ToxStrategies

Innovative solutions
Sound science


September 30, 2021

Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835

Subject: GRAS Notification – Allulose

Dear Sir:

On behalf of Tate & Lyle., ToxStrategies, Inc. (its agent) is submitting, for FDA review, a copy of the GRAS notification as required. The enclosed document provides notice of a claim that the food ingredient, allulose, described in the enclosed notification is exempt from the premarket approval requirement of the Federal Food, Drug, and Cosmetic Act because it has been determined to be generally recognized as safe (GRAS), based on scientific procedures, for addition to food. This is a resubmission of GRN 893 that was withdrawn on May 6, 2020.

In addition, non-safety related data and information (marked as confidential; Exhibit 2) are attached to the GRAS notice that are to be shared with the Food Safety Inspection Service (FSIS) of the U.S. Department of Agriculture (USDA).

If you have any questions or require additional information, please do not hesitate to contact me at 630-352-0303, or dschmitt@toxstrategies.com.

Sincerely,

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

# GRAS Determination of Allulose for Use as an Ingredient in Human Food

**SEPTEMBER 29, 2021**

Tox Strategies

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# GRAS Determination of Allulose for Use as an Ingredient in Human Food

**SUBMITTED BY:**

Tate & Lyle
5450 Prairie Stone Parkway
Hoffman Estates, IL 60192

**SUBMITTED TO:**

U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
HFS-200
5001 Paint Branch Parkway
College Park MD 20740-3835

**CONTACT FOR TECHNICAL OR OTHER INFORMATION**

Donald F. Schmitt, MPH
ToxStrategies, Inc.
931 W. 75th St., Suite 137, PMB 255
Naperville, IL 60565

**September 29, 2021**

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## List of Acronyms

| | |
|---|---|
| ADME | absorption, distribution, metabolism, and excretion |
| AUC | area under the curve |
| bw | body weight |
| CDC | Centers for Disease Control and Prevention |
| cGMP | current Good Manufacturing Practice |
| CAS | Chemical Abstracts Service |
| CEDI | cumulative estimated daily intake |
| CFR | Code of Federal Regulations |
| CFU | colony-forming units |
| COA | Certificate of Analysis |
| dpm | disintegrations per minute |
| FDA | U.S. Food and Drug Administration |
| GRAS | Generally Recognized as Safe |
| GRN | Generally Recognized as Safe Notification |
| $LD_{50}$ | lethal dose |
| NHANES | US National Health and Nutrition Examination Survey |
| NOAEL | no-observed-adverse-effect level |
| SCFA | short-chain fatty acid |
| USDA | United States Department of Agriculture |
| WWEIA | What We Eat in America |

# § 170.225 Part 1, GRAS Notice: Signed Statements and Certification

## (1) GRAS Notice Submission

Tate & Lyle (T&L), through its agent, ToxStrategies, Inc., hereby notifies the U.S. Food and Drug Administration (FDA) of the submission of a Generally Recognized as Safe (GRAS) notice for the use of allulose in selected foods for human consumption, in accordance with Subpart E of 21 CFR § 170.

## (2) Name and Address

Tate & Lyle
5450 Prairie Stone Parkway
Hoffman Estates, IL 60192

## (3) Name of Notified Substance

The name of the substance that is the subject of this GRAS determination is the monosaccharide allulose.

## (4) Intended Use in Food

The allulose ingredient is proposed for use in nine new food types including (1) nutritional beverages; (2) nutritional beverages intended for children; (3) sweetened alcoholic malt beverages; (4) alcoholic premixed cocktails; (5) grain-free, no sugar, high protein RTE cereals; (6) nutrition bars; (7) ketchup and barbecue sauces; (8) dried cranberries; and (9) meat- and poultry-based jerky, in addition to those foods included in GRNs 400, 498, 693 and 828 (i.e., select low calorie, reduced calorie, or sugar-free foods including bakery products, beverages, cereals, chewing gums, confections and frostings, frozen dairy desserts, yogurt and frozen yogurt, dressings for salads, gelatins, pudding and fillings, hard and soft candies, jams and jellies, sugar, sugar substitutes, sweet sauces and syrups, fat based creams, medical foods and coffee mix). Higher use levels are also proposed for existing categories for ready-to-eat (RTE) and cooked cereals including regular and low calorie, reduced calorie, and sugar-free RTE and cooked cereals; (see Table 9). Allulose has 70% of the sweetness of sugar but provides negligible energy, and therefore is an excellent substitute for sugar to reduce sugar and energy intake.

## (5) Statutory Basis for GRAS Determination

T&L, through its agent, ToxStrategies, confirms that the allulose ingredient, which meets the specifications described herein, has been determined to be GRAS through scientific procedures in accordance with 21 CFR § 170.30(a) and (b).

## (6) Premarket Approval Statement

T&L further asserts that the use of the allulose ingredient, as described herein, is exempt from the pre-market approval requirements of the Federal Food, Drug, and Cosmetic Act, based on a conclusion that the substance is GRAS under the conditions of its intended use.

## (7) Availability of Information

The data and information that serve as the basis for this GRAS determination, as well any information that has become available since the GRAS determination, will be sent on request, or are available for the FDA's review and copying during customary business hours from ToxStrategies, Inc., Naperville, IL.

## (8) Data and Information Confidentiality Statement

None of the data and information in the GRAS notice are exempt from disclosure under the Freedom of Information Act, 5 U.S.C. 552.

## (9) GRAS Certification

To the best of our knowledge, the GRAS determination is a complete, representative, and balanced document. T&L is not aware of any information that would be inconsistent with a finding that the proposed uses and use levels of the allulose ingredient in food, meeting the appropriate specifications described herein, and used according to current Good Manufacturing Practice (cGMP), is GRAS. Recent reviews of the scientific literature revealed no potential adverse health concerns.

## (10) Name/Position of Notifier

[redacted]

Sept. 30, 2021
Date

Donald F. Schmitt, M.P.H.
Senior Managing Scientist
ToxStrategies, Inc.
Agent for Tate & Lyle

## (11) FSIS Statement

The allulose ingredient will be used as a sweetener in selected meat/poultry products at a maximum use level of 15% under the jurisdiction of USDA/SFSIS. Allulose adds a sweet flavor to meat and/or decreases saltiness.

# § 170.230 Part 2, Identity, Method of Manufacture, Specifications, and Physical or Technical Effect

## A. Identity

Allulose is produced from corn glucose by enzymatic epimerization. It contains negligible residual amounts of other related monosaccharides and impurities (Table 2 and Appendix A).

## B. Common or Usual Name

D-Allulose or D-psicose. The names D-allulose and D-psicose are used interchangeably in literature but refer to the same substance. The ingredient will be referred to as allulose throughout this document.

## C. CAS Registry Number

CAS No. 551-68-8

## D. Trade Name

The trade name of T&L's allulose product is DOLCIA PRIMA® allulose.

## E. Empirical Formula and Chemical Structure of Allulose

The empirical formula for allulose is $C_6H_{12}O_6$. The chemical names are D-ribo-2-hexulose, D-ribo-2-ketohexose. The molecular weight of allulose is 180.16 g/mol. The chemical structure of allulose is represented in Figure 1.

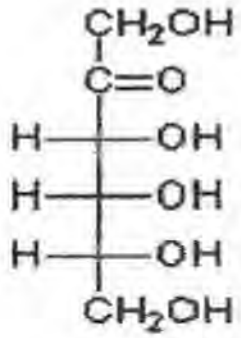



***Figure 1. Structural formula of allulose***

## F. Allulose Composition

DOLCIA PRIMA® allulose is obtained from starch derived from corn (*Zea mays* L.); see Table 1.

***Table 1. Taxonomic classification of the raw material source of allulose***

| Classification | Corn |
|---|---|
| Kingdom | Plantae |
| Phylum | Magnoliophyta |
| Class | Liliopsida |
| Order | Poales |
| Family | Poaceae |
| Genus | *Zea* |
| Species | *Zea mays* L. |

DOLCIA PRIMA® Allulose is composed predominantly of allulose (> 95% in syrup version, or > 99.1% in crystalline version), with the remainder being composed of only a small quantity of fructose and other di- and tri-saccharides typically found in carbohydrate syrups (Table 2).

***Table 2. Composition of allulose***

| Components | Liquid Syrup | Crystalline |
|---|---|---|
| Allulose | >95%, dry basis | >99.1%, dry basis |
| Non-allulose saccharides | <5%, dry basis | <2%, dry basis |

## G. Manufacturing Process

A process flow diagram for the allulose product is shown below (Figure 2).

The starting material is typical corn (U.S. Grade #2 Dent Corn [dried grain]), and the intermediate products are monosaccharides (glucose and fructose). All enzymes used in the process are safe and suitable for food uses and consistent with enzymes identified in previous GRAS notifications (including their sources). The allulose ingredient is produced in two forms: syrup and crystalline powder. The manufacturing process is conducted under Good Manufacturing Practices (GMP) for both end products and is identical in every step but the last.

- U.S. Grade #2 Dent Corn (dried grain) is subjected to traditional wet-milling processes to produce germ, fiber, protein, and starch fractions. For the production of allulose, the starch fraction is used.
- The starch fraction (polymeric glucose; amylose and amylopectin) is converted to corn syrup (maltose and higher oligosaccharides) and ultimately to D-glucose by enzymatic hydrolysis using standard manufacturing techniques.

- D-glucose is isomerized to D-fructose using safe and suitable glucoisomerases.
- D-fructose is separated from the bulk of D-glucose by chromatography to greater than 85% (w/w) purity.
- Fructose is then epimerized to D-allulose using D-psicose 3-epimerase.
- The resulting mixture of D-allulose and D-fructose is separated by chromatography to ≥95% D-allulose and ≤5% non-allulose saccharides (including fructose, glucose).
- This enriched D-allulose stream concentrated and passed through activated granular carbon and an ion exchange resin.

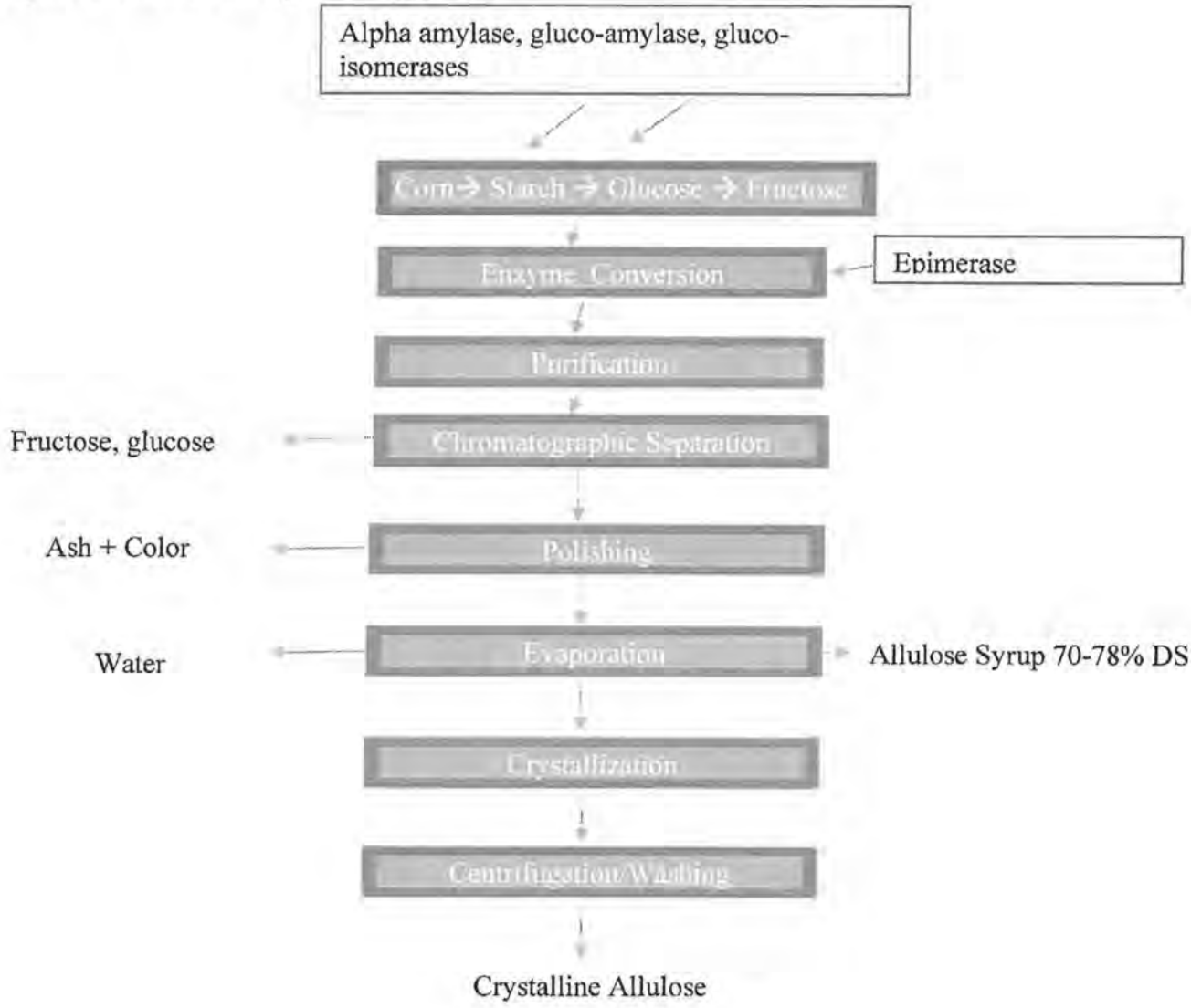
**For the syrup form, the final step consists of:**

Using an evaporator, the solution is concentrated to a final density of 71%–78% solids.

**For the crystalline form, the final step consists of:**

The solution is concentrated, crystallized, centrifuged, washed, and dried.

***Figure 2. Allulose manufacturing process***




All processing aids employed in the manufacturing process are safe and suitable for use in the production of food ingredients (see Table 3).

