcoholic beverages, and products under the jurisdiction of the United States Department of Agriculture). The notice informs us of NORDWISE's view that these uses of *L. plantarum* DSM 21379 are GRAS through scientific procedures.

NORDWISE describes *L. plantarum* DSM 21379 as a white to beige colored powder and states that *L. plantarum* DSM 21379 is a non-pathogenic, non-toxigenic, Gram-positive, rod-shaped, anaerobic, non-spore-forming, non-motile bacterium. NORDWISE notes that the strain was isolated from a one-year-old healthy child in 1995 and has been deposited in the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) culture collection with the depository number DSM 21379. NORDWISE describes the taxonomic analysis for the identity of the strain. NORDWISE also discusses the results of phenotypic and genomic analyses to confirm the strain's identity and states that the strain is not genetically modified. NORDWISE discusses the results of phenotypic and genotypic characterization performed on *L. plantarum* DSM 21379 and states that *L. plantarum* DSM 21379 has no genes for pathogenicity, virulence factors, toxins, and antibiotic resistance. NORDWISE states that the amounts of biogenic amines produced by the bacterium do not pose a threat to human health.

NORDWISE describes the manufacture of *L. plantarum* DSM 21379 by fermentation of a pure culture under controlled conditions. After fermentation, the biomass is collected by centrifugation. The collected bacterial cells are mixed with cryoprotectants, lyophilized, milled, and sieved. The resulting powder is mixed with

excipients to obtain the final product. NORDWISE states that *L. plantarum* DSM 21379 is manufactured under current good manufacturing practices and that all raw materials and processing aids are food grade and are used in accordance with applicable U.S. regulations, are GRAS for their intended use, or are the subject of an effective food contact notification. NORDWISE states that the raw materials used in the manufacturing process are not derived from major allergens and *L. plantarum* DSM 21379 does not contain any major allergens.

NORDWISE provides specifications for *L. plantarum* DSM 21379 that include total bacterial count ($\geq 3.5 \times 10^{11}$ CFU/g), and limits for heavy metals, including lead (< 0.1 mg/kg) and microorganisms, including *Escherichia coli* (not detected in 1 g), *Salmonella* spp. (not detected in 25 g), and *Listeria monocytogenes* (not detected in 25 g). NORDWISE provides results from the analyses of three non-consecutive batches to demonstrate that *L. plantarum* DSM 21379 can be manufactured to meet these specifications. NORDWISE states that *L. plantarum* DSM 21379 is stable for 24 months when stored at 4 or 20 °C in aluminum foil pouches.

NORDWISE estimates the dietary exposure to *L. plantarum* DSM 21379 from the intended uses to be 1×10^{11} CFU/person/d based on the assumption that an individual consumes 20 servings of food a day and that all servings of food contain *L. plantarum* DSM 21379 at the maximum use level of 5×10^{9} CFU/serving. NORDWISE states that the ingredient is substitutional for other strains of *L. plantarum* and therefore, there will be no increase in the cumulative dietary exposure to *L. plantarum* from the intended uses of *L. plantarum* DSM 21379.

NORDWISE discusses data and information used to support the safety of *L. plantarum* DSM 21379, including a history of safe use of *L. plantarum* in various fermented foods. NORDWISE incorporates into their notice and provides summaries of the information pertaining to the safety of live *L. plantarum* in food discussed in GRNs 000685, 000722, 000847, 000946, 000953, and 001113.[1] NORDWISE states that the reported opportunistic infection cases caused by certain *L. plantarum* strains only occurred in patients who were either immunocompromised or had predisposed conditions such as cancer. NORDWISE summarizes a published toxicology study and human trials on *L. plantarum* DSM 21379 and states that no adverse effects were observed at the test doses in these studies.

Based on the totality of the data and information, NORDWISE concludes that *L. plantarum* DSM 21379 is GRAS for its intended use.

[1] The subjects of GRNs 000685, 000722, 000847, 000946, 000953, and 001113 are various *L. plantarum* strains. We evaluated these notices and responded in letters dated October 31, 2017, February 16, 2018, September 30, 2019, February 5, 2021, February 5, 2021 and July 20, 2023, respectively, stating that we had no questions at the time regarding the notifiers' GRAS conclusions.

Standards of Identity

In the notice, NORDWISE states its intention to use *L. plantarum* DSM 21379 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, & 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 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 21379 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 Nutrition Center of Excellence. The Office of Pre-Market 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 NORDWISE's notice concluding that *L. plantarum* DSM 21379 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 21379. Accordingly, our response should not be construed to be a statement that foods containing *L. plantarum* DSM 21379, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that NORDWISE provided, as well as other information available to FDA, we have no questions at this time regarding NORDWISE's conclusion that *L. plantarum* DSM 21379 is GRAS under its intended conditions of use. This letter is not an affirmation that *L. plantarum* DSM 21379 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 001245 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
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Susan J. Carlson, Ph.D.
Director
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