



Bryan Tunland
 Tunland and Associates, LLC
 10306 74th Street, NE
 Otsego, Minnesota 55301

Re: GRAS Notice No. GRN 001019

Dear Mr. Tunland:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001019. We received the notice that you submitted on behalf of Inulina Y Miel de Agave S.A. de C.V. (IMAG) on January 11, 2021 and filed it on November 30, 2021. IMAG submitted amendments to the notice on April 18, 2022, November 10, 2022, November 14, 2022, and November 16, 2022, providing additional information regarding the composition, manufacturing process, specifications for heavy metals, and maximum use levels.

The subject of the notice is agave mixed fructans from *Agave tequilana* Weber var. *azul* (agave mixed fructans) for use as a bulking agent, texturizing agent, or source of reduced energy carbohydrate as a sugar replacer, fat replacer, and/or texture modifier in select foods and use levels as specified in Table 1.¹ The notice informs us of IMAG’s view that these uses of agave mixed fructans are GRAS through scientific procedures.

Table 1. Intended food categories and use levels for agave mixed fructans

Food Category ^a	Agave mixed fructans maximum use level (% or g/serving)	Agave mixed fructans maximum use level (mL or g/serving) ^b
Acidophilus milk (fermented milk beverages)	2	4.8 mL
Bars: all types, including breakfast bars, granola bars, energy bars, and diet/meal replacement bars	10	4 to 7 g
Baby foods and beverages: all types, including ready-to-eat (RTE) and dry baby food (excluding infant formula)	1 g/serving	7 to 60 g
Breakfast cereals, all types of RTE	5 g/serving	0.75 to 3 g
Beverages, juices, and juice drinks: fruit juices and drinks, including ades, cocktails, cider, nectar, and	1.5	5.4 mL

¹ IMAG states that agave mixed fructans is not intended for use in infant formula and meat and poultry products under the jurisdiction of the U.S. Department of Agriculture.

Food Category ^a	Agave mixed fructans maximum use level (% or g/serving)	Agave mixed fructans maximum use level (mL or g/serving) ^b
smoothies, vegetable juices, flavored waters, soy drinks, gelatin drinks, and lightly carbonated beverages, including ready-to-drink (RTD) beverages and dry mixes ^c (excludes citrus juices and highly carbonated beverages)		
Beverages, meal replacement and meal supplement including RTD and dry mixes ^c	5	12 mL
Beverages, milk-based: dairy-based beverages, including RTD and dry mixes ^c	1	2.4 mL
Biscuits: reduced calorie (energy)	6	3.3 g
Breads: yeast leavened breads, rolls and buns	0.5	0.25 g
Breads: reduced calorie (energy), fiber enriched, or with added calcium (includes muffins and quick breads)	6	3.3 g
Cakes, lite: fat free/reduced fat/ reduced sugar/reduced calorie baked goods (includes cakes, brownies, and pastries)	5	2 to 6.25 g
Candy, hard dietetic	15	8.25 g
Candy, soft dietetic	5	1.5 g
Cheese (cream type)	5	1.5 g
Cheese (processed cheese and cheese products)	5	1.5 g
Cheese used in pasta fillings	5	2.75 g
Condiments: including catsup and mustard	5	0.75 mL
Cookies, reduced calorie (energy), reduced sugar	8	2.4 g
Crackers: snack-type, including savory, sandwich, whole grain (excluding plain crackers such as saltines, matzo crackers or oyster crackers)	6	1.8 g
Dessert toppings, lite: fat free/reduced fat marshmallow cream, non-dairy whipped toppings	6	1.8 mL
Dessert toppings (excluding whipped toppings)	2	0.6 mL
French fry coatings ^d	1.7	0.51 g
Frozen dairy desserts, lite: fat free/reduced fat/ reduced sugar/ reduced energy (calorie) ice creams and dairy-based frozen desserts, including novelties and frozen yogurt	8	12.88 mL
Icings and glazes, fat free/reduced fat/ reduced sugar/reduced calorie	5	1.5 g
Jams and jellies, fat free/reduced fat/ reduced sugar/reduced calorie	2	0.4 g
Mousse, reduced fat/reduced calorie	3	3.6 mL

