Marisa O. Rihner
Senior Managing Consultant
SafeBridge Regulatory & Life Sciences Group
154 Hansen Road, Suite 201
Charlottesville, VA 22911

Re: GRAS Notice No. GRN 001073

Dear Ms. Rihner:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001073. We received the notice that you submitted on behalf of AgriFiber Solutions, LLC (AgriFiber) on June 7, 2022, and filed it on August 31, 2022. AgriFiber submitted amendments to the notice on November 15, 2022, February 9, 2023, and March 21, 2023, that reduced the specification limit for yeasts and molds, included limits for heavy metals in the specifications and provided additional batch analyses, clarified maximum use levels for certain food categories, discussed additional safety information, provided an updated allergen statement, and updated the point of contact.

The subject of the notice is corn bran arabinoxylan for use as a formulation aid (binder, gelling agent, texturizer, stabilizer, thickener and/or emulsifier) and a source of dietary fiber in various foods at maximum use levels as specified in Table 1 (below). The notice informs us of AgriFiber's view that these uses of corn bran arabinoxylan are GRAS through scientific procedures.

Table 1. Food uses of corn bran arabinoxylan and corresponding maximum use levels

Food uses	**Maximum use level (%)**
Baked goods and baking mixes	3.0-12.7 (54.3 in croutons)
Fruit juice drinks and nectars (including powdered concentrates), fruit drinks, fruit flavored drinks, "energy" drinks, sports drinks, and fluid replacement beverages	1.0
Cheese (including cheese spreads and imitation cheese)	0.75
Candy (chocolate and non-chocolate) and chewing gum	1.0
Coatings and breadings for meat, poultry, fish, and vegetables	2.0
Custards, puddings, and gelatin desserts	3.0
Cream, cream substitutes, sour cream, and whipped cream	1.5

Food uses	**Maximum use level (%)**
Dips, salad dressings (including mayonnaise), sauces, and gravies	3.0
Egg substitute omelets, scrambled, or fried; egg casseroles, souffle, quiches, and egg foo young	1.5
Fillings for baked goods	3.0
Flavored fluid milk and milk drinks	1.5
Ice cream and ice cream novelties; frozen yogurt, gelato, and sherbet	1.0
Cereal and nutrition bars	9.5
Pasta and noodles, cooked	2.7
Processed fruits and fruits juices; processed vegetables and vegetable juices (except legumes)	1.0
Coffee and tea	1.5
Plant-based dairy alternatives (milk, desserts, and yogurt alternatives)	1.5
Plant-based meat alternatives	2.0
Nutritional beverages for adults, ready-to-drink	1.6
Cereals, ready-to-eat (RTE): biscuit-type, high fiber, and puffed	6.3, 9.5, and 25.3, respectively
Smoothies and grain drinks	1.6
Snack foods (chips, popcorn, crackers, and pretzels/snack mix)	12.7
Soups (RTE, condensed, and dry)	3.0
Yogurt	3.0

Our use of the term, “corn bran arabinoxylan” 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.

AgriFiber provides information about the identity and composition of corn bran arabinoxylan. AgriFiber describes corn bran arabinoxylan as a tan to brown powder obtained from corn bran and containing 74-90% dietary fiber (arabinoxylan). Arabinoxylan is a polysaccharide consisting of a xylose backbone with arabinose at the branching points and galactose in the side chains. AgriFiber states that corn bran arabinoxylan primarily contains water-soluble arabinoxylan with an average degree of polymerization of 2,500. AgriFiber notes that arabinoxylans are abundant in the cell walls of various cereal grains.

AgriFiber states that the manufacturing process of corn bran arabinoxylan starts by

adding hot water to corn bran to form a slurry and adjusting the pH to 5-7.5. α-Amylase is added to hydrolyze the starch, followed by sodium hydroxide, and the mixture is allowed to react until a designated viscosity is reached. The solids are separated and washed with water. The remaining supernatant and water washes are combined, and the pH is adjusted to approximately neutral. The solution is further processed by the addition of endo-β-1,4-xylanase[1] to achieve target hydrolysis. The solids are separated and the supernatant is subjected to ultra- and diafiltration processes. The resulting concentrate is then dried, milled, and sieved to yield the final product. AgriFiber states corn bran arabinoxylan is manufactured in accordance with good manufacturing practices and that all raw materials and processing aids are food grade and are used in accordance with applicable U.S. regulations or have been previously determined to be GRAS for their intended use.

AgriFiber provides specifications for corn bran arabinoxylan that include total dietary fiber (arabinoxylan) (74-90%), limits for ash (<6%), moisture (<9%), lead, arsenic, cadmium, and mercury (each <0.1 mg/kg), and microorganisms. AgriFiber provides results from the analyses of three non-consecutive batches to demonstrate that corn bran arabinoxylan can be manufactured to meet these specifications. AgriFiber states that corn bran arabinoxylan is expected to be stable for at least two years when stored in a sealed container under cool and dry conditions.