***Table 3. Processing aids***

| **Processing aid** | **CAS Number** | **Purpose** | **21 CFR Citations/GRN Numbers** |
|---|---|---|---|
| Alpha-amylase from *Aspergillus oryzae* | 9001-19-8 | Hydrolysis of starch | 21 CFR 172.892; 21 CFR 184.1012; GRN Nos. 22, 24, 79, 126, 594, 664, 751 |
| Glucoamylase from *Aspergillus niger* | 977031-46-1 | Hydrolysis of starch | 21 CFR 172.892; GRN Nos. 372, 657 |

| | | | |
|---|---|---|---|
| Glucosiomerase from a genetically modified strain of *Streptomyces rubiginosus* (strain DP-Pzn37) | 9005-00-9 | Conversion of D-glucose to D-fructose | 21 CFR 184.1372 |
| D-psicose 3-epimerase from a genetically modified strain of *E. coli* K12 | 1219591-85-1 | Conversion of D-fructose to allulose | See footnote* |
| Activated carbon | 64365-11-3 | Purification | 21 CFR 175.250; 21 CFR 172.615 |

* The *E. coli* production microorganism is derived from the wild-type *E. coli* K12 strain. *E. coli* K-12 has a documented history of safe use. Its derivatives are currently used in a large number of drugs, specialty chemicals, and large- scale industrial applications including in the production of amino acids for use as food ingredients. *E. coli* K12 is a nonpathogenic and nontoxigenic host organism and belongs to risk group 1 in the classification of human etiologic agents (NIH, 2002). It is one of the most extensively studied bacteria and has been used in genetic studies and biotechnology research in laboratories worldwide. A synthetic gene was designed and used to assure that no extraneous donor DNA was transferred to the production organism. (NIH 2002) Department of Health and Human Services, National Institutes of Health. Guidelines for Research involving Recombinant DNA Molecules, April 2002. In addition, the safety of the enzyme was based on the Pariza and Johnson Decision Tree (2001) that clearly showed that it is safe for the intended use (see Appendix A; Pariza, MW and Johnson, EA. 2001). Evaluating the safety of microbial enzyme preparations used in food processing: update for a new century. Regul Toxicol Pharmacol 33:173-186).

All enzymes, reagents, and processing aids used in the production of allulose are safe and suitable, food grade, and in conformity with US regulations (i.e., alpha-amylase, glucoamylase, glucoisomerases, epimerase, activated carbon). They are commonly used in food ingredient manufacturing processes and all production processes used are processes traditionally used in food manufacturing. The epimerase enzyme is purchased from CODEXIS. The enzyme never comingles with the final product but the possible presence of the enzyme in the allulose product has been evaluated (see Appendix E; analytical results for the presence of epimerase enzyme in the allulose product and the ELISA analytical method employed). The epimerase enzyme was self-determined as GRAS in 2014. The conclusion and signature page of the GRAS Panel that evaluated the safety and GRAS status (based on scientific procedures) of the epimerase enzyme is also attached in Appendix E.

## H. Product Specifications

Specifications for the allulose product are presented in Table 4. A comparison of non-consecutive lots of product to the specifications below can be found in Tables 5 and 6. Results of analyses for additional microbiological parameters are presented in Table 7. All analytical methods used to analyze batches of allulose against its specifications have been validated for that purpose.

***Table 4. Specifications for allulose***

| Parameter | Liquid Syrup | Crystalline Granules |
|---|---|---|
| Appearance | Colorless to slightly yellow | Off white |
| Allulose (%, dry basis) | >95 | >99.1 |
| Total non-allulose saccharides (%) | <5 | <0.9 |
| Dry solids (%) | 70-78 | n/a |
| Moisture (%) | n/a | <0.5 |
| pH | 3.0 – 4.5 | n/a |
| Ash (%) | n/a | <0.5 |
| $SO_2$ (ppm) | <10 | <10 |
| Total plate count (cfu/10g) | <200 | <200 |
| Yeast (cfu/10g) | ≤10 | ≤10 |
| Mold (cfu/10g) | ≤10 | ≤10 |
| Arsenic (ppm) | <0.1 | <0.1 |
| Cadmium (ppm) | <0.1 | <0.1 |
| Lead (ppm) | <0.1 | <0.1 |
| Mercury (ppm) | <0.01 | <0.01 |

n/a = not applicable

***Table 5. Analytical results for three non-consecutive lots of allulose syrup***

| Specification | | Lot No. YP19DO3774 | Lot No. YP19G01863 | Lot No. YP18D03177 |
|---|---|---|---|---|
| Allulose (%, dry basis) | >95 | 96.2 | 96.3 | 96.3 |
| Total non-allulose saccharides (%) | <5 | 2.6 | 2.9 | 2.4 |
| Dry solids (%) | 70-78 | 70.8 | 70.5 | 71.0 |
| pH | 3.0 – 4.5 | 4.2 | 3.9 | 4.3 |
| Sulfur dioxide (ppm) | <10 | <10 | <10 | <10 |
| Total plate count (cfu/10g) | <200 | <10 | <10 | <10 |
| Yeast (cfu/10g) | ≤10 | <10 | <10 | <10 |
| Mold (cfu/10g) | ≤10 | <10 | <10 | <10 |
| Arsenic (ppm) | <0.1 | 0.016 | 0.011 | 0.024 |

| | | | | |
|---|---|---|---|---|
| Cadmium (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Lead (ppm) | <0.1 | <0.005 | <0.005 | 0.006 |
| Mercury (ppm) | <0.01 | <0.005 | <0.005 | <0.005 |

***Table 6. Analytical results for three non-consecutive lots of crystalline allulose***

| **Specification** | | **Lot No. LO18J90596** | **Lot No. LO19F90351** | **Lot No. LO18J90294** |
|---|---|---|---|---|
| Allulose (%, dry basis) | >99.1 | 99.4 | 99.8 | 99.2 |
| Total non-allulose saccharides (%) | <0.9 | 0.27 | 0.06 | 0.29 |
| Moisture (%) | <0.5 | 0.14 | 0.12 | 0.10 |
| Ash (%) | <0.5 | <0.1 | <0.1 | <0.1 |
| Sulfur dioxide (ppm) | <10 | <10 | <10 | <10 |
| Total plate count (cfu/10g) | <200 | <10 | 10 | 10 |
| Yeast (cfu/10g) | ≤10 | <10 | 10 | <10 |
| Mold (cfu/10g) | ≤10 | <10 | 10 | <10 |
| Arsenic (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Cadmium (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Lead (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Mercury (ppm) | <0.01 | <0.005 | <0.005 | <0.005 |

***Table 7. Other microbiological criteria for three non-consecutive lots of liquid syrup and crystalline allulose***

| **Microbiological Criteria** | | | | |
|---|---|---|---|---|
| **Allulose Syrup** | | **Lot No. YP19DO3774** | **Lot No. YP19G01863** | **Lot No. YP18D03177** |
| *E. coli* (cfu/10g) | ND | ND | ND | ND |
| *Salmonella* (cfu/25g) | Negative | Negative | Negative | Negative |
| **Crystalline Allulose** | | **Lot No. LO18J90596** | **Lot No. LO19F90351** | **Lot No. LO18J90294** |
| *E. coli* (cfu/10g) | ND | ND | ND | ND |
| *Salmonella* (cfu/25g) | Negative | Negative | Negative | Negative |

ND = not detected

The analytical results for the allulose ingredient summarized in the above tables and included in the Certificates of Analysis (COAs) in Appendix B confirm that the finished product meets the analytical specifications. The results also demonstrate that T&L's manufacturing process results in a consistently reproducible product and confirm the lack of significant levels of impurities and/or contaminants (e.g., heavy metals, microbiological contaminants). In addition, the corn starting material is periodically analyzed for the presence of pesticides and mycotoxins as part of Tate & Lyle's standard Quality Assurance processes.

Regarding heavy metals analyses, the method employed for the analysis of arsenic is a validated internal Tate & Lyle method designated as R method 2837 and is based upon AOAC 2011.19 and AOAC 993.14 (modified). The method employed for the analysis of cadmium is a validated internal Tate & Lyle method designated as R method 2837 and is based upon AOAC 2011.19 and AOAC 993.14 (modified). The method employed for the analysis of mercury is a validated internal Tate & Lyle method designated as R method 2832 and is based upon AOAC 2011.19 and AOAC 993.14 (modified). The method employed for analysis of *E.coli* is TN10512L, is an internal method, which references ISO21528-1:2017. The method TN10512L is validated for the intended use. The method employed for analysis of *Salmonella* is TN10547, is an internal validated method for the intended use that references ISO6579-1:2017.

## I. Stability Data

The results of stability testing conducted using liquid allulose, DOLCIA PRIMA® LS brand, at temperatures of 4°C, 25°C, and 35°C demonstrate its stability through the end of the product's shelf-life in the syrup version up to 9 months. In contrast, stability studies on DOLCIA PRIMA® DS crystalline allulose show that this material is stable for up to 30 months. See Appendix C for stability testing data.

# § 170.235 Part 3, Dietary Exposure

## Current Uses

Allulose is naturally present in small quantities in many common foods, such as in dried fruits (e.g., figs, raisins, fried dough, brown sugar and ketchup). Allulose amounts are usually below 1%. Table 8 describes the quantities of naturally occurring allulose in foods (Oshima et al., 2006).

***Table 8. D-allulose content in foods***

| Item | mg/100 g food |
|---|---|
| **Bakery products** | |
| Sponge cake | 11.0 |
| Corn snack | 47.0 |
| Rice cracker | 27.3 |
| Cookie | 26.7 |
| Brown sugar drop | 76.5 |
| Fried dough cake | 95.6 |
| Chocolate chip cookies | 6.4 |
| Cereal | 2.2 |
| **Dishes** | |
| Fish broiled with soy | 39.1 |
| Simmered dishes of dried radish strips | 8.1 |
| Fermented soybeans | 7.8 |
| **Seasonings and beverages** | |
| Caramel sauce | 83.0 |
| Brown sugar | 71.1 |
| Meat sauce | 15.8 |
| Demiglace | 16.3 |
| Maple syrup | 57.9 |
| Ketchup | 39.8 |
| Worcester sauce | 130.6 |
| Coke® (sic) | 38.3 |
| Coffee | 0.5 |
| Fruit juice | 21.5 |
| Tomato juice | 2.4 |

| Item | mg/100 g food |
|---|---|
| **Fruits** | |
| Dried fig | 29.6 |
| Dried kiwi fruit | 9.4 |
| Raisin | 38.7 |
| Canned peaches | 1.5 |
| Can of mandarin oranges | 8.4 |
| Canned cherries | 2.0 |

Allulose is added to select foods as a sweetener, per previous GRAS notifications, and these foods include bakery products, chewing gum, hard candies, frozen dairy desserts, carbonated beverages, non-carbonated beverages, soft candies, yogurt, ready-to-eat cereals, coffee mix, jams/jellies, confections and frostings, dressings for salads, gelatins, pudding and fillings, sweet sauces/syrups, and fat-based creams. Intake assessments of allulose in US populations were conducted as part of GRAS notification nos. 400, 498, 693, and 828.

## Proposed Uses

The focus of this GRAS determination is for the use of allulose as a sweetener in additonal food categories including those in the publicly available GRN's in which FDA has issued "no questions" letters. Higher use levels are also proposed in two existing food categories covered in prior GRAS notifications.

Table 9 below summarizes the food categories and associated use levels. An intake assessment was conducted to estimate the mean and 90$^{th}$ percentile daily intakes of allulose based on its intended use in foods as shown in Appendix D.

The EDI of allulose were generated from dietary recalls collected as part of the *What We Eat in America* (WWEIA) component of the combined 2015-2018 National Health and Nutrition Examination Surveys (NHANES) data files (NCHS 2018, 2020). Exponent developed allulose EDIs on a per capita and per user basis for the U.S. population ages 2 years (y) and older and the following five subpopulations: (1) infants and young children <2 y, (2) children 2-12 y, (3) adolescents 13-18 y, (4) adult females 19 y and older, and (5) adult males 19 y and older. Estimates were generated in units of grams allulose per day (g/day) and grams allulose per kilogram body weight per day (g/kg-bw/day). The sections below summarize the data, methods, and results.

Background dietary intake of allulose was determined based on the existing food uses and use levels of allulose as described in U.S. GRAS Notices (GRNs) 400 (CJ Cheiljedang, 2011), 498 (Matsutani Chemical Industry Company, Ltd 2013), 693 (Samyang Corporation, 2017), and 828 (Samyang Corporation, 2018). These uses of allulose are summarized in Table 9 by food category and corresponding use levels. For the purpose of estimating

background allulose intake from existing food uses, the maximum use level from all GRNs for a given food type was used in the assessment.

