U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Yesong Pu
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Shandong Province 271613
CHINA

Re: GRAS Notice No. GRN 001342

Dear Yesong Pu:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001342. We received Shandong Fukuan Biological Engineering CO., LTD (Fukuan Bio)'s notice on November 26, 2025, and filed it on July 8, 2026. Fukuan Bio submitted amendments to the notice on September 14, 2026, and September 17, 2026, that clarified the identity of the production organism, the manufacturing process, analytical methods, and intended use of the ingredient.

The subject of the notice is D-psicose, produced using D-psicose 3-epimerase from *Ruminiclostridium cellulolyticum* "H10" expressed in *Bacillus subtilis* CGMCC 7596, for use as a sweetener in the food categories and at the maximum levels shown in Table 1, excluding infant formula, or in products under the jurisdiction of the United States Department of Agriculture. The notice informs us of Fukuan Bio's view that these uses of D-psicose are GRAS through scientific procedures.

**Table 1: Intended food categories and maximum use levels for D-psicose.**

| Food Category | Maximum Use Level (%) |
|---|---|
| Bakery products (rolls, cakes, pies, pastries, and cookies; low-calorie or dietetic) | 10 |
| Non-alcoholic beverages (low- and reduced-calorie, sugar-free) | 3.5 |
| Hard candy | 50 |
| Soft candy (low- and reduced-calorie, sugar-free) | 25 |
| Chewing gum | 50 |
| Cereals, regular | 2 |
| Cereals (low- and reduced-calorie, sugar-free) | 5 |
| Coffee mix | 30 |
| Confections and frostings | 5 |
| Dressings for salads | 5 |

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| Frozen dairy desserts (ice cream, soft serve, sorbet; low- and reduced-calorie, sugar-free) | 5 |
| Gelatins, puddings, and fillings (low- and reduced-calorie, sugar-free) | 10 |
| Fat-based creams | 10 |
| Jams and jellies | 10 |
| Sugar | 10 |
| Sugar substitutes | 100 |
| Sweet sauces and syrups (low- and reduced-calorie, sugar-free) | 10 |
| Yogurt and frozen yogurt (low- and reduced-calorie, sugar-free) | 5 |
| Alcoholic beverages (pre-mixed cocktails, wine coolers, and malt beverages; low- and reduced-calorie) | 3.5 |

Fukuan Bio provides information on the identity of D-psicose (also known as D-allulose). Fukuan Bio describes D-psicose as a white to yellowish powder containing ≥ 98% (dry weight basis (DW)) D-psicose or a pale-yellow liquid containing ≥ 95% (DW) D-psicose. D-psicose is a monosaccharide (C-3 epimer of D-fructose) with a molecular weight of 180.16 g/mol and the CAS Registry No. 551-68-8.

Fukuan Bio describes the method of manufacture of D-psicose. D-psicose is manufactured from D-fructose by enzymatic epimerization in the presence of D-psicose 3-epimerase produced by recombinant *Bacillus subtilis* CGMCC 7596 expressing a gene encoding D-psicose 3-epimerase from *Ruminiclostridium cellulolyticum* "H10." Fukuan Bio states that *B. subtilis* CGMCC 7596 is non-pathogenic and non-toxigenic and is deposited in the China General Microbiological Culture Collection Center with the deposit number CGMCC 7596.

The *B. subtilis* CGMCC 7596 cells are grown by fermentation, and the resulting culture broth is combined with D-fructose in the reaction tank to carry out the enzymatic conversion. After the reaction is complete, the mixture is subjected to heat-treatment to inactivate the enzyme and kill any remaining cells. The resulting mixture is decolorized with activated carbon and then filtered. The filtrate is subjected to separation chromatography and eluted with water. The eluate is heated, treated with ethanol, followed by vacuum concentration and sterilization to obtain a D-psicose syrup product. The syrup may be crystallized with the addition of ethanol under controlled temperature conditions, and the resulting crystals are obtained by centrifugation and washed and dried to obtain crystalline D-psicose. Fukuan Bio states that D-psicose is manufactured in accordance with current good manufacturing practices and that all raw materials and processing aids are food grade and are used in accordance with U.S. regulations, are GRAS for their intended use, or are the subject of an effective food contact notification.

Fukuan Bio provides specifications for D-psicose that include D-psicose content (≥95% in syrup or ≥98% in powder, DW), and limits for fructose (≤3% in syrup or ≤1.5% in powder, DW), glucose (≤2% in syrup or ≤0.5% in powder, DW), moisture (≥70% dry solids in syrup or ≤1% loss on drying in powder), ash (≤0.5% in syrup or ≤0.1% in powder), residual ethanol (≤1,000 mg/kg, both forms), arsenic (≤0.1 mg/kg, both

forms), cadmium (≤0.1 mg/kg, both forms), lead (≤0.1 mg/kg, both forms), mercury (≤0.1 mg/kg, both forms), and microorganisms, including *Salmonella* (negative/25 g, both forms) and *Staphylococcus aureus* (<10 colony forming units (CFU)/g, both forms). Fukuan Bio provides the results from the analyses of three non-consecutive batches each of the syrup and powder forms to demonstrate that D-psicose can be manufactured to meet the specifications. Fukuan Bio provides the results of stability studies conducted with both product forms. Fukuan Bio reports that crystalline D-psicose was stable for 24 months at 25°C and 60% relative humidity, and D-psicose syrup was stable for 8 months at 35°C and 75 days at 45°C.