AgriFiber estimates the dietary exposure to corn bran arabinoxylan from its intended uses using food consumption data from the 2015-2018 National Health and Nutrition Examination Survey (NHANES). AgriFiber estimates eaters-only dietary exposure to corn bran arabinoxylan to be 21.6 g/person (p)/d (0.37 g/kg body weight (bw)/d) at the mean and 35.3 g/p/d (0.73 g/kg bw/d) at the 90th percentile for the U.S. population aged 1 year and older.

To estimate dietary exposure to dietary fiber, AgriFiber applies the maximum specification limit for total dietary fiber (arabinoxylan) of 90% to the dietary exposure estimates for the intended uses of corn bran arabinoxylan. For the U.S. population aged 1 year and older, the eaters-only dietary exposure to dietary fiber from the intended uses of corn bran arabinoxylan is estimated to be 19.4 g/p/d (0.33 mg/kg bw/d) at the mean and 31.8 g/p/d (0.66 mg/kg bw/d) at the 90th percentile. AgriFiber states that the intended uses of corn bran arabinoxylan will be substitutional for other dietary fiber ingredients and concludes that the cumulative dietary exposure to dietary fiber is not expected to increase.

AgriFiber discusses the data and information supporting the safety of corn bran arabinoxylan. AgriFiber notes that the structure of corn bran arabinoxylan is not a substrate for human digestive enzymes and that corn bran arabinoxylan reaches the proximal colon largely undigested. In the colon, corn bran arabinoxylan is expected to be degraded by microbiota releasing arabinoxylan oligosaccharides (AXOS) and xylooligosaccharides (XOS) which are expected to undergo additional fermentation.

[1] AgriFiber states that endo-β-1,4-xylanase enzyme preparation is the subject of GRN 000628. We evaluated GRN 000628 and responded in a letter dated September 14, 2016, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

AgriFiber states that while traditional toxicology studies have not been performed on corn bran arabinoxylan, published safety studies have been performed on structurally comparable arabinoxylans and their hydrolysis products such as AXOS and XOS. AgriFiber compares the test articles in published studies to its corn bran arabinoxylan and notes that corn bran arabinoxylan contains the same carbohydrate and polyphenolic moieties present in the test articles subject to toxicological evaluation. AgriFiber discusses published safety data including acute, subchronic, teratogenicity, and genotoxicity studies using arabinoxylan isolated from Ispaghula husk and sugarcane bagasse; wheat bran AXOS; and XOS from corn cobs as test articles which demonstrated no treatment-related adverse effects or mutagenicity. AgriFiber states that while the branching structure between fibers may impact the rate or pattern of microbial fermentation, it would not impact safety. Thus, AgriFiber concludes on the basis of compositional similarity and lack of differences that would impact safety, that published toxicological data for arabinoxylan, AXOS, and XOS, including NOAELs of at least 2,500 mg/kg bw/d are relevant to corn bran arabinoxylan.

AgriFiber discusses a published clinical study in which corn bran arabinoxylan consumed by adults was demonstrated to be safe and well tolerated. AgriFiber includes summaries of additional clinical studies with arabinoxylans, AXOS, XOS, or AXOS-rich wheat bran extract in adults and children to support the safe use of corn bran arabinoxylan. AgriFiber states that corn bran arabinoxylan is free of the nine major allergens and the potential for an allergenic response is lower than that associated with the consumption of corn. AgriFiber addresses the presence of antinutrients in its ingredient and states that levels of antinutrients are negligible and do not raise safety concerns for the intended use.

Based on the totality of data and information described above, AgriFiber concludes that corn bran arabinoxylan is generally recognized as safe for its intended uses.

Standards of Identity

In the notice, AgriFiber states its intention to use corn bran arabinoxylan 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 corn bran arabinoxylan 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. Office of Food Additive Safety (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.[2]

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. AgriFiber notes that corn bran arabinoxylan is a tan to brown powder. As such, the use of corn bran arabinoxylan 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 001073 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 the 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 AgriFiber's notice concluding that corn bran arabinoxylan 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 corn bran arabinoxylan. Accordingly, our response should not be construed to be a statement that foods containing corn bran arabinoxylan, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that AgriFiber provided, as well as other information available to FDA, we have no questions at this time regarding AgriFiber's conclusion that corn bran arabinoxylan is GRAS under its intended conditions of use. This letter is not an affirmation that corn bran arabinoxylan is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient

[2] The definition of "dietary fiber" in 21 CFR 101.9(c)(6)(i) was added by FDA's final rule revising the nutrition and supplement facts labels (81 FR 33742, May 27, 2016). This final rule, among other things, defines dietary fiber as non-digestible soluble and insoluble carbohydrates (with three or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with three or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health.

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 001073 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2023.03.21 17:43:30 -04'00'

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