Kayla Preece, N.D.
AIBMR Life Sciences, Inc.
2800 E. Madison Street
Suite 202
Seattle, WA 98112

Re: GRAS Notice No. GRN 000906

Dear Dr. Preece:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000906. We received the notice that you submitted on behalf of Société d'Exploitation de Produits pour les Industries Chimiques (SEPPIC) on January 30, 2020, and filed it on March 9, 2020. SEPPIC submitted amendments to the notice on May 19, 2020, June 12, 2020, July 14, 2020, and August 21, 2020, that clarified aspects of the intended use, manufacturing process, specifications, dietary exposure, and safety studies.

The subject of the notice is wheat seed polar lipids (WSPL) for use as an ingredient in fruit and vegetable juice drinks at a level of 0.1 mg/g.[1] The notice informs us of SEPPIC's view that this use of WSPL is GRAS through scientific procedures.

Our use of the term, "wheat seed polar lipids," in this letter is not our recommendation of that term as an appropriate common or usual name for declaring the substance in accordance with FDA's labeling requirements. Under 21 CFR 101.4, each ingredient must be declared by its common or usual name. In addition, 21 CFR 102.5 outlines general principles to use when establishing common or usual names for nonstandardized foods. Issues associated with labeling and the common or usual name of a food ingredient 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 (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "wheat seed polar lipids."

SEPPIC provides information on the source, identity, and composition of WSPL. SEPPIC states that WSPL is produced from the seed of wheat (*Triticum aestivum*) and is described as a beige to light yellow powder containing ≥90% polar lipids (≥50% sphingolipids, ≥40% digalactosyldiacylglycerol (DGDG)), and ~5% triglycerides.

[1] In the June 12, 2020, amendment, SEPPIC states that the intended use of WSPL is now limited to fruit and vegetable juice drinks. In the August 21, 2020, amendment, SEPPIC clarifies that WSPL uses do not include categories where standards of identity apply.

SEPPIC describes the method of manufacture of WSPL, stating that all materials used in the process are food grade and that WSPL is manufactured according to current good manufacturing practices. According to SEPPIC, purified wheat flour is extracted with ethanol by mechanical stirring. Solids are separated by filtration under vacuum and the filtrate containing the lipids is concentrated under vacuum. The resulting oil is dispersed in acetone and then the acetone fraction containing triglycerides is separated by decantation. The remaining fraction is filtered under vacuum to yield a polar lipid paste. The paste is dried under vacuum to evaporate acetone, and the resulting coarse powder is further dried, crushed, and sieved to yield the final WSPL powder.

SEPPIC provides specifications for WSPL that include total sphingolipids (≥50%, including glycosphingolipids), DGDG (≥40%), total nitrogen linked with polar lipids (≥0.6%), acid value (<15 mg potassium hydroxide/g), peroxide value (<10 mEq/kg), loss on drying (<5%), dry extract (>95%), residual gluten (<20 mg/kg), and limits for arsenic, cadmium, mercury (each ≤0.1 mg/kg), lead (≤0.2 mg/kg), residual solvents (acetone <30 mg/kg and ethanol <5000 mg/kg), and microorganisms. SEPPIC provides the results of the analysis of three nonconsecutive batches to demonstrate that WSPL can be manufactured to meet the specifications.

SEPPIC estimates the dietary exposure to WSPL based on the intended use and food consumption data from the What We Eat in America component of the 2013-2014 National Health and Nutrition Examination Survey. SEPPIC estimates dietary exposure to WSPL for the U.S. population (consumers ages 2 years and older) to be 20 mg/person (p)/day (d) (0.4 mg/kg body weight (bw)/d) at the mean and 31 mg/p/d (0.7 mg/kg bw/d) at the 90th percentile. SEPPIC notes that based on the specifications established for WSPL, the 90th percentile dietary exposure to sphingolipids and DGDG is estimated to be 15 mg/p/d and 12 mg/p/d, respectively.

SEPPIC discusses the safety of the intended use of WSPL, which is enriched in sphingolipids and DGDG. SEPPIC states that sphingolipids and DGDG are commonly found in many foods, such as wheat, eggs, milk, cheese, apples, barley, and pumpkin, and have been shown to be safely and regularly consumed in the U.S. SEPPIC provides publicly available information showing that consumers frequently consume the same levels of sphingolipids and DGDG that would result from the intended use of WSPL. The metabolism and safety of sphingolipids and DGDG at this level of consumption are well established and generally recognized in the scientific community.

SEPPIC further corroborates the safety of the intended use of WSPL by discussing several unpublished studies, including a 28-day oral toxicity study and several genotoxicity studies (i.e., bacterial reverse mutation, *in vitro* mammalian chromosomal aberration, and *in vivo* mammalian micronucleus tests). SEPPIC states that these studies did not show any adverse effects or evidence of genotoxicity.

Based on the totality of the data and information, SEPPIC concludes that WSPL 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 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 WSPL 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 ONFL. OFAS 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. WSPL derived from wheat seed requires labeling under the FD&C Act because it contains protein derived from wheat.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In the notice, SEPPIC describes WSPL as a beige to light yellow powder. As such, the use of WSPL in food products may constitute a color additive use under section 201(t)(1) of the FD&C Act and FDA's implementing regulations in 21 CFR Part 70. Under section 201(t)(1) and 21 CFR 70.3(f), a color additive is a material that is a dye, pigment, or other substance made by a synthetic process or similar artifice, or is extracted, isolated, or otherwise derived from a vegetable, animal, mineral, or other source. Under 21 CFR 70.3(g), a material that otherwise meets the definition of a color additive can be exempt from that definition if it is used (or is intended to be used) solely for a purpose or purposes other than coloring. Our response to GRN 000906 is not an approval for use as a color additive nor is it a finding of the Secretary of the Department of Health and Human Services within the meaning of section 721(b)(4) of the FD&C Act. Questions about color additives should be directed to the Division of Food Ingredients in OFAS.

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

Conclusions

Based on the information that SEPPIC provided, as well as other information available to FDA, we have no questions at this time regarding SEPPIC's conclusion that WSPL is GRAS under its intended conditions of use. This letter is not an affirmation that WSPL 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 000906 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2020.08.24 09:51:30 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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