U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Amy Mozingo
GRAS Associates, LLC
11810 Grand Park Ave, Suite 500
North Bethesda, MD 20852

Re: GRAS Notice No. GRN 001323

Dear Ms. Mozingo:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001323. We received the GRAS notice that you submitted on behalf of Shandong Bailong Chuangyuan Bio-Tech Co., LTD (SBC) on August 19, 2025 and filed it on April 20, 2026. SBC submitted amendments to the notice on July 6, 2026, August 12, 2026 and September 1, 2026 that clarified the production strain identity, manufacturing process, specifications, dietary exposure, self-limiting level of use, and safety information.

The subject of the notice is D-psicose, produced using D-psicose 3-epimerase from *Clostridium cellulolyticum* ATCC 35319 expressed in *Bacillus subtilis* CGMCC 13152, for use as a sweetener and humectant in the food categories and at the maximum levels shown in Table 1, excluding use in infant formula, infant foods, or in products under the jurisdiction of the United States Department of Agriculture. The notice informs us of SBC'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 candies (low- and reduced-calorie, sugar-free) | 50 |
| Soft candies (low- and reduced-calorie, sugar-free) | 25 |
| Chewing gum | 50 |
| Cereals, regular, low-calorie, reduced-sugar, sugar-free | 10 |
| Coffee mix | 30 |
| Confections and frostings | 5 |
| Dressings for salads | 5 |
| Frozen dairy desserts (ice cream, soft serve, sorbet; low- and reduced-calorie, sugar-free) | 5 |
| Gelatins, puddings, and fillings (low- and reduced-calorie, sugar- | 10 |

| Food Category | Maximum Use Level (%) |
|---|---|
| free) | |
| 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 (regular and frozen, low- and reduced-calorie, sugar-free) | 5 |
| Alcoholic beverages (pre-mixed cocktails, wine coolers, and malt beverages; low- and reduced-calorie) | 3.5 |
| Nutritional drinks and mixes | 2.5 |

SBC describes D-psicose (also known as D-allulose) as a white crystalline powder containing ≥ 98.5% (dry weight basis (DW)) D-psicose or a colorless to light 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.

SBC states that D-psicose is manufactured from either unmodified corn starch or from the enzymatic epimerization of D-fructose in the presence of D-psicose 3-epimerase produced by fermentation of non-pathogenic and non-toxigenic *B. subtilis* CGMCC 13152 expressing a gene encoding D-psicose 3-epimerase from *C. cellulolyticum* ATCC 35319. SBC describes the genetic construction of the production microorganism *B. subtilis* CGMCC 13152 and confirms that it is removed after fermentation.

In the first step, unmodified cornstarch is converted to D-fructose by a series of enzymatic reactions using the α-amylase enzyme from *B. stearothermophilus* expressed in *B. licheniformis,* glucoamylase from *Penicillium oxalicum* expressed in *Aspergillus niger*, and glucose isomerase from *Streptomyces rubiginosus*. SBC states that the first step is omitted if D-fructose is selected as an alternative starting material. In the second step, *B. subtilis* CGMCC 13152 cells expressing D-psicose 3-epimerase are grown by fermentation and used to convert D-fructose to D-psicose. The resulting D-psicose solution is decolorized using activated carbon, subjected to ion exchange chromatography, concentrated, and further purified through separation chromatography to remove residual D-fructose and other sugars, followed by additional decolorization, ion exchange chromatography, and vacuum concentration to yield D-psicose syrup. The syrup is further concentrated, crystallized, centrifuged, and dried to yield D-psicose powder. SBC 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 applicable U.S. regulations, are GRAS for their intended uses, or are the subject of an effective food contact notification.

SBC provides specifications for D-psicose that include D-psicose content (≥98.5% in powder or ≥95% in syrup, DW), and limits for moisture (≤1% in powder, DW), ash (≤0.5%), lead (≤0.1 mg/kg), arsenic (≤0.1 mg/kg), cadmium (≤0.1 mg/kg), and microorganisms, including *Salmonella* serovars (absent in 25 g) and *Staphylococcus aureus* (absent in 25 g). SBC provides the results from the analyses of five non-

consecutive batches, each of the powder and syrup forms, to demonstrate that D-psicose can be manufactured to meet the specifications. Based on the results from accelerated stability studies (40 °C and 75% relative humidity), SBC concludes that D-psicose powder and syrup are stable for 24- and 12-months, respectively.

SBC estimates the eaters-only dietary exposure to D-psicose from the intended uses to be 7.28 g/person (p)/d (0.10 g/kg body weight (bw)/d) at the mean and 18.11 g/p/d (0.26 g/kg bw/d) at the 90th percentile for the U.S. population aged 2 years and older based on food consumption data from the 2017–March 2020 National Health and Nutrition Examination Survey (NHANES). SBC states that the intended uses of D-psicose are substitutional for those described in prior GRAS notices for D-psicose and incorporates the most recent eaters-only cumulative dietary exposure estimates from GRN 001057[1] into the notice: 12.3 g/p/d at the mean and 24.5 g/p/d at the pseudo-90th percentile[2] for the U.S. population aged 2 years and older. SBC notes that because the intended uses of D-psicose are substitutional for the uses in prior GRAS notices for D-psicose, an increase in the cumulative dietary exposure to D-psicose is not expected.

SBC summarizes publicly available safety data for D-psicose from prior GRAS notices for D-psicose (GRNs 000400, 000498, 000693, 000828, 001024, 001029, 001057, 001188, and 001193)[3] and from updated literature searches through June 2025. SBC discusses studies on D-psicose absorption, distribution, metabolism, and excretion (ADME), acute (rats and dogs) 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, SBC concludes that D-psicose is non-genotoxic and non-carcinogenic. SBC states that no adverse effects attributable to D-psicose were observed in multiple animal studies including in 90-day studies (1670-2000 mg/kg bw/d) and in a chronic study (approximately 1300 mg/kg bw/d). Additionally, SBC discusses a reproductive toxicity study in rats in which no adverse effects were observed up to the highest dose tested (2000 mg/kg bw/d). SBC discusses multiple human tolerance studies on the safety of orally consumed D-psicose. SBC 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. SBC 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 data and information described above, SBC concludes that D-psicose is GRAS for its intended uses.

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[1] 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.
[2] The pseudo-90th percentile dietary exposure approximates the dietary exposure at the 90th 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 GRNs 000400,000498, 000693, 000828, 001024, 001029, 001057, 001188 and 001193 was D-psicose. We evaluated those GRNs and responded in letters dated June 18, 2012, June 12, 2014, August 28, 2017, March 2, 2020, March 2, 2023, August 4, 2023, January 25, 2024, November 19, 2024 and December 12, 2024 respectively, stating that we had no questions at that time regarding each notifier's GRAS conclusion.

**Standards of Identity**

In the notice, SBC 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, 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 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 SBC'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 SBC provided, as well as other information available to FDA, we have no questions at this time regarding SBC'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

001323 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J. CARLSON -S

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