Food Category ^a	Agave mixed fructans maximum use level (% or g/serving)	Agave mixed fructans maximum use level (mL or g/serving) ^b
Pasta, fresh such as spaghetti, fettuccini, linguini, tortellini, ravioli or lasagna (excluding noodles)	4	5.6 g
Pasta, precooked macaroni	4	5.6 g
Pizza crust	5	2.75 g
Potatoes, mashed: prepared or frozen (excluding dry mix types)	3	4.2 g
Pretzels, soft	5	1.5 g
Salad dressings, lite: fat free/reduced fat/reduced calorie, including mayonnaise salad dressings and mayonnaise-type dressings	5	0.75 to 1.5 g
Sauces and gravies: entrée, dipping and condiment sauces such as Alfredo, BBQ, cheese, clam Hollandaise, pasta, pizza, soy, sweet and sour and white sauces, salsa, and gravies (excluding tomato sauce and paste)	2	0.6 mL
Snack chips, fat free/reduced fat, including chips and extruded snacks	3	0.9 g
Soups, dry	3	7.35 g
Spreads, fat free/reduced fat margarines and margarine-like table spreads	10	1.5 mL
Surimi, imitation crab and reconstructed seafood	3	1.65 g
Syrups, lite: reduced calorie, including flavored pancake syrups	2	0.6 mL
Tortillas, reduced fat	3	1.65 g
Vegetarian patties/crumbles	2	1.7 g
Yogurt, fat free/reduced fat	3	5.1 g

^a IMAG notes that the food uses and use levels are based on uses and use levels from GRN 000118 and GRN 000854.

^b Maximum use level of agave mixed fructans is calculated based on serving sizes corresponding to reference amounts commonly consumed as set forth in 21 CFR 101.12 and maximum use level percentage.

^c IMAG states that maximum use levels are based on g of agave mixed fructans per 100 g prepared beverage or sauce.

^d IMAG notes that the maximum use level is given per 100 g of consumed coated French fries.

Our use of the term, “agave mixed fructans,” 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 “agave mixed fructans.”

IMAG provides information on the source, identity, and composition of agave mixed fructans. IMAG states that agave mixed fructans are extracted from the pines or stems of mature *A. tequilana* Weber var. *azul*. Agave mixed fructans are oligo- and polysaccharides that consist of fructose units joined by $\beta(2-1)$ and $\beta(2-6)$ linkages and contain one internally or one terminally linked glucose unit per molecule. IMAG describes agave mixed fructans as a white to slight beige powder or a white to slightly amber liquid with a mean degree of polymerization (DP) of 11.9 ranging from 2 to 70 fructose units. IMAG notes that agave mixed fructans contain 98-100% total carbohydrates on a dry basis which include $\geq 92\%$ agave mixed fructans, and 8% of mono- and disaccharides that consist of primarily fructose, glucose, and sucrose.

IMAG describes the method of manufacture of agave mixed fructans. Harvested agave pines are rinsed with water, milled, and extracted with water at temperatures between 30 °C and 50 °C to yield raw agave juice. After removing the extracted and milled pines, the raw agave juice is transferred to a settling tank to allow proteins and pectic substances to precipitate. The precipitate-containing juice undergoes a series of filtration steps to remove particulate matter, microorganisms, raphides of calcium oxalate, and turbidity. The resulting juice is sterilized at 104 °C, concentrated to a dry matter (DM) content of 68°-72° Brix to give the liquid form of agave mixed fructans. The powder form is produced by concentrating the sterilized juice to a DM of 40 to 45% by evaporation followed by spray drying to greater than 95% DM. IMAG states that agave mixed fructans are manufactured under current good manufacturing practices using food-grade starting materials and processing aids, which are used in accordance with U.S. regulations.