*Table 9. Maximum allulose use levels by food type of foods and beverages*

| | | | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | **Food Category** | **Description of Foods Selected for Analysis** | **Proposed New Uses** | **Existing GRAS Uses*** | **Combined existing GRAS and proposed uses **** |
| 1 | Baked products (bread, muffin, cake and cookies, pastries), dietetic, low calorie, reduced calorie, sugar-free | Sweetened bread/rolls, muffin, and cakes and cookies – all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 10 | 10 |
| 2 | Beverages | | | | |
| 2a | Non-alcoholic beverages, low calorie, reduced calorie, sugar-free | Sweetened coffees, teas, soft drinks, energy drinks, juice drinks, fruit drinks, fruit flavored drinks, flavored/carbonated waters, and enhanced/fortified waters – all identified as low calorie, reduced calorie, or sugar-free. | NA | 3.5 | 3.5 |
| 2b | Nutritional beverages | Nutritional beverages within the "nutritional beverages" and "protein and nutritional powders"WWEIA categories not included as part of the existing GRAS uses in medical foods | 2.5 | NA | 2.5 |
| 2c | Nutritional beverages intended for children (i.e., PediaSure) | PediaSure | 3.5 | NA | 3.5 |
| 2d | Alcoholic malt beverage, sweetened | Sweetened alcoholic malt beverage (food code 93106000), which includes products such as hard lemonade, hard punch, hard tea, etc. | 3.5 | NA | 3.5 |
| 2e | Alcoholic premixed cocktails | All cocktails with added sugar | 3.0 | NA | 3.0 |
| 3 | Candy, hard and soft | | | | |
| 3a | Hard candy (includes pressed candy and mints), low calorie, reduced calorie, sugar-free | Hard candy – low calorie, reduced calorie, sugar-free, or NFS†. | NA | 70 | 70 |
| 3b | Soft candy, low calorie, reduced calorie, sugar-free | Soft candy – low calorie, reduced calorie, sugar-free. | NA | 25 | 25 |

| | Food Category | Description of Foods Selected for Analysis | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | | | Proposed New Uses | Existing GRAS Uses* | Combine dexisting GRAS and proposed uses ** |
| 4 | Chewing gum | Regular and sugar-free chewing gum. | NA | 50 | 50 |
| 5 | Cereals, ready-to-eat (RTE) and cooked | | | | |
| 5a | RTE and cooked, regular | RTE and cooked cereals identified as containingadded sugar. | 12 | 2 | 12 |
| 5b | RTE and cooked, low calorie, reduced calorie, sugar-free | RTE and cooked cereals identified as low calorie, reduced sugar, or sugar-free. | 12 | 5 | 12 |
| 5c | RTE cereals with <5% sugar | RTE cereals with <5% added sugar excluding cereals with no added sugar. | NA | 10 | 10 |
| 5d | Grain-free, no sugar, high protein RTE cereal | No grain-free, no sugar, high protein RTE cereals were reported consumed, hence, zero-sugar added RTE cereals were selected as surrogates. | 20 | NA | 20 |
| 6 | Coffee mix | Sweetened non-reconstituted coffee mixes. | NA | 30 | 30 |
| 7 | Confections & Frostings | Frostings and icings and marshmallows. | NA | 5 | 5 |
| 8 | Dressings for salads | Salad dressings including mayonnaise. | NA | 5 | 5 |
| 9 | Frozen dairy (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free | Desserts including ice cream, soft serve, sorbet - all identified as low calorie, reduced calorie,sugar-free, or NFS†. | NA | 5 | 5 |
| 10 | Gelatins, pudding & fillings | | | | |
| 10a | Gelatins, pudding & fillings, low calorie, reduced calorie, sugar-free | Gelatins and puddings - all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 10 | 10 |
| 10b | Fat-based cream (used in modified fat/calorie cookies, cakes, pastries, pie) | Fat-based cream filling in cookies, cakes, pastries, pies. | NA | 10 | 10 |
| 11 | Nutrition bars | Meal replacement bars, protein bars, energy bars, etc. | 25 | NA | 25 |
| 12 | Jams & Jellies | Jams, jellies, and pastes, all types. | NA | 10 | 10 |

| | | | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | **Food Category** | **Description of Foods Selected for Analysis** | **Proposed New Uses** | **Existing GRAS Uses*** | **Combine dexisting GRAS and proposed uses **** |
| 13 | Sugar | Sugar added in home preparations including white sugar, brown sugar, cinnamon sugar, raw sugar, honey, molasses, and not specified. | NA | 10 | 10 |
| 14 | Sugar substitutes | Sugar substitutes. | NA | 100 | 100 |
| 15 | Sweet sauces & syrups, low calorie, reduced calorie, sugar-free | Sweet sauces & syrups - all identified as low calorie, reduced calorie, sugar-free, dietetic orNFS†. | NA | 10 | 10 |
| 16 | Ketchup and barbecue sauces | Ketchup and barbecue sauces. | 10 | NA | 10 |
| 17 | Yogurt and frozen yogurt, low calorie, reduced calorie, sugar-free | Yogurt and frozen yogurt - all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 5 | 5 |
| 18 | Medical foods | Nutritional drinks such as Boost, Ensure, and Glucerna to provide a surrogate for medical foods. | NA | 15 | 15 |
| 19 | Cranberries, dried | Dried cranberries (i.e., Craisins). | 25 | NA | 25 |
| 20 | Jerky (meat or poultry based) | Jerky (meat or poultry based). | 15 | NA | 15 |

* Based on current food uses and use levels of allulose as described in U.S. GRNs 400 (CJ Cheiljedang, 2011), 498 (Matsutani Chemical Industry Company, Ltd2013), 693 (Samyang Corporation, 2017), and 828 (Samyang Corporation, 2018).

† NFS refers to food codes described as "not-further-specified;" providing a generic description to the food reported consumed (i.e., dietetic topping).NA: Not applicable.

** Maximum use levels applied in estimating cumulative intake from proposed and existing GRAS uses

## Food Consumption Data

Estimated food intakes of allulose were based on food consumption records collected in the WWEIA component of NHANES conducted in 2015-2016 and 2017-2018 (NHANES 2015-2018). This continuous survey uses a complex multistage probability sample designed to be representative of the civilian U.S. population (NCHS 2018, 2020). The NHANES datasets provide nationally representative nutrition and health data and prevalence estimates for nutrition and health status measures in the USA. Statistical weights are provided by the National Center for Health Statistics (NCHS) to adjust for the differential probabilities of selection.

As part of the examination, trained dietary interviewers collected detailed information on all foods and beverages consumed by respondents in the previous 24-hour time period (midnight to midnight). A second dietary recall was administered by telephone three to ten days after the first dietary interview, but not on the same day of the week as the first interview. The dietary component of the survey is conducted as a partnership between the U.S. Department of Agriculture (USDA) and the U.S. Department of Health and Human Services (DHHS). DHHS is responsible for the sample design and data collection, and USDA is responsible for the survey's dietary data collection methodology, maintenance of the databases used to code and process the data, and data review and processing. A total of 13,666 individuals in the survey period 2015- 2018 provided 2 complete days of dietary recalls.

## Selection of Representative Food Codes

Food codes corresponding to each of the food categories to which allulose can currently be added to or is proposed to be added were identified in the WWEIA, NHANES 2015-2018. Foods in which only a component is of interest for the addition of allulose (e.g., dressing as part of a salad, jelly in a sandwich, icing on a cake) were also identified. Food descriptions and the "additional description" details provided for some food codes were reviewed as part of the process to select representative foods and food mixtures to include in the analysis.

For relevant food mixtures, the proportion of the food code (as a percentage of total weight) corresponding to the component of interest was identified and only this portion of the food weight was used to determine the amount of allulose that may be added. Exponent used USDA's Food and Nutrient Database for Dietary Studies (FNDDS)2017-2018 (USDA, 2018) to translate the food as consumed into its corresponding ingredients based on percent weight. Additional details on the identification of the portion of food mixtures assumed to contain allulose are presented in sections below.The list of the food codes included in the analysis is provided in Appendix D.

***Confection & Frosting and Gelatins, Pudding & Fillings***

The average proportion of frosting/icing in baked goods was assumed to be 30% for cakes/cupcakes, 25% for brownies, 30% for cookies, and 20% for pastries. Likewise, the

average filling proportion was assumed to be 30% for cookies and 15% for pastries.These proportions were based on frosting/icing or filling contribution between baked goods with and without icing/frosting or filling using portion weight information from the FNDDS.

***Sugar and Sugar Substitutes***

Food codes for sugar and sugar substitutes were identified and assigned the maximum use levels of allulose as specified in Table 1. The WWEIA food codes also include food mixtures that may contain a sweetener added during home preparation. To capture these potential existing uses of allulose as a sugar substitute assumed to occur at the consumer level, food descriptions containing "homemade", "home recipe", "prepared with", "made with", "made from", "with sugar", "sugar added", "sweetened", or "presweetened" were identified and reviewed. When the food was assumed to represent a home preparation, the sugar or sugar substitute portion of the mixture was identified and included in the analysis. The Food Patterns Equivalent Database (FPED) was used to identify the concentration of added sugars in these mixtures (USDA, 2020). For example, sugar portions of the food codes for "Cornbread, made from home recipe" and"Apple, dried, cooked, with sugar" were assumed to contain allulose in the analysis.

For beverage food codes identified as presumably sweetened by the consumer, Exponent used USDA's FPED database to determine the proportion of sugar in the beverage mixtures. This proportion was included in the analysis for the sugar and sugar substitute existing uses.

## Analysis

For each WWEIA NHANES respondent on each day of dietary recall, intake of allulose was calculated as the amount of the select food or food ingredient (g) corresponding to either background existing GRAS uses or proposed uses and multiplied by the maximum allulose use level of that food as shown in Table 9. Contributions from all foods consumed during the two days of recall were summed and the resulting value was divided by two to result in an estimate of 2-day average allulose intake for each respondent. Intakes of allulose derived on a body weight (bw) basis were calculated using each participant's measured body weight.

Summaries of the estimated allulose intake by the population ages 2 y and older and subpopulations of infants and children <2 y, children 2-12 y, adolescents 13-18 y, adult females 19 y and older, and adult males 19 y and older were derived from the allulose intakes calculated for each respondent. Estimates of intake for the population groups were calculated on a *per user* basis and a *per capita* basis, in units of gram allulose per day (g/day) and gram allulose per kilogram body weight per day (g/kg-bw/day). In this analysis, a "user" is anyone who reported consuming a food with allulose added on either of the survey days. The resulting values represent estimates of allulose intake assuming the maximum use level of allulose.

The 2-day average intakes by each individual were estimated using Exponent's Foods Analysis and Residue Evaluation Program (FARE® version 14.06) software, which uses the statistically weighted values from the survey in its analyses. The statistical weights compensate for variable probabilities of selection, adjust for non-response, and provide intake estimates that are representative of the U.S. population.

***Cumulative EDI (CEDI)***

To estimate the CEDI for allulose, food uses of allulose from background food uses and proposed uses together were considered. Specifically, intake of allulose was calculated as the amount of the select food or food ingredient (in grams) from either background existing GRAS and/or proposed uses and multiplied by the maximum allulose level associated with the combined GRAS and proposed uses of that food as shown in Table 9.

## Results

The two-day average intake estimates of allulose at the mean and 90$^{th}$ percentile of intake was derived using dietary records from NHANES 2015-2018 for the U.S. population 2+ years of age and subpopulations of infants and young children, children, adolescents, adult females, and adult males. The EDI of allulose from background and proposed uses are summarized in Tables 10 and 11, respectively. The allulose CEDI from the combined background and proposed uses are summarized in Table 12.

***Background EDI***

Among the U.S. population 2+ y, 92% consumed one or more foods containing allulose from background uses (i.e., GRAS uses from GRNs 400, 498, 693, and 828; Table 10). The estimated daily intake of allulose from background uses at the per user mean and 90th percentile of intake among this population is 6.69 g/day (0.09 g/kg-bw/day) and 16.39 g/day (0.23 g/kg-bw/day), respectively. Per user mean intake of allulose from background uses ranged from 1.50 g/day among infants <2 y to 8.68 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.14 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 3.63 g/day among infants <2 y to 22.71 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2 y at 0.34 g/kg-bw/day allulose.

The total per user mean and 90$^{th}$ percentile intake estimates of allulose based on NHANES data and reported for the U.S. population by GRNs 400, 498, 693 and 828 ranged from 9-12.55 g/day and 24.8-30 g/day, respectively. The per user mean and 90$^{th}$ percentile intake estimates in the present analysis are approximately 26% and 34% lower, respectively, than those estimates in the GRNs. In order to understand the downward shift of allulose intake observed in the more recent NHANES data, Exponent generated and compared two sets of allulose intake estimates using NHANES 2015- 2018 and NHANES 2007-2010 for the food uses reported in GRN 498 (see Appendix C of Exponent Intake Assessment Report; Appendix D of this GRN). Lower allulose intake

estimates in the present analysis appear to be due to a shift in dietary patterns of non-alcoholic low calorie, reduced calorie, sugar-free beverages. Specifically, the percent users and intake of non-alcoholic beverages (low calorie, reduced calorie, sugar-free) have decreased from 32% in NHANES 2007-2010 to 21% in NHANES 2015-2018 with a decreased intake among consumers of non- alcoholic beverages in NHANES 2015-2018. A trend analysis conducted by Bleich et al.(2018) similarly reported an observed decline in beverage and sugar-sweetened beverage consumption for children and adults from 2003 to 2014. There was also a reduction in intake of regular cereal contributing to lower allulose intakes, i.e., a decrease in percent users (46% in NHANES 2007-2010 versus 33% in NHANES 2015-2018) and lower intake amounts in NHANES 2015-2018. This reduction, however, did not result from changes in dietary patterns but instead was due to differences in the food selection methodology between GRN 498 and the current assessment. The food selection of regular cereals in the present analysis was limited to cereals with added sugar since allulose would not be added to cereals with no added sugar, whereas all cereals excluding low calorie, reduced calorie, and sugar-free cereals were included in the assessment for GRN 498 under regular cereals. The estimated allulose intake from existing background uses in this analysis relies on the most currently available dietary data from NHANES (2015-2018) and shows a lower allulose intake as compared to previously reported allulose EDIs from GRNs 400, 498, 693, and 828.

**Table 10. Two-day average EDI of allulose from background uses by the U.S. population 2+ years and subpopulations**

| | | | Per Capita | | Per User | |
|---|---|---|---|---|---|---|
| | N* | % User | Mean | 90th Percentile | Mean | 90th Percentile |
| Background Allulose EDIs (g/day) | | | | | | |
| U.S. 2+ y | 11650 | 92 | 6.18 | 15.15 | 6.69 | 16.39 |
| Infants <2 y | 391 | 48 | 0.72 | 1.94 | 1.50 | 3.63 |
| Children 2-12 y | 2566 | 95 | 2.89 | 6.71 | 3.04 | 6.98 |
| Adolescents 13-18 y | 1257 | 88 | 3.27 | 7.62 | 3.70 | 8.33 |
| Males 19+ y | 3696 | 92 | 7.97 | 20.70 | 8.68 | 22.71 |
| Females 19+ y | 4131 | 93 | 6.30 | 16.44 | 6.79 | 17.45 |
| Background Allulose EDIs (g/kg-bw/day) | | | | | | |
| U.S. 2+ y | 11650 | 92 | 0.09 | 0.22 | 0.09 | 0.23 |
| Infants <2 y | 391 | 48 | 0.07 | 0.16 | 0.14 | 0.34 |
| Children 2-12 y | 2566 | 95 | 0.11 | 0.27 | 0.12 | 0.28 |
| Adolescents 13-18 y | 1257 | 88 | 0.05 | 0.12 | 0.06 | 0.14 |
| Males 19+ y | 3696 | 92 | 0.09 | 0.23 | 0.10 | 0.25 |
| Females 19+ y | 4131 | 93 | 0.08 | 0.21 | 0.09 | 0.22 |

*Unweighted number of users; % user, *per capita*, and *per user* estimates were based on NHANES 2015-2018 and derived using the statistical weights provided by the NCHS.