Fukuan Bio states that the intended uses of D-psicose are the same as those described in GRN 001024[1] and incorporates the dietary exposure estimates from GRN 001024 into the notice. Fukuan Bio states that the eaters-only dietary exposure to D-psicose from the intended uses is 9.4 g/person (p)/d (0.13 g/kg body weight (bw)/d) at the mean and 22.7 g/p/d (0.32 g/kg bw/d) at the 90$^{th}$ percentile for the U.S. population aged 2 years and older based on food consumption data from the 2017–2018 National Health and Nutrition Examination Survey (NHANES). Fukuan Bio notes that because the intended uses of D-psicose are substitutional for previous uses, a change in the cumulative dietary exposure to D-psicose is not expected. Fukuan Bio estimates the eaters-only cumulative dietary exposure from all uses of D-psicose to be 11.9 g/p/d at the mean and 23.9 g/p/d at the pseudo-90th percentile[2] for the U.S. population aged 2 years and older and notes that these estimates are consistent with those presented in GRN 001057.[3]

Fukuan Bio summarizes publicly available safety data for D-psicose from prior GRNs for D-psicose (see GRNs 000400, 000498, 000693, 000828, 001024, 001029, 001057, 001148, 001188, and 001193)[4] and from updated literature searches through October 2025. Fukuan Bio discusses studies on D-psicose absorption, distribution, metabolism, and excretion (ADME), acute (rats) and subchronic (rats and dogs) toxicity, reproductive and developmental toxicity, mutagenicity, genotoxicity, chronic toxicity in animals, and clinical studies involving human tolerance. Based on these data, Fukuan

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[1] The subject of GRN 001024 is D-psicose. We evaluated GRN 001024 and responded in a letter dated March 2, 2023, stating that we had no questions at that time regarding the notifier's GRAS conclusion.

[2] The pseudo-90$^{th}$ percentile dietary exposure approximates the dietary exposure at the 90$^{th}$ percentile by doubling the mean dietary exposure as described in FDA's "Guidance for Industry: Estimating Dietary Intake of Substances in Food" (https://www.fda.gov/regulatory-information/search-fda-guidancedocuments/guidance-industry-estimating-dietary-intake-substances-food).

[3] The subject of GRN 001057 is D-psicose. We evaluated GRN 001057 and responded in a letter dated January 25, 2024, stating that we had no questions at that time regarding the notifier's GRAS conclusion. GRN 001057 expanded the intended uses beyond those in GRN 001024. FDA notes that the eaters-only cumulative dietary exposure in the GRN 001057 response letter was stated to be 12.3 g/p/d at the mean and 24.5 g/p/d at the pseudo-90$^{th}$ percentile for the US population aged 2 years and older.

[4] The subject of GRNs 000400, 000498, 000693, 000828, 001029, 001148, 001188, and 001193 is D-psicose. We evaluated these GRNs and responded in letters dated June 18, 2012, June 12, 2014, August 28, 2017, March 2, 2020, August 4, 2023, September 30, 2024, November 19, 2024, and December 12, 2024, respectively, stating that we had no questions at that time regarding each notifier's GRAS conclusion.

Bio concludes that D-psicose is non-genotoxic and non-carcinogenic. Fukuan Bio states that no adverse effects attributable to D-psicose were observed in multiple animal studies including in 90-day studies (200–5,000 mg/kg bw/d) and in a chronic study (1,280 mg/kg bw/d). Additionally, Fukuan Bio discusses a reproductive toxicity study in rats in which no adverse effects were observed up to the highest dose tested (2,000 mg/kg bw/d). Fukuan Bio discusses multiple human tolerance studies on the safety of orally consumed D-psicose. Fukuan Bio states that up to 0.5 g/kg bw for men and 0.6 g/kg bw for women of D-psicose were well tolerated. Fukuan Bio states that its intended conditions of use of D-psicose are identical to those previously evaluated by FDA and does not identify additional issues of toxicological concern.

Based on the totality of information, Fukuan Bio concludes that D-psicose is GRAS for its intended use.

**Standards of Identity**

In the notice, Fukuan Bio states its intention to use D-psicose 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 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 D-psicose 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 Fukuan Bio's notice concluding that D-psicose 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 D-psicose. Accordingly, our response should not be construed to be a statement that foods containing D-psicose,

if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

**Conclusions**

Based on the information that Fukuan Bio provided, as well as other information available to FDA, we have no questions at this time regarding Fukuan Bio's conclusion that D-psicose is GRAS under its intended conditions of use. This letter is not an affirmation that D-psicose 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 001342 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J. CARLSON -S

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