IMAG provides the specifications for the liquid and powder forms of agave mixed fructans, which include: a minimum content of total carbohydrates ($\geq 99\%$, DM basis) and agave mixed fructans ($\geq 92\%$, DM basis), fructose ($\leq 6\%$, DM basis), glucose ($\leq 2\%$, DM basis), sucrose ($\leq 2\%$, DM basis), ash ($\leq 0.3\%$, DM basis), moisture (28-32% (liquid), $\leq 4\%$ (powder)), pH (≥ 5.5 (liquid), > 5.5 (powder)), Brix degrees for the liquid (68-72° Brix), lead (< 0.015 mg/kg), mercury (0.003 mg/kg), cadmium (< 0.001 mg/kg), arsenic (< 0.020 mg/kg), and limits for mycotoxins and microorganisms. IMAG provides results from 4 non-consecutive batches to demonstrate that agave mixed fructans meet the stated specifications. Based on stability data for the powder form, IMAG states that agave mixed fructans are stable for at least three years.

IMAG states that the use of agave mixed fructans is intended to provide an alternative source of nondigestible fructans. IMAG notes that the intended use is substitutional for the intended uses in GRN 000854² and therefore, there will not be an increase in the overall dietary exposure to agave mixed fructans. IMAG incorporates the average and 90th percentile dietary exposure estimates from GRN 000854 of 10.1 g/p/d and 19.2

² The subject of GRN 000854 is agave mixed fructans from *Agave tequilana*. We evaluated this notice and responded in a letter dated August 10, 2012, stating that we had no questions at the time regarding the notifier’s GRAS conclusion.

g/p/d, respectively for the U.S. population aged 2 years and older. IMAG states that inulin-type fructans occur naturally in a variety of edible fruits and vegetables and reports a background average dietary exposure to inulin-type fructans from the diet to be 1–4 g/d at the 97th percentile in the U.S.

IMAG discusses publicly available data and information supporting the safety of agave mixed fructans extracted from the stems of *A. tequilana* Weber var. *azul*. IMAG notes the previous and widespread safe consumption of linear and mixed fructans as components of dietary fruits, vegetables, and grains. IMAG indicates that the safety of agave mixed fructans is further supported by the data and information discussed in GRN 000118.³ IMAG states that the intended uses of its agave mixed fructans will be substitutional for other inulin-based food ingredients.

IMAG describes published laboratory animal and human studies pertaining to the metabolic fate of inulin and inulin-type fructans. IMAG states that inulin-type fructans are resistant to digestion and absorption in the upper gastrointestinal tract and will reach the large intestines intact and be subject to fermentation by colonic microflora. IMAG summarizes published laboratory animal, genotoxicity, and human studies conducted using agave mixed fructans and other compositionally similar fructans. IMAG discusses published human studies of agave mixed fructans and other fructans demonstrating that agave mixed fructans are well tolerated following oral exposure. IMAG notes conclusions in the published literature that inulin-type fructans are safe for human consumption as a dietary fiber at levels up to 20 g/d of inulin and/or oligofructose. Regarding allergenicity, IMAG concludes that agave mixed fructans will not present an allergenic concern to consumers based on the weight of evidence in the literature.

IMAG conducted an updated literature search through June 2020 to identify available safety information related to agave mixed fructans. IMAG did not identify any safety concerns or information that would contradict its GRAS conclusion.

Based on the totality of information, IMAG concludes that agave mixed fructans is GRAS under the conditions of intended use.

Standards of Identity

In the notice, IMAG states its intention to use agave mixed fructans in several food categories, including foods for which standards of identity exist, located in Title 21 of the CFR. 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 FD&C Act, a food is misbranded if its labeling is false or

³ The subject of GRN 000118 is inulin. We evaluated this notice and its supplement, and responded in letters dated May 5, 2003 and January 16, 2008, respectively, stating that we had no questions at that time regarding the notifier's GRAS conclusions.

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 agave mixed fructans 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 in the Center for Food Safety and Applied Nutrition. 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.

Section 301(ll) of the Federal Food, Drug, and Cosmetic Act (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 IMAG's notice concluding that agave mixed fructans 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 agave mixed fructans. Accordingly, our response should not be construed to be a statement that foods containing agave mixed fructans, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that IMAG provided, as well as other information available to FDA, we have no questions at this time regarding IMAG's conclusion that agave mixed fructans is GRAS under its intended conditions of use. This letter is not an affirmation that agave mixed fructans 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 001019 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J.
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