***Proposed Uses EDI***

Among the U.S. population 2+ y, 64% consumed one or more foods containing allulose from proposed uses (Table 11). The estimated daily intake of allulose from proposed

uses at the per user mean and 90th percentile of intake among this population is 5.92 g/day (0.10 g/kg-bw/day) and 13.47 g/day (0.22 g/kg-bw/day), respectively. Per user mean intake of allulose from proposed uses ranged from 3.61 g/day among infants < 2 y to 6.94 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.32 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 7.74 g/day among infants <2 y to 16.34 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2 y at 0.66 g/kg-bw/day allulose.

**Table 11. Two-day average EDI of allulose from all intended uses by the U.S. population 2+ years and subpopulations**

| | | | Per Capita | | Per User | |
|---|---|---|---|---|---|---|
| | N* | % User | Mean | 90th Percentile | Mean | 90th Percentile |
| Allulose EDIs from Proposed Uses (g/day) | | | | | | |
| U.S. 2+ y | 7831 | 64 | 3.78 | 10.35 | 5.92 | 13.47 |
| Infants <2 y | 252 | 31 | 1.13 | 2.64 | 3.61 | 7.74 |
| Children 2-12 y | 2078 | 75 | 3.16 | 7.88 | 4.20 | 8.58 |
| Adolescents 13-18 y | 942 | 67 | 3.40 | 9.58 | 5.09 | 11.00 |
| Males 19+ y | 2316 | 63 | 4.37 | 12.39 | 6.94 | 16.34 |
| Females 19+ y | 2495 | 60 | 3.54 | 10.33 | 5.89 | 13.91 |
| Allulose EDIs from Proposed Uses (g/kg-bw/day) | | | | | | |
| U.S. 2+ y | 7831 | 64 | 0.06 | 0.17 | 0.10 | 0.22 |
| Infants <2 y | 252 | 31 | 0.10 | 0.23 | 0.32 | 0.66 |
| Children 2-12 y | 2078 | 75 | 0.13 | 0.30 | 0.17 | 0.34 |
| Adolescents 13-18 y | 942 | 67 | 0.05 | 0.15 | 0.08 | 0.17 |
| Males 19+ y | 2316 | 63 | 0.05 | 0.14 | 0.08 | 0.19 |
| Females 19+ y | 2495 | 60 | 0.05 | 0.15 | 0.08 | 0.19 |

* Unweighted number of users; % user, *per capita*, and *per user* estimates were based on NHANES 2015-2018 and derived using the statistical weights provided by the NCHS.

***Cumulative EDI (CEDI)***

In the U.S. population 2+ y, 95% consumed one or more foods containing allulose from background and/or proposed uses. The allulose CEDI at the per user mean and 90th percentile of intake among this population is 10.09 g/day (0.15 g/kg-bw/day) and 23.53 g/day (0.35 g/kg-bw/day), respectively (Table 4). Per user mean allulose CEDI ranged from 3.33 g/day among infants <2 y to 12.61 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.30 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 7.18 g/day among infants <2 y to 29.86 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2y at 0.65 g/kg-bw/day allulose.

**Table 12. Two-day average CEDI of allulose from background uses and all proposeduses combined by the U.S. population 2+ y and subpopulations**

| | | | Per Capita | | Per User | |
|---|---|---|---|---|---|---|
| | N * | % User | Mean | 90th Percentile | Mean | 90th Percentile |
| Allulose CEDIs (g/day) | | | | | | |
| U.S. 2+ y | 12017 | 95 | 9.60 | 22.65 | 10.09 | 23.53 |
| Infants <2 y | 409 | 50 | 1.66 | 4.75 | 3.33 | 7.18 |
| Children 2-12 y | 2632 | 97 | 5.63 | 12.04 | 5.83 | 12.36 |
| Adolescents 13-18 y | 1320 | 92 | 6.28 | 13.39 | 6.79 | 13.55 |
| Males 19+ y | 3828 | 95 | 12.00 | 28.84 | 12.61 | 29.86 |
| Females 19+ y | 4237 | 95 | 9.48 | 23.27 | 9.99 | 24.05 |
| Allulose CEDIs (g/kg-bw/day) | | | | | | |
| U.S. 2+ y | 12017 | 95 | 0.14 | 0.34 | 0.15 | 0.35 |
| Infants <2 y | 409 | 50 | 0.15 | 0.40 | 0.30 | 0.65 |
| Children 2-12 y | 2632 | 97 | 0.22 | 0.48 | 0.23 | 0.49 |
| Adolescents 13-18 y | 1320 | 92 | 0.10 | 0.22 | 0.11 | 0.22 |
| Males 19+ y | 3828 | 95 | 0.13 | 0.32 | 0.14 | 0.33 |
| Females 19+ y | 4237 | 95 | 0.13 | 0.30 | 0.14 | 0.32 |

*Unweighted number of users; % user, *per capita*, and *per user* estimates were based on NHANES 2015-2018 and derived using the statistical weights provided by the NCHS.

## § 170.240 Part 4, Self-Limiting Levels of Use

The use of allulose in foods is considered to be self-limiting, for technological reasons such as product flavor profile, which could affect consumer acceptability.

## § 170.245 Part 5, Experience Based on Common Use in Food

The statutory basis for our conclusion of the GRAS status of allulose for the proposed food uses in the notice is based on scientific procedures and not common use in food.

# § 170.250 Part 6, GRAS Narrative

## History of Use and Regulatory Approval

Allulose is considered GRAS for use in selected foods for human consumption (FDA, 2012, 2014, 2017, 2020; Table 13). Extensive published information and data have been submitted to and reviewed by FDA as part of the various GRNs for allulose ingredients.

***Table 13. Regulatory approvals for use of allulose in human food***

| Year Approved | Country | Submission |
|---|---|---|
| 2012 | USA | GRN 400; D-psicose |
| 2014 | USA | GRN 498; D-psicose |
| 2017 | USA | GRN 693; D-psicose |
| 2020 | USA | GRN 828; D-psicose |
| 2015 | Mexico | Allulose as a non-nutritive sweetener |
| 2015 | Chile | Allulose as an ingredient |
| 2017 | Colombia | Allulose as an ingredient |
| 2017 | Costa Rica | Allulose as a food ingredient |
| 2017 | South Korea | Allulose as a "processed saccharide product" |
| 2017 | Singapore | Allulose as a food ingredient |

## Safety

*Introduction*

Allulose has been added to food as an alternative sweetener and has a history of safe use. Multiple GRAS "no questions" letters have been issued (GRNs 400, 498, 693, and 828) with respect to the conclusion regarding the safety of the intended uses and use levels of allulose in foods in which it serves as a sugar replacer/sweetener at levels up to 100% (FDA, 2012, 2014, 2017. 2020). Clinical and preclinical studies with allulose have been conducted to examine its general toxicity and gastrointestinal tolerance and are summarized in the following sections, many similar references and discussion can also be found in the GRNs noted above (Tables 14 and 15).

*Absorption, Distribution, Metabolism, and Excretion (ADME)*

GRN Nos. 400, 498, 693, and 828 have previously reviewed and summarized the ADME properties of allulose. Human studies have reported that allulose is rapidly absorbed in

the small intestine and is mostly excreted in urine within 48 hours, although it is not significantly metabolized (Iida et al., 2010). Additionally, several rodent studies indicate that allulose is absorbed after oral administration and eliminated after both oral and intravenous administration (Matsuo et al., 2003; Tsukamoto et al., 2014; Whistler et al., 1974).

Animal studies

Whistler et al. (1974) conducted a study with intravenous administration of 15 mg of $^{14}C$-labeled allulose to rats (150–200 g bodyweight), collecting urine samples and carbon dioxide exhaled for six hours following the intervention for analysis. It was demonstrated that only 0.6% of the monosaccharide was excreted through respiration; the vast majority (97%–98%) was eliminated through the urine (35.4%), which suggests that the allulose is metabolized in small quantities and eliminated very quickly through the kidneys. In the same study, following oral administration of the monosaccharide, about 70% was excreted in the urine in the first 7 hours, demonstrating that allulose passed through the wall of the small intestine and as in the intravenous administration, entered the bloodstream and was eliminated primarily by the kidneys (Whistler et al., 1974).

Following oral administration to Wistar rats, Matsuo et al. (2003) investigated the absorption, excretion, and fermentation of allulose. In the absorption test, 18 animals (6 weeks old; average weight 140 ± 4 g) were given a single dose of 5 g/kg bw of allulose, then divided into three groups for the collection of blood samples and quick removal of the organs at 1, 3, and 7 hours after ingestion (Matsuo et al., 2003). A progressive reduction in the serum concentration of allulose was observed, with a more pronounced drop after the first hour, as well as in the level contained in the small intestine, with quantities of the monosaccharide being detected at 6%–10% after 1 hour, 2%–3% after 3 hours, and 1%–3% after 7 hours. In the stomach, levels of 26%-37% were found after 1 hour, 0.4%-0.6% after 3 hours, and nothing after 7 hours post-intervention. By comparison, in the cecum, despite not having been detected after the first hour, there was an increase in the concentration of the monosaccharide after 3 (11% to 18%) and 7 hours (10% to 19%) (Matsuo et al., 2003).

Tsukamoto et al. (2014) administered $^{14}C$-labeled D-psicose intravenously and by oral gavage at a dose of 100 mg/kg bw to Wistar rats. After oral administration, D-psicose appeared rapidly in the bloodstream, while peak liver and kidney concentrations occurred 60 minutes post-administration. At 120 minutes, D-psicose concentrations decreased in the liver and kidney and were highest in urine, indicating rapid elimination (Figure 3). Seven days after oral administration, the appearance of D-psicose in the body was less than 1% of the original dose. Following intravenous administration, the D-psicose concentration in the blood was decreased with a half-life of 57 minutes, and the excretion in urine was approximately 50% within 1 hour. Similar to the results obtained following oral administration, accumulation in organs was primarily in the liver (Tsukamoto et al., 2014).

In an excretion test conducted by Matsuo et al. (2003), samples of urine and feces were collected at 24–hour intervals for three days from eight Wistar rats, six weeks old, and having an average weight of 138 ± 4 g, that had been given a single dose of 5 g/kg bw of allulose. Twenty-four hours after administration, 11%–15% of the quantity ingested was detected in the urine, and 8%–13% in the feces. In the following two periods (48 and 72 hours), no additional residual monosaccharide was found, thus suggesting that practically all of the allulose was eliminated during the first hour.

Human studies

In a study by Iida et al. (2010), following oral ingestion of 0.08, 0.17, or 0.33 g/kg bw of D-psicose, excretion rates in urine were measured for up to 48 hours in 14 humans. In the first 12 hours, urine excretion rates ranged from 54% to 63%, depending on dose, then decreased to 3% to 6% by 24 to 48 hours following administration. Cumulative excretion rate measured at 48 hours for the lowest dose (0.08 g/kg bw) was 78.8% ± 11.7%, whereas the 0.33-g/kg bw dose was 66.2% ± 12.6% (Iida et al., 2010).

To evaluate the absorption, distribution, metabolism, and excretion (ADME) of allulose in humans, a single dose containing 15 g Dolcia Prima® allulose containing a defined quantity of marked [$^{14}$C(U)] allulose was administered to eight healthy male adult individuals (Atiee, 2015; unpublished). In the first 6 hours after ingestion, exhaled air, as well as samples of blood, urine, and feces, were collected at previously established times over the course of the first 7 days. Analytical results from the blood samples showed that the monosaccharide was absorbed quickly, with the maximum mean plasma concentrations reached in the first hour after ingestion (Atiee, 2015; unpublished).

Work in humans by Atiee, 2015 (unpublished), suggested further that allulose is not metabolized for energy in humans as only 6% of a total of 80 samples of exhaled air collected following the administration of $^{14}$C-labeled allulose showed detectable levels of measurable $^{14}CO_2$. Levels above the minimum detection limit of the equipment (50 disintegrations per minute [dpm]) were detected and reported. Of the five samples with detectable levels of measurable $^{14}CO_2$, the highest concentration found was only 79.29 dpm which indicated that allulose is not metabolized for energy in humans (Atiee, 2015; unpublished).

After analysis of human samples of urine and feces, collected following the administration of $^{14}$C-labeled allulose, Atiee, 2015 (unpublished) confirmed that the urinary tract represents the primary route of allulose elimination. For seven participants, 84% to 93% of the ingested dose was recovered in the urine and feces samples. Only one individual showed very low recovery in the urine, less than 50% of the marked $^{14}$C, when compared to all of the other participants. This was most likely due to incomplete urine collection by this subject who was therefore considered to be an outlier of the group studied (Atiee, 2015; unpublished).

The ADME studies described above demonstrate that there are similarities in how allulose is absorbed, metabolized, and eliminated from the body in both animals and humans.

## Animal Studies

*Acute Toxicity*

The acute toxicity of allulose was investigated by Matsuo et al. (2002a). Five groups of eight male Wistar rats each were administered a single oral dose of allulose (8, 11, 14, 17, or 20 g/kg bw). Three rats receiving 14 g/kg bw, three rats receiving 17 g/kg bw, and eight rats receiving 20 g/kg of allulose died within 2 days of allulose administration. The authors calculated the $LD_{50}$ value of 16.3 g/kg by the Behrens-Karber method and 15.8 g/kg by the Litchfield-Wilcoxon method.

These $LD_{50}$ values are of the same magnitude as for other commonly consumed carbohydrates (e.g., fructose [14.7 g/kg-bw] and erythritol [15.3 g/kg-bw]). Compounds with $LD_{50}$ values of >5 g/kg bw in rats are classified as "practically non-toxic," and compounds with $LD_{50}$ values of >15 g/kg bw as "relatively harmless" (Altug, 2003).

Nishi et al. (2016) conducted a study in dogs, reporting that a single oral dose of 1 or 4 g/kg bw allulose did not cause any treatment-related abnormalities in dogs. All dogs were active and had good appetites throughout the study period. Blood glucose concentrations decreased slightly, without a rise in plasma insulin concentration 2 hours after D-allulose administration. Plasma alkaline phosphatase activities showed a mild and transient increase between 12 and 48 hours after D-allulose administration. The data suggest that a single oral dose of up to 4 g/kg bw of D-allulose does not result in severe toxicity in dogs.

*Subchronic toxicity*

A 90-day oral sub-chronic toxicity study was undertaken with allulose (Matsuo et al., 2012). In this study, male Wistar rats (3 weeks old) were fed diets containing either 3% allulose or sucrose for 90 days. The body-weight gain and intra-abdominal adipose tissue weight did not differ between the sucrose and the allulose groups. The weights of the liver and kidneys were significantly higher in the allulose group than in the sucrose group. However, no gross pathological findings were evident at dietary doses of 3% allulose or were correlated with hypertrophy of the liver and kidney. The erythrocyte and leukocyte counts were observed to be statistically higher in the allulose group, but the authors concluded that the differences from the control group were small and considered not toxicologically significant. Therefore, the authors concluded that no adverse effects were shown, and the authors derived a NOAEL for allulose as 3% of the diet (equivalent to 1,670 mg/kg bw/day) which was the highest level tested.

Another 90-day oral sub-chronic toxicity study was undertaken to investigate a high allulose syrup (85%) in male Wistar rats (Matsuo and Ishii, 2011), as compared to the previous study diet containing 3% of allulose (see above Matsuo et al., 2012). The body weight gain and intra-abdominal adipose tissue weight did not differ between the control and allulose group. Also, weights of the tissues did not differ. In clinical chemistry and hematological analyses, no differences were found. No gross pathological findings were evident at dietary doses of 4.3% allulose syrup (approximately 2,000 mg/kg bw/day). The

authors conclude that similar to the 3% allulose (powder) diet, a diet containing 85% concentrated allulose syrup (average 3.7% allulose) did not induce any adverse effects.

Sub-chronic toxicity was assessed in a 34-day feeding study in 4-week-old Wistar rats (Matsuo et al., 2002a). Eight groups of seven male Wistar rats/group were fed a diet containing 0 (control), 10%, 20%, 30%, and 40% allulose. One rat on the 30% allulose diet and five rats on the 40% allulose diet died during the experimental period. It should be noted that the 30 and 40% dietary levels administered were extremely high, resulted in the deaths described above, and can be considered inappropriate for a toxicity study of this design. Higher concentrations of allulose resulted in decreased body weight gain and food efficiency. The authors concluded that the decreases in body weight gain in the 10% and 20% groups were attributable to a decrease in food intake and were not considered to be of toxicological significance. A laxative effect was noted but was transient and was not observed after 4 days. Rats fed the 30% and 40% allulose diet were able to regain body weight and food intake during the first 7 days of the feeding period, suggesting that the effects may have been transitory. The authors reported that allulose concentrations of up to 20% of the diet did not show adverse effects.

*Chronic toxicity*

Long-term toxicity of allulose was investigated by Yagi and Matsuo (2009) in male Wistar rats receiving a diet containing 3% allulose (or 1,280 mg/kg bw/d) or 3% sucrose (1,220 mg/kg bw/day) for 12–18 months. The authors found that allulose administration resulted in a lower body weight gain and lower intra-abdominal adipose tissue weight than in rats fed the sucrose diet. Relative weights of liver and kidney were significantly higher in the allulose group than in the sucrose group, but this was not considered toxicologically significant. General hematology or serum chemistry tests were within the normal ranges for all animals and did not differ between the sucrose and allulose groups. Hemoglobin (Hb) and mean corpuscular volume (MCV) at 18 months were significantly greater in the allulose group than in the sucrose group, but no differences were observed in any of the related hematology values. The histopathological data demonstrated that there were no toxicologically significant findings in rats fed 3% allulose. The authors concluded that administration of allulose at 3% in the diet for 12–18 months (1,280 mg/kg bw/day) did not result in any adverse effects in rats.

***Table 14. Summary of the toxicity studies supporting the safety of allulose***

| Animals | Doses | Duration | Endpoints Evaluated | Results Found | Reference |
|---|---|---|---|---|---|
| Dogs | 1 and 4 g/kg bw | One day by gavage | Acute toxicity-food intake and selected clinical chemistry | Safe up to the tested dose of 4 g/k bw | Nishi et al. (2016) |
| Male *Wistar* rats | 8, 11, 14, 17 & 20 g/kg bw | One day by gavage | Acute toxicity | $LD_{50}$ = 16.3 g/kg bw | Matsuo et al. (2002a) |
| Young *Wistar* rats | 10%, 20%, 30% and 40% in the diet | 34 days | Food intake, weight gain, and organ weights | No adverse effects reported up to 20% in diet | Matsuo et al. (2002b) |

| | | | | | |
|---|---|---|---|---|---|
| Male *Wistar* rats | 3.0% or 4.3% in the diet | 90 days | Serum biochemistry, hematology, histology, and macroscopic exams | Safe up to the tested dose of 4.3% (estimated to be approx. 2 g/kg bw/d) | Matsuo and Ishii (2011) |
| Male *Wistar* rats | 3.0% (1.67 g/kg bw/d) in the diet | 90 days | Serum biochemistry, hematology, histology, and macroscopic exams | Safe at the tested dose of 3% (1.67 g/kg bw/d) | Matsuo et al (2012) |
| Male *Wistar* rats | 3.0% (1,280 mg/kg bw/d) in the diet | 12-18 months | Food intake, weight gain, organ weights; serum biochemistry, hematology, histology | Safe at the tested dose (NOAEL >1,280 mg/kg bw/d) | Yagi and Matsuo (2009) |

*Reproductive toxicity*

Kim et al. (2019) evaluated the reproductive toxicity of D-allulose in rats. They assessed reproduction and offspring growth following gavage administration of D-allulose to parental rats at dosage levels of 0, 500, 1000, and 2000 mg/kg-bw. Female rats were dosed continuously from 2 weeks prior to mating until day 21 of lactation, while males were dosed for the 10-week period before mating. No direct toxicity or mortality was evident following D-allulose administration, and no changes in body weight or food consumption were observed in the test article or control groups. No significant alterations in precoital time, copulation index, fertility index (male), or pregnancy index (male) were observed between groups. Relative to the control group, there was also no effect of D-allulose treatment on pregnancy rates, implantation, pregnancy length, gender ratios, viability indexes, lactation indexes, prenatal death rates, or the number of live young at time of birth. Organ weights and associated indexes were also comparable between groups at the time of sacrifice, and treatment with D-allulose was not linked to any obvious manifestations on necropsy or histopathological examination. In the F1 generation offspring, the body weights of pups born to parents administered D-allulose (500, 1000, and 2000 mg/kg-bw) were slightly higher on days 1–9 postnatally, relative to controls ($p < 0.05$),; however, after day 9, the body-weight effects were no longer evident. The NOAEL for D-allulose was considered to be 2000 mg/kg-bw, the highest dose level tested, for both parental animals and their offspring.

*Mutagenicity/genotoxicity*

GRN 400 included the results of an Ames test that did not find evidence of mutagenic potential, and also reported on both a micronucleus test and chromosomal aberration test that found no evidence of genetic toxicity following exposure to allulose.

As yet unpublished studies of mutagenicity and genotoxicity were conducted *in vitro* and are considered supportive of the lack of genotoxicity of allulose as demonstrated in previous allulose GRNs (Nos. 400, 498, 693). The results of an Ames assay and micronucleus test did not show any evidence of mutagenic or genotoxic potential (Li, 2015-unpublished; Neft, 2015-unpublished).

## Human Studies

Clinical studies conducted in humans have also evaluated the tolerability and occurrence of adverse effects related to consumption of allulose by healthy populations.

In general, the studies demonstrated the acceptability of different quantities of allulose. Like other ingredients, such as polyols and other monosaccharides (e.g., fructose, tagatose), or fibers and some digestion-resistant oligosaccharides, the consumption of large quantities of the ingredient can cause gastrointestinal discomfort, this effect being a temporary symptom of the adaptation of the gut flora and therefore without toxicological significance.

Previously, and even at the beginning of the 20$^{th}$ century, it was very common to consume greater quantities of raw, whole foods and foods rich in non-digestible fiber and carbohydrates, and the gastrointestinal systems of the population were better adapted to dealing with high concentrations of such compounds without presenting any temporary symptoms or discomfort through the ingestion of high doses (e.g., 120–160 g/day; Leach and Sobolik, 2010; Shoemaker, 1927). Over time, due to changes in eating habits and lifestyle, and with a significant reduction in the ingestion of fiber and other non-digestible carbohydrates, there has been a proportional reduction in the tolerance levels of the gut flora to the consumption of non-digestible ingredients.

More recent studies have demonstrated the ability of the gut flora to adapt to various levels of allulose over time, such as the clinical study of Iida et al. (2007) summarized below, which observed good tolerability for daily consumption of up to 31.0–33.3 g/day of allulose in healthy individuals.

Han et al. (2018) investigated gastrointestinal tolerance in 30 healthy adults (15 males and 15 females), ages 21–30 years old. Two experiments were conducted. In the first experiment, the study participants were given daily single doses of allulose starting at 0.1 g/kg bw/day and increasing by 0.1 g/kg bw/day every week until gastrointestinal symptoms were observed, at which time the study was terminated. In the fifth week, some participants developed gastrointestinal symptoms, and the study was stopped. The maximum tolerated dose in this study was 0.4 g/kg bw/day (when all of the allulose was consumed as a single dose). This maximum tolerated single dose was then used by Han et al. (2018) to conduct a second study in which the same protocol was followed as the first study, with the difference that, this time, the allulose was consumed in portions throughout the day, similar to how meals and snacks are consumed by people. In this case, the maximum tolerated dose was 0.9 g/kg bw/day, or about 54 g/day for a 60-kg adult.

Iida et al. (2007) investigated the effects of the use of allulose on gastrointestinal symptoms in five healthy men and five healthy women, aged between 20 and 30 years. For this purpose, all of the volunteers were given, at the beginning, 0.4 g/kg bw/day of allulose, increasing 0.1 g/kg bw/day up to a maximum of 0.9 g/kg bw/day, for six days. All of the test sample was consumed by the participants in a single sitting during the day. While two participants did not report any adverse effects, even at the highest doses, some

cases of diarrhea were reported with the administration of doses between 0.6 and 0.8 g/kg bw/day: one man ingesting 0.6 g/kg bw/day, two women at 0.7 g/kg bw/day, and two men and three women at 0.8 g/kg bw/day. The study concluded that the maximum tolerance levels were 0.5 g/kg bw/day (or 33.3 g/day), for men, and 0.6 g/kg bw/day (or 31.0 g/day), for women.

This clinical study of Iida et al. (2007) established a dose-response relationship for the onset of diarrhea in humans, showing that in men the maximum tolerated dose was 0.5 g/kg bw, whereas in women, it was 0.6 g/kg bw (above these doses, gastrointestinal effects such as abdominal pain, gas formation, and diarrhea occurred). Thus, it was established that, for humans, the NOAEL for allulose is 0.5 g/kg bw (33.3 g/day) for men and 0.6 g/kg bw (31 g/day) for women (Iida et al., 2007; FDA, 2012, 2014, 2017).

It is noteworthy that these no-effect levels for human subjects from Iida et al. (2007) are based on single doses of allulose, where the daily dose was consumed completely in one sitting. The actual threshold is even higher if the allulose was consumed in portions throughout the day, as one would when consuming meals and snacks daily (Han et al., 2018).

Another clinical safety study of long-term use was performed with 17 healthy volunteers, evaluating the effects of consuming 15 g/day of allulose (n=8) or glucose (n=9) for 12 consecutive weeks. According to the results observed, there were no adverse effects or changes in several hematological and biochemical parameters used in clinical toxicology studies (Hayashi et al., 2010). Four years later, a randomized, double-blind clinical trial in 34 individuals (n=17 each for allulose and control groups) evaluated the effect of 30 g/day of syrup containing 6% allulose (i.e., 1.8 g/day of allulose) and various amounts of other sugars for 12 weeks. During the treatment phase, the subjects consumed either a test drink or a control drink 30 minutes before breakfast on a daily basis. No adverse effects were found in relation to hepatic and renal function, nor any alterations in the biochemical and hematological parameters of the group consuming 1.8 g/day of allulose (Hayashi et al., 2014).

A typical dose of allulose (0.35 g/kg bw, in 100 mL solution) during a clinical study with healthy volunteers revealed that intestinal absorption may range from 66.2% to 80% of the dose initially ingested, while not being converted to energy. The absorption rate of different types of sugars correlates well with the provided laxative effect and the consequent no-observed-effect level. This is because the lower the absorption rate, the greater the intestinal fermentation and, consequently, the laxative effect, hence, lowering the no-effect level. For sorbitol, for example, which has a low intestinal absorption rate, the NOAEL is 0.15–0.17 g/kg bw for men, and 0.24–0.30 g/kg bw for women. For erythritol, which is better absorbed in the small intestine (90%), the NOAEL for tolerance is 0.66 g/kg bw for men, and 0.8 g/kg bw for women. Therefore, with an absorption rate slightly lower than that of erythritol, allulose would also be expected to have a slightly lower threshold for GI intolerance. This is reflected in the previously reported NOAEL of 0.5 g/kg bw (33.3 g/day) for men and 0.6 g/kg bw (31 g/day) for women (Iida et al., 2007; FDA, 2012, 2014, 2017).

In summary, the studies (Table 17) demonstrated the tolerability of different quantities of allulose. Like other ingredients, such as polyols and other monosaccharides (e.g., fructose, tagatose), or fibers and some digestion-resistant oligosaccharides, the consumption of large quantities of the ingredient can cause certain gastrointestinal discomfort; this effect is a temporary symptom of the organism adapting and therefore is without toxicological significance.

*Table 15. Clinical trials conducted with administration of Dolcia Prima® allulose*

| References | Main Characteristics of the Human Studies on Allulose | Doses with No Adverse Effects in Human Subjects |
|---|---|---|
| **Human Studies on Allulose** | | |
| Iida et al. (2008) | – Total combined n=28;<br>– Doses 0, 2.5, 5.0, and 7.5 g;<br>– Ages 20–39;<br>– Healthy individuals (male and female). | 7.5 g (highest single dose tested) |
| Hayashi et al. (2010) | – n=17;<br>– Healthy individuals-men and women-given allulose (n=8) or glucose (n=9);<br>– Dose 15 g/day, for 12 weeks. | 15 g/day (one dose level tested) |
| Iida et al. (2007) | – n=10 (5 males and 5 females);<br>– Age 20-30 years;<br>– Given 0.4–0.9 g/kg bw/day in increments of 0.1 g/kg bw/day;<br>– Dosing was once a day at 10 am, followed by 1 week of no allulose ingestion, and then the higher dose was consumed;<br>– 6 treatment days, over 6–7 weeks. | Up to 0.5 g/kg bw/day was tolerated well by men, and 0.6 g/kg bw/day was tolerated well by women, when consumed as a single dose. This equates to up to 33.3 g/serving, for men and 31 g/serving for women (based on the study participants, or about 30-36 g/serving for 60-kg bw adults in general) |
| Hayashi et al. (2014) | – N=34 (males and females; 17 in allulose group and 17 in control group)<br>– Given 1.8 g/day of allulose in 30 g of syrup, over 12 weeks. | 1.8 g/day (one dose level tested) |
| Han et al. (2018) | – n=30 (15 males and 15 females);<br>– Age 21-30 years;<br>– Given daily doses of allulose increasing every week until gastrointestinal symptoms observed;<br>– Study duration about 8 weeks, for allulose consumption throughout the day, and about 5 weeks, for single daily dose exposures. | 0.9 g/kg bw/day, or 54 g/day, for a 60-kg bw adult, when allulose is consumed in portions throughout the day.<br>0.4 g/kg bw/day, or 24 g, for a 60-kg bw adult well-tolerated, as a single bolus dose consumed at one time. |
| **Human Studies on Dolcia Prima® Allulose** | | |
| Kendall et al. (2014) | – n=10;<br>– Healthy subjects given allulose or glucose. | 25 g (single dose tested) |
| Wolever et al. (2014) | – n=12 healthy adults; N=12 adults with type II diabetes<br>– Given allulose or glucose. | 25 g (single dose tested) |
| Noronha et al. (2018) | – n=24;<br>– Given single doses of 0, 5.0 or 10 g allulose, in a solution containing 75 g glucose. | 10 g (highest dose tested) |

## Effect on Insulinemic and Glycemic Response

In addition to the more classical ADME studies, other clinical studies and experiments on animals have been conducted to observe the effects of allulose on glycemia and/or insulinemia.

*Animal studies*

Matsuo and Izumori (2009) conducted a research study on the effects of allulose on the postprandial glycemic response in 6-month-old male Wistar rats. Animals were given 2.0 g/kg bw of sucrose, maltose, or soluble starch supplemented with 0.2 g/kg bw of allulose or fructose. An inhibitory effect of allulose was observed on the glycemic response of the other sugars, significantly suppressing the increase in glycemia that normally occurs after the ingestion of carbohydrates. In the case of starch, while not statistically significant, a trend was observed indicating the same inhibitory effect of a reduction in the glycemic response by allulose. Based on the findings of Matsuo and Izumori (2009), it can be concluded that allulose does not induce a glycemic response per se, and also suppresses the glycemic response of other carbohydrates.

Baek et al. (2010) reported the results of a comparative study on the effects of ingesting different types of carbohydrates on glycemic response, the release of insulin, and lipid profiles using as a a model diabetic *C57BL/6J* rats. Rats were orally administered 200 mg/kg bw of allulose, glucose, fructose, or water (control), for 28 days. In addition to no adverse effects being observed that were associated with the intervention with the monosaccharide used, they also demonstrated that allulose was capable of maintaining the initial glycemic level between 276 and 305 mg/dL for the entire intervention period, whereas all of the other test groups showed glycemia that was twice as high ($p < 0.05$). Moreover, allulose was demonstrated to be safe, significantly increasing the tolerance to glucose ($p < 0.05$) and even reversing the hepatic concentrations of triglycerides (37.9%) and total cholesterol (62.9%) without any effect on the serum insulin concentration (Baek et al., 2010).

Human studies

Iida et al. (2008) published the results of their study on the effects of ingesting allulose on glycemic and insulinemic response in healthy individuals. In this blind, crossover, and randomized study, eleven men and nine women aged between 20 and 39 years consumed a single dose of four test beverages containing 75 g of maltodextrin and supplemented with 0 g, 2.5 g, 5 g, or 7.5 g of allulose, with minimum intervals of one week between the different forms of intervention. In parallel, eight participants were given 7.5 g of allulose in isolated form to evaluate the effect of consuming the pure monosaccharide on the concentration of plasma insulin and glucose (Iida et al., 2008). Blood samples were collected before initiation of the intervention and also at an interval of 30 minutes, up to 2 hours after the interventions. The results showed that, besides the absence of adverse effects related to the intervention, the independent consumption of the monosaccharide did not influence the glycemic and insulinemic levels of the individuals (Iida et al., 2008).

Another clinical research study was conducted by Hayashi et al. (2010) to investigate the safety and effect of allulose on postprandial blood glucose levels in adult men and women, including borderline diabetic patients. A randomized double-blind, placebo-controlled, crossover experiment of single ingestion was conducted on 26 subjects who consumed 0 or 5 g of allulose in tea with a standard meal. Blood glucose levels at fasting and 30, 60, 90, and 120 min after the meal were compared. The blood glucose level was significantly lower 30 and 60 min after the meal with allulose ($p < 0:01$, $p < 0:05$), and a significant decrease was also shown in the area under the curve ($p < 0:01$). The results suggest that allulose had the effect of suppressing the postprandial blood glucose elevation, mainly in borderline diabetic cases. Another randomized double-blind placebo-controlled parallel-group experiment of long-term ingestion was conducted on 17 normal subjects who ingested 5 g of allulose (n=8) or D-glucose (n=9) with meals three times a day (total 15 g/day) for 12 continuous weeks. No adverse effects or clinical problems from the continuous ingestion of allulose were reported (Hayashi et al., 2010).

In a double-blind, randomized, multi-center, controlled study that evaluated and tested the effect of single doses of 0 (control), 5.0, or 10 g of allulose, added in a solution containing 75 g of glucose, at glycemia up to 120 minutes in 24 subjects (12 males and 12 females aged 66 ± 1.2 years; BMI 27.0 ± 0.9 kg/m$^2$; diabetes duration 11.3 ± 1.7 years; HbA1c 50.0 ± 1.3 mmol/mol [6.7 ± 0.1%] with type-2 diabetes (Noronha et al., 2018). The study showed that allulose is able to reduce significantly the plasma glucose iAUC by 8% at 10 g, when compared with the control (717.4±38.3 versus 777.5±39.9 mmol·min/L, p=0.015) with a linear dose-response gradient between the reduction in plasma glucose iAUC and dose (p=0.016). Allulose also significantly reduced several related secondary and exploratory outcome measures at 5.0 g (plasma glucose absolute mean and total AUC) and at 10 g (plasma glucose absolute mean, absolute and incremental maximum concentration [Cmax], and total AUC) ($p<0.0125$). There was no effect of fructose at any dose. Although allulose showed statistically significant reductions in plasma glucose iAUC compared with fructose at both 5.0 g, 10 g, and pooled doses, these reductions were within the prespecified equivalence margins of ±20%.

Two unpublished clinical studies were conducted to evaluate the glycemic response of Dolcia Prima® allulose in healthy individuals and diabetics (Kendall et al., 2014-unpublished; Wolever et al., 2014-unpublished).

While the first study evaluated the effects on glycemia in 10 healthy adult individuals, the second study measured the glycemia and insulinemia of 12 healthy adults and 12 patients with type-2 diabetes. In both studies, beverages supplemented with 25 g of Dolcia Prima® allulose, or 25 g of glucose (control) were administered, with the glycemic and/or the insulinemic response measured before and 15, 30, 45, 60, 90, and 120 minutes after the intervention. It was demonstrated that the ingestion of 25 g of the allulose did not cause a glycemic or insulinemic peak above fasting levels in either the healthy or diabetic population (Kendall et al., 2014-unpublished; Wolever et al., 2014-unpublished).

After reviewing the effects of allulose on glycemia and insulinemia, Chung et al. (2012) concluded that the monosaccharide contributed to maintaining appropriate levels of plasma glucose and insulin, characterizing it as a safe and strategic alternative ingredient for substitution of the sugars in the diet of individuals who are at high risk of developing type-2 diabetes.

## Safety Summary

Based on the preclinical and clinical safety studies summarized above, the following can be concluded:

- Regulatory authorities have reviewed the safety of allulose and found it to be safe for use in human food. Numerous studies and publications support the safety of allulose, including *in vitro* studies, *in vivo* animal studies, and clinical studies in humans.

- A summary of the most relevant studies on allulose ADME, acute and subchronic toxicity, reproductive and developmental toxicity, mutagenicity and genotoxicity, and chronic toxicity in animals along with clinical studies have been summarized and reviewed. The compositional profile of allulose presents no obvious safety concerns. As a result, allulose has been reviewed and approved in several countries for addition to food for human consumption.

- ADME data on allulose are available in both animals and humans, and the data are similar for both.

- Allulose is rapidly absorbed such that large bolus doses are more likely to have an impact on laxation than smaller cumulative doses. As such, clinical studies have demonstrated that the tolerability of allulose is highly dependent on the mode and timeline of ingestion. Individual tolerance develops with continued ingestion over time. Mild GI intolerance is considered a physiological response to osmotic loading, is of no toxicological significance, is generally self-limiting, and not severe or indicative of toxicity per se but is a short-term individual tolerability issue similar to other foods (dried fruit) or food ingredients (fructose), and other sweeteners such as polyols like sorbitol, mannitol, erythritol, and xylitol.

- No adverse effects attributable to allulose were observed in multiple animal studies including in 90-day studies (1670 - 2000 mg/kg bw/day) and in a chronic study (approximately 1300 mg/kg bw/day).

- Data are available from a number of human studies in both sexes, healthy individuals, and sensitive subpopulations such as diabetics.

- No effects were observed in multiple human studies, except gastrointestinal intolerance at very high dose levels. Gastrointestinal intolerance is related to the presence of excess indigestible material in the gastrointestinal tract and is

temporary and reversible. This type of symptom is usually transient and is not considered to be of toxicological significance (IOM, 2002). It is not unique to allulose; similar effects are observed with other sweeteners, such as polyols like sorbitol, mannitol, and xylitol.

- Allulose can be considered safe for human consumption at up to 63 g/day, when consumed in portions throughout the day as one would typically, based on multiple meals or snacks throughout the day (Han et al., 2018), and up to 24–36 g (0.4 – 0.6 g/kg/day for a 60 kg individual) can be consumed in one sitting (Han et al., 2018; Iida et al., 2007).

- In summary, the published study data, additional unpublished supporting data, and previous reviews by regulatory authorities (e.g., GRN Nos. 400, 498, 693, 828), support the conclusion that Tate & Lyle's allulose ingredient is safe for its intended use as a sweetener, at the proposed use levels in specified foods.

# Basis for the GRAS Determination

## Introduction

The regulatory framework for determining whether a substance can be considered GRAS in accordance with section 201(s) (21 U.S.C. § 321(s)) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301 et. Seq.) ("the Act") is set forth at 21 CFR 170.30, which states:

> General recognition of safety may be based only on the view of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. The basis of such views may be either (1) scientific procedures or (2) in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food. General recognition of safety requires common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food.
>
> General recognition of safety based upon scientific procedures shall require the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation for the ingredient. General recognition of safety through scientific procedures shall ordinarily be based upon published studies, which may be corroborated by unpublished studies and other data and information.

These criteria are applied in the analysis below to determine whether the use of allulose in selected human food that is the subject of this GRAS determination is GRAS based on scientific procedures. All data relied upon in this GRAS determination are publicly available and generally known, and therefore meet the "general recognition" standard

under the Federal Food, Drug, and Cosmetic Act. Unpublished study data are included only as supportive and corroborative of the publicly available data and information.

## Safety Determination

The subject of this GRAS determination is the use of allulose as a sweetener in selected foods. Allulose is currently marketed for use in food for human consumption. This GRAS determination supports additional new uses. Regulatory authorities have reviewed the extensive safety database on allulose and found no issues of concern with respect to its use in human food at the proposed use levels. Numerous studies have been conducted and published and unpublished data are available that provide support for the safety of the intended uses of allulose, including *in vitro* studies and *in vivo* animal studies (i.e., acute and subchronic toxicity, mutagenicity and genotoxicity, chronic toxicity), as well as clinical studies in adults.

Allulose is considered GRAS for use in food for human consumption (GRNs 400, 498, 693, 828) (FDA, 2012, 2014, 2017, 2020). To date, Tate & Lyle's allulose ingredient has been approved for direct use in foods by the U.S. FDA, and regulatory bodies in Mexico, Chile, Columbia, Costa Rica, Singapore, and South Korea.

The safety of orally administered allulose has been characterized extensively in the publicly available preclinical and clinical study literature. The compositional profiles and specifications for both Tate & Lyle's proposed allulose syrup and crystalline products present no obvious safety concerns. Finally, similar allulose products have been reviewed and approved around the world for addition to food.

## General Recognition of the Safety of Allulose

The intended use of the allulose ingredient in human food has been determined to be safe through scientific procedures set forth in 21 CFR§170.3(b), thus satisfying the so-called "technical" element of the GRAS determination, based on the following:

- Allulose is manufactured from corn, following current cGMP for food (21 CFR § Part 110). The raw materials and processing aids used in the manufacturing process are food grade and/or approved for use in food. The allulose ingredient has been characterized appropriately, contains a minimum of 95%–98% alluose (syrup and crystalline forms, respectively), and meets appropriate food-grade specifications.

- There is a body of common knowledge of historical human consumption of allulose from foods containing allulose. Allulose is naturally present in small quantities in many common foods, such as in dried fruits (e.g., figs, raisins, fried dough, brown sugar, and ketchup). The additional intended uses will be in sweetened alcoholic malt beverages; alcoholic premixed cocktails; ready-to-eat (RTE) and cooked cereals including regular and low calorie, reduced calorie, and sugar-free RTE and cooked cereals; grain-free, no sugar, high protein RTE

cereals; nutrition bars; ketchup and barbecue sauces; dried cranberries; meat- and poultry-based jerky, and nutritional beverages.

- Allulose is rapidly absorbed such that large bolus doses are more likely to have an impact on laxation than smaller cumulative doses. As such, clinical studies have demonstrated that the tolerability of allulose is highly dependent on the mode and timeline of ingestion. Individual tolerance develops with continued ingestion over time. Mild GI intolerance is considered a physiological response to osmotic loading of no toxicological significance, is generally self-limiting, and not severe or indicative of toxicity per se, but is a short-term individual tolerability issue as with other foods (dried fruit) or food ingredients (fructose), and other sweeteners such as polyols like sorbitol, mannitol, and xylitol.

- Allulose is currently added to food, and multiple GRAS "no-questions" letters have been issued (GRNs 400, 498, 693, 828) that support the safe use of allulose in foods in which it serves as a sugar replacement/sweetener at 90$^{th}$ percentile daily intake levels for ages 2+ of up to approximately 30 g/day. GRN 498 stated the following, "*A potential side effect of D-allulose is gastrointestinal discomfort when ingested in large quantities. It is well-known that this type of side effect is transient. As consumption levels of non-digestible carbohydrates decreased throughout the 20th century, human tolerance levels also decreased. This tolerance and loss of tolerance suggests that the gastrointestinal symptoms associated with high intakes of non-digestible carbohydrates are likely transient and can improve over time. This type of symptom is usually transient and is not considered to be of toxicological significance*".

- The clinical study of Iida et al. (2007) established a dose-response relationship for the onset of diarrhea in humans, showing that in men the maximum tolerated dose was 0.5 g/kg bw, whereas in women, it was 0.6 g/kg bw (above these doses, gastrointestinal effects such as abdominal pain, gas formation, and diarrhea occurred). Thus, it was established that, for humans, the NOAEL for the onset of diarrhea in humans from consuming allulose is 0.5 g/kg bw (33.3 g/day) for men and 0.6 g/kg bw (31 g/day) for women (Iida et al., 2007; FDA, 2012, 2014, 2017).

- Among the U.S. population 2+ y, 95% consumed one or more foods containing allulose from background and/or proposed uses. The allulose CEDI at the per user mean and 90th percentile of intake among this population is 10.09 g/day (0.15 g/kg-bw/day) and 23.53 g/day (0.35 g/kg-bw/day), respectively. Per user mean allulose CEDI ranged from 3.33 g/day among infants <2 y to 12.61 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.30 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 7.18 g/day among infants <2 y to 29.86 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2y at 0.65 g/kg-bw/day allulose.

- In the current analysis, a downward shift of allulose intake was observed

using more recent NHANES data (i.e., NHANES 2015-2018) as compared to total allulose intakes reported by GRNs 400, 498, 693, and 828. The total per user mean and 90$^{th}$ percentile intake estimates of allulose based on older NHANES 2007-2010 data and reported for the U.S. population by GRNs 400, 498, 693 and 828 ranged from 9 - 12.55 g/day and 24.8 - 30 g/day, respectively. Allulose intake estimates from background uses in the present analysis (NHANES 2015-2018) at the per user mean and 90$^{th}$ percentile are 6.69 g/day and 16.39 g/day, respectively. These estimates at the per user mean and 90$^{th}$ percentile are at least 26% and 34% lower, respectively, than those estimates in the previous GRNs.

- Lower allulose intake estimates in the present analysis appear to be due to a shift in dietary patterns of non-alcoholic low calorie, reduced calorie, sugar-free beverages. Specifically, the percent users and intake of non-alcoholic beverages (low calorie, reduced calorie, sugar-free) have decreased from 32% in NHANES 2007-2010 to 21% in NHANES 2015-2018 with a decreased intake among consumers of non- alcoholic beverages in NHANES 2015-2018. A trend analysis conducted by Bleich et al.(2018) similarly reported an observed decline in beverage and sugar-sweetened beverage consumption for children and adults from 2003 to 2014. There was also a reduction in intake of regular cereal contributing to lower allulose intakes, i.e., a decrease in percent users (46% in NHANES 2007-2010 versus 33% in NHANES 2015-2018) and lower intake amounts in NHANES 2015-2018. This reduction, however, did not result from changes in dietary patterns but instead was due to differences in the food selection methodology between GRN 498 and the current assessment. The food selection of regular cereals in the present analysis was limited to cereals with added sugar since allulose would not be added to cereals with no added sugar, whereas all cereals excluding low calorie, reduced calorie, and sugar-free cereals were included in the assessment for GRN 498 under regular cereals. The estimated allulose intake from existing background uses in this analysis relies on the most currently available dietary data from NHANES (2015-2018) and shows a lower allulose intake as compared to previously reported allulose EDIs from GRNs 400, 498, 693, and 828 (see Exponent intake assessment report Appendix C).

- Allulose can be considered safe for human consumption up to 24–36 g (0.4 – 0.6 g/kg/day for a 60 kg individual) when consumed in one sitting. As summarized above, the 90$^{th}$ percentile estimated total daily intake for the US population, ages 2+ is 23.53 g/day; this is likely an overestimate of intake as it assumes allulose is used in all intended foods at the maximum intended use level.

- No safety/toxicity concerns related to consumption of allulose are evident, beyond that of gastrointestinal intolerance at high bolus doses. Even at the 90$^{th}$ percentile, the estimated total daily intake for the US population, ages 2+ of 23.53 g/day is conservative, and as such, tolerability should be of limited concern.

- Regulatory authorities have reviewed the extensive safety study database for allulose and found no issues of concern with respect to its use in human food at the proposed use levels. Numerous studies have been conducted and published in support of the safety of allulose, including *in vitro* studies and *in vivo* animal studies (i.e., acute and subchronic toxicity, mutagenicity and genotoxicity, chronic toxicity), as well as clinical studies in adults. No adverse effects attributable to allulose were observed in multiple animal studies; in 90-day studies (1670 - 2000 mg/kg bw/day) and in a chronic study (approximately 1300 mg/kg bw/day).

- The body of publicly available scientific literature on the consumption and safety of allulose is sufficient to support the safety and GRAS determination to support the proposed new uses of the allulose ingredient.

Because this safety evaluation was based on generally available and widely accepted data and information, it also satisfies the so-called "common knowledge" element of a GRAS determination.

Determination of the safety and GRAS status of this allulose ingredient for the specified uses that is the subject of this self-determination has been made through the deliberations of a GRAS Panel of qualified experts convened by Tate & Lyle and comprised of Michael Carakostas, DVM, Ph.D., Stanley M. Tarka, Jr., Ph.D., F.A.T.S., and Thomas A. Vollmuth, Ph.D. These individuals are qualified by scientific training and experience to evaluate the safety of substances intended to be added to food. They have critically reviewed and evaluated the publicly available information summarized in this document and have individually and collectively concluded that the allulose ingredient, produced in a manner consistent with cGMP and meeting the specifications described herein, is safe under its intended conditions of use.

The Panel further unanimously concluded that use of this allulose ingredient in these additional specified human foods described herein is GRAS based on scientific procedures, and that other experts qualified to assess the safety of food and food ingredients for human consumption would concur with these conclusions. The Panel's GRAS opinion is included as Exhibit 1 to this document.

It is also Tate & Lyle's opinion that other qualified scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion. Tate & Lyle has concluded that the allulose ingredient is GRAS under the intended conditions of use on the basis of scientific procedures; and therefore, it is excluded from the definition of a food additive and may be marketed and sold for its intended purpose in the U.S. without the promulgation of a food additive regulation under Title 21 of the CFR.

Tate & Lyle is not aware of any information that would be inconsistent with a finding that the use of the allulose ingredient in food for human consumption, meeting appropriate specifications, and used according to GMP, is GRAS. Recent reviews of the scientific literature revealed no potential adverse health concerns.

# § 170.255 Part 7, Supporting Data and Information

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APPENDIX A

# Pariza and Johnson Decision Tree

Appendix 4 - Analysis of Safety Based on Pariza/Johnson Decision Tree

Guidelines have been published for the safety assessment of microbial enzyme preparations (Pariza and Johnson, 2001). The guidelines have proven to be a useful tool in safety assessments for the production and use of numerous food enzymes. The safety assessment of a given enzyme preparation is based upon an evaluation of the toxigenic potential of the production organism. The responses below follow the pathway indicated in the decision tree. The outcome of this analysis is that the epimerase enzyme preparation is accepted as safe for its intended use.

1. Is the production strain genetically modified? Yes, go to 2.

2. Is the production strain modified using r DNA techniques? Yes, go to 3a.

3. a. Does the expressed enzyme product which is encoded by the introduced DNA have a history of safe us? This epimerase enzyme is novel but the epimerase enzyme has been used previously to make a food sweetener that was the subject of a GRAS Notification that has been reviewed by FDA (GRN 400); Yes, go to 3c.

   c. Is the test article free of transferable antibiotic resistance gene DNA? No, go to 3d.

   d. Does the resistance gene(s) code for resistance to a drug substances used in the treatment of disease agents in man or animal? Due to its toxicity characteristics, chloramphenicol is not a clinically important antibiotic. No, go to 3e.

e. Is all other introduced DNA well characterized and free of attributes that would render it unsafe for constructing microorganisms to be used to produce food-grade products? **Yes, go to 4.**

4. **Is the introduced DNA randomly integrated into the chromosome? No, go to 6.**

6. **Is the production strain derived from a safe lineage, as previously demonstrated by repeated assessment via this evaluation procedure? Yes, *E. Coli* K-12 is a well established strain with a history of safe use. Accept.**

APPENDIX B

# COAs and Other Analytical Data

# TATE & LYLE

CONSISTENTLY FIRST IN RENEWABLE INGREDIENTS
ICD CERTIFICATE OF ANALYSIS

| | |
|---|---|
| PRODUCT: Dolcia Prima LS | PO# : N.A |
| Report Date: 09/22/2019 | Order # : NA |
| Sent to: N.A | Date Shipped: |
| Vendor: N.A | N.A |

## Analytical Data

Sample Number: Dolcia Prima LS YP19D03774

Manufacture Date May 6, 2019

| Analysis | Unit | Result | Specification | Methods |
|---|---|---|---|---|
| Color | n/a | Colorless | Off white | Visual inspection |
| Allulose | % dsb | 96.2 | ≥95% | Saccharide distribution – TN67435 |
| Total non allulose saccharides | % dsb | 2.6 | ≤5% | Saccharide distribution – TN67435 |
| pH | | 4.2 | 3.0-4.5 | pH – TN60710 |
| Dry solids | % | 70.8 | 70% to78% | DS RI M – TN27501 |
| Total plate count | CFU/10 g | <10 | ≤200 CFU/10 g | Total Plate Count – TN10565; TN10560 |
| E. Coli. | CFU/10 g | None detected | None detected | E. coli – TN 10512L |
| Salmonella | CFU/ 25 g | Negative | Negative | *Salmonella* – TN 10547 |
| Yeast | CFU/10 g | <10 | ≤10 CFU/10 g | Mold & Yeast – TN10600 |
| Mold | CFU/10 g | <10 | ≤10 CFU/10 g | Mold & Yeast – TN10600 |
| SO2 | ppm | <10 | <10 ppm | Sulphur dioxide – TN80055 |
| Arsenic | ppb | 15.8 | <0.10 ppm | Elemental Analysis of Heavy Metals - R 2837 |
| Lead | ppb | 5.6 | <0.10 ppm | Elemental Analysis of Heavy Metals - R 2837 |
| Cadmium | ppb | <5 | <0.1 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Mercury | ppb | <5 | <0.01 ppm | Elemental Analysis of Mercury - R method 2832 |

Shana Bender – Manager Analytical

3/25/2020
Date

# TATE & LYLE

CONSISTENTLY FIRST IN RENEWABLE INGREDIENTS
ICD CERTIFICATE OF ANALYSIS

| | |
|---|---|
| PRODUCT: Dolcia Prima LS | PO# : N.A |
| Report Date: 09/22/2019 | Order # : NA |
| Sent to: N.A | Date Shipped: |
| Contact: N.A | N.A |

## Analytical Data

Sample Number: Dolcia Prima LS YP19G01863

Manufacture Date: April 27, 2019

| Analysis | Unit | Result | Specification | Methods |
|---|---|---|---|---|
| Color | n/a | Colorless | Colourless to slightly yellow | Visual inspection |
| Allulose | % dsb | 96.34 | ≥95% | Saccharide distribution – TN67435 |
| Total non allulose saccharides | % dsb | 2.87 | ≤5% | Saccharide distribution – TN67434 |
| pH | % | 3.9 | 3.0-4.5 | pH – TN60710 |
| Dry solids | % | 70.5 | 70% to78% | DS RI - TN27501 |
| Total plate count | CFU/10 g | <10 | ≤200 CFU/10 g | Total Plate Count – TN10565; TN10560 |
| E. Coli. | CFU/10 g | None detected | None detected | *E. coli* TN 10512L |
| Salmonella | CFU/ 25 g | Negative | negative | *Salmonella* – TN 10547 |
| Yeast | CFU/10 g | <10 | ≤10 CFU/10 g | Mold & Yeast – TN10600 |
| Mold | CFU/10 g | <10 | ≤10 CFU/10 g | Mold&Yeast – TN10600 |
| SO2 | ppm | <10 | <10 ppm | Sulphur dioxide – TN80055 |
| Arsenic | ppb | 11.4 | <0.10 ppm | Elemental Analysis of Heavy Metals - R method 2837 |
| Lead | ppb | <5 | <0.10 ppm | Elemental Analysis of Heavy Metals - R method 2837 |
| Cadmium | ppb | <5 | <0.1 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Mercury | ppb | <5 | <0.01 ppm | Elemental Analysis of Mercury - R method 2832 |

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CONSISTENTLY FIRST IN RENEWABLE INGREDIENTS
ICD CERTIFICATE OF ANALYSIS

| | |
|---|---|
| PRODUCT: Dolcia Prima LS | PO# : N.A |
| Report Date: 09/22/2019 | Order# : N.A |
| Sent to: N.A<br>Contact: N.A | Date Shipped:<br>N.A |

## Analytical Data

Sample Number: Dolcia Prima LS YP18D03177
Manufacture Date April 13, 2018

| Analysis | Unit | Result | Specification | Methods |
|---|---|---|---|---|
| Color | n/a | Colorless | Colourless to slightly yellow | Visual inspection |
| Allulose | % dsb | 96.3 | ≤95% | Saccharide distribution -- TN67435 |
| Total non allulose saccharides | % dsb | 2.4 | ≤5% | Saccharide distribution – TN67435 |
| pH | | 4.3 | 3.0-4.5 | pH – TN60710 |
| Dry solids | % | 71 | 70% to78% | DS RI – TN27501 |
| Total plate count | CFU/10 g | <10 | ≤200 CFU/10 g | Total Plate Count – TN10565; TN10560 |
| E. Coli. | CFU/10 g | None detected | None detected | E. Coli - TN 10512L |
| Salmonella | CFU/ 25 g | Negative | Negative | *Salmonella* – TN 10547 |
| Yeast | CFU/10 g | <10 | ≤10 CFU/10 g | Mold & Yeast – TN10600 |
| Mold | CFU/10 g | <10 | ≤10 CFU/10 g | Mold & Yeast – TN10600 |
| SO2 | ppm | <10 | <10 ppm | Sulphur dioxide – TN80055 |
| Arsenic | ppb | 23.8 | <0.10 ppm | Elemental Analysis of Heavy Metals - R method 2837 |
| Lead | ppb | 6 | <0.10 ppm | Elemental Analysis of Heavy Metals - R method 2837 |
| Cadmium | ppb | <5 | <0.1 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Mercury | ppb | <5 | <0.01 ppm | Elemental Analysis of Mercury - R method 2832 |

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# TATE & LYLE

CONSISTENTLY FIRST IN RENEWABLE INGREDIENTS
ICD CERTIFICATE OF ANALYSIS

| | |
|---|---|
| Product: Dolcia Prima DS | P●# : N.A |
| Report Date: 09/22/2019 | Order # : NA |
| Sent to: | Date Shipped: N.A |

## Analytical Data

Sample Number: Dolcia Prima DS LO18J90596
Manufacture Date November 15, 2018

| Analysis | Unit | Result | Specification | Methods |
|---|---|---|---|---|
| Color | n/a | Off white | Off white | Visual inspection |
| Screen | % | 0.1 | <5% | |
| screen | % | 7 | <10% | |
| Allulose | % dsb | 99.35 | ≥99.10% | Saccharide distribution – TN67450 |
| Total non allulose saccharides | % dsb | 0.27 | ≤0.90% | Saccharide distribution TN67435 |
| moisture | %dsb | 0.14 | ≤0.50% | Moisture – TN46040 |
| Ash | % dsb | <0.1% | <0.5% | Ash – TN 09580 |
| Total plate count | CFU/g | <10 | ≤200 CFU/g | Total Plate Count – TN10565 |
| E. Coli. | CFU/ g | None detected | None detected | *E. coli* – TN 10412L |
| Salmonella | CFU/ 25 g | Negative | Negative | *Salmonella* TN 10510 |
| Yeast | CFU/ g | <10 | ≤10 CFU/g | Mold & Yeast – TN47010 |
| Mold | CFU/10 g | <10 | ≤10 CFU/g | Mold & Yeast – TN47010 |
| SO2 | ppm | <10 | <10 ppm | Sulphur dioxide – TN80055 |
| Arsenic | ppb | <5 | <0.10 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Lead | ppb | <5 | <0.10 ppm | Elemental Analysis of Heavy Metals - R method 2837 |
| Cadmium | ppb | <5 | <0.1 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Mercury | ppb | <5 | <0.01 ppm | Elemental Analysis of Mercury - R method 2832 |

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3/25/2020
Date

# TATE & LYLE

CONSISTENTLY FIRST IN RENEWABLE INGREDIENTS
ICD CERTIFICATE OF ANALYSIS

| | |
|---|---|
| PRODUCT: Dolcia Prima DS | PO# : N.A |
| Report Date: 09/22/2019 | Order # : NA |
| Sent to: N.A | Date Shipped: |
| Contact: N.A | N.A |

## Analytical Data

Sample Number: Dolcia Prima DS LO19F90351

Manufacture Date: June 3, 2019

| Analysis | Unit | Result | Specification | Methods |
|---|---|---|---|---|
| Color | n/a | Off white | Off white | Visual inspection |
| Screen | # 10 | 0.1 | <5% | |
| screen | # 200 | 3 | <10% | |
| Allulose | % dsb | 99.74 | ≥99.1% | Saccharide distribution – TN67450 |
| Total non allulose saccharides | % dsb | 0.06 | ≤0.9% | Saccharide distribution – TN67434 |
| moisture | %dsb | 0.12 | ≤0.5% | Moisture – TN46040 |
| Ash | % dsb | <0.1% | <0.5% | Ash – TN 09580 |
| Total plate count | CFU/ g | 10 | ≤200 CFU/g | Total Plate Count – TN10565; TN10560 |
| E. Coli. | CFU/10 g | None detected | None detected | *E. Coli* TN10512L |
| Salmonella | CFU/ 25 g | Negative | Negative | *Salmonella* TN 10547 |
| Yeast | CFU/g | 10 | ≤10 CFU/ g | Mold & Yeast – TN47010 |
| Mold | CFU/10 g | 10 | ≤10 CFU/ g | Mold & Yeast – TN47010 |
| SO2 | ppm | <10 | <10 ppm | Sulphur dioxide – TN80055 |
| Arsenic | ppb | <5 | <0.10 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Lead | ppb | <5 | <0.10 ppm | Elemental Analysis of Heavy Metals - R method 2837 |
| Cadmium | ppb | <5 | <0.1 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Mercury | ppb | <5 | <0.01 ppm | Elemental Analysis of Mercury - R method 2832 |

This is signed by

Shana Fenler

Shana Bender – Manager Analytical

3/25/2020

Date

# TATE & LYLE

CONSISTENTLY FIRST IN RENEWABLE INGREDIENTS
ICD CERTIFICATE OF ANALYSIS

| | |
|---|---|
| Product: Dolcia Prima DS | PO# : N.A |
| Report Date: 09/22/2019 | Order # : NA |
| Sent to: N.A | Date Shipped: |
| Contact: N.A | N.A |

## Analytical Data

Sample Number: Dolcia Prima DS LO18J90294

Manufacture Date October 3, 2019

| Analysis | Unit | Result | Specification | Methods |
|---|---|---|---|---|
| Color | n/a | Colorless | Off white | Visual inspection |
| Screen US#10 | % | 0.1 | <5% | |
| Screen US #200 | % | 6.6 | <10% | |
| Allulose | % dsb | 99.19 | ≥99.1% | Saccharide distribution – TN67450 |
| Total non allulose saccharides | % dsb | 0.29 | <0.9% | Saccharide distribution – TN67435 |
| moisture | %dsb | 0.1 | ≤0.5% | Moisture – TN46040 |
| Ash | % dsb | <0.1% | <0.5% | Ash – TN 09580 |
| Total plate count | CFU/g | 10 | ≤200 CFU/g | Total Plate Count –TN10560 |
| E. *Coli.* | CFU/g | None detected | None detected | E. *Coli* - TN10512 |
| *Salmonella* | CFU/ g | Negative | Negative | *Salmonella* TN 10547 |
| Yeast | CFU/g | <10 | ≤10 CFU/g | Mold & Yeast – TN47010 |
| Mold | CFU/g | <10 | ≤10 CFU/g | Mold & Yeast – TN47010 |
| SO2 | ppm | <10 | <10 ppm | Sulphur dioxide – TN80055 |
| Arsenic | ppb | <5 | <0.10 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Lead | Ppb | <5 | <0.10 ppm | Elemental Analysis of Heavy Metals - R method 2837 |
| Cadmium | Ppb | <5 | <0.1 ppm | Elemental Analysis of Heavy Metals – R method 2837 |
| Mercury | ppb | <5 | <0.01 ppm | Elemental Analysis of Mercury - R method 2832 |

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3/25/2020
Date

APPENDIX C

# Stability Testing Data

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## Shelf Life Stability
## DOLCIA PRIMA® LS Allulose Syrup
## DOLCIA PRIMA® DS Crystalline Allulose

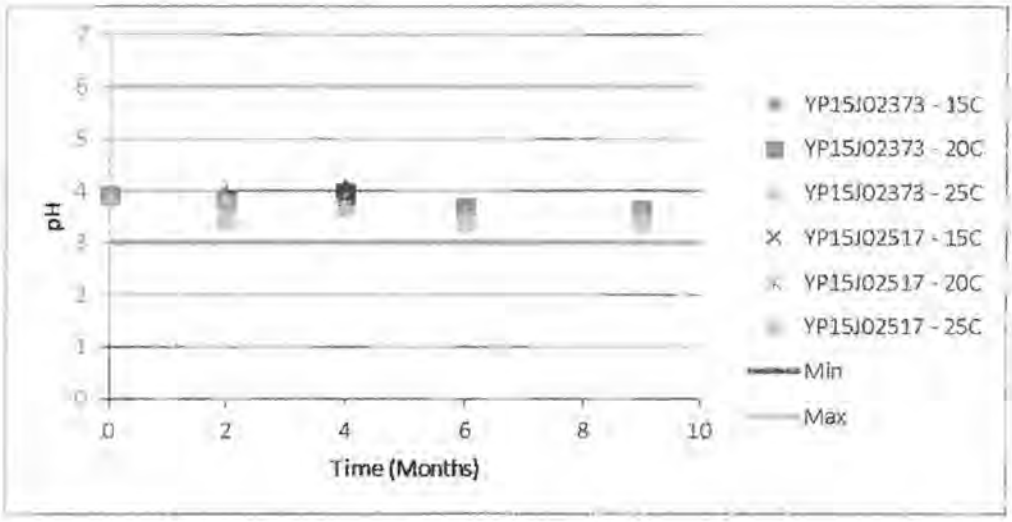
Based on the studies summarized below, the shelf life of DOLCIA PRIMA® LS Allulose Syrup is shown to be at least 9 months when stored at the recommended storage temperature, i.e. 25° C. In this study, the test samples were stored in tightly sealed glass jars in a dark chamber at ambient humidity.

The shelf life of DOLCIA PRIMA® DS Crystalline Allulose is shown to be at least 26 months when stored at the recommended storage conditions of 25° C, <50% RH. In this study, the samples were heat sealed in pouches made from the plastic bag liner which provides a moisture barrier in the DOLCIA PRIMA® DS bag. These pouches were stored in a dark chamber with humidity controlled to <50% RH.

### A. pH Stability

The pH of DOLCIA PRIMA® Allulose Syrup decreased gradually throughout shelf-life study at all temperatures tested (Figure 1). The material remained within specification for duration of the 9 month period at 25°C and below.

Figure 1. pH Stability of DOLCIA PRIMA® LS Allulose Syrup

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## B. Color Stability of DOLCIA PRIMA® LS Allulose Syrup

One of the key factors that define the end of shelf life for a syrup is color development. As shown in Figure 2, the rate of color development is strongly influenced by temperature. No color generation was seen at 4°C, and only a mild color increase was seen at 25°C over 6 months. Based on color, the syrup should be kept at 25°C for any storage beyond 1 month. Extended storage at these recommended conditions is shown in Figure 3.

Figure 2. Color Stability of DOLCIA PRIMA® Allulose Syrup 4°C – 35°C

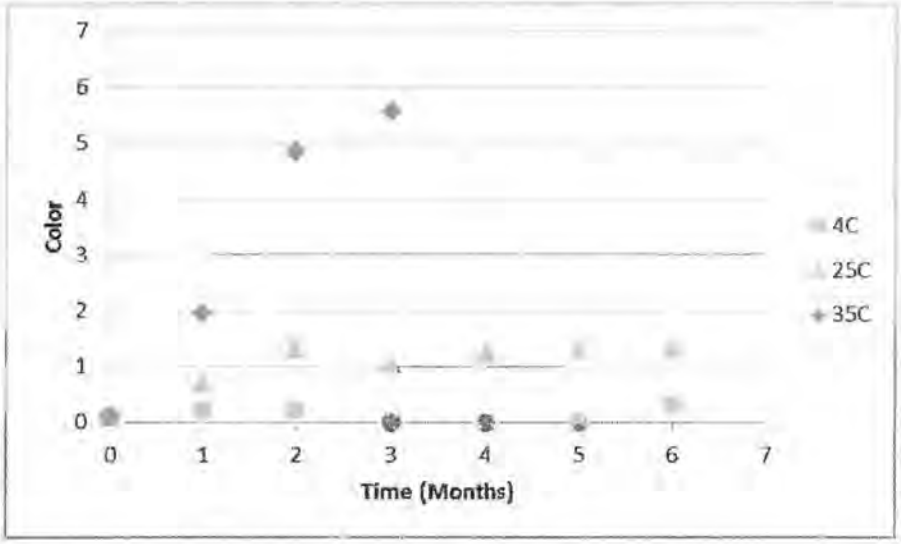
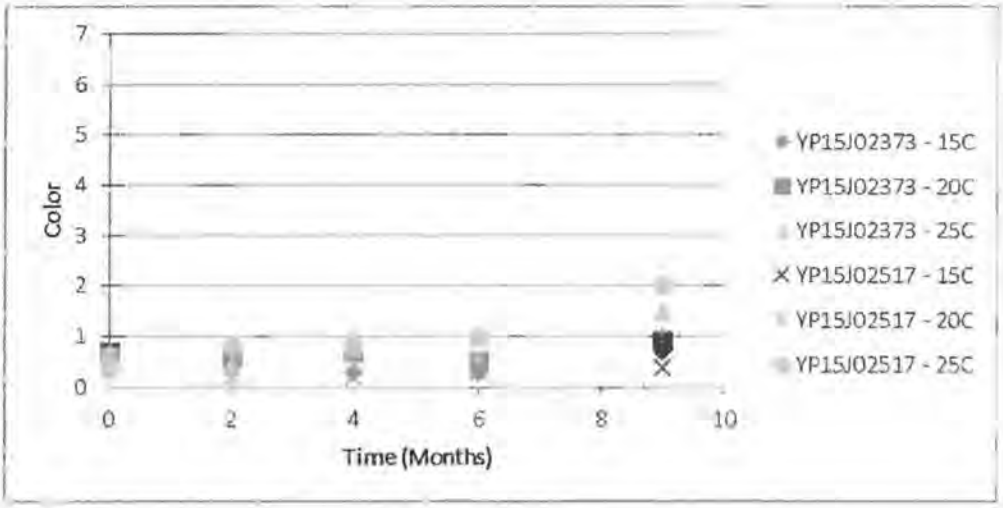



Figure 3. Color Stability of DOLCIA PRIMA® LS Allulose Syrup at 15°C, 20°C, and 25°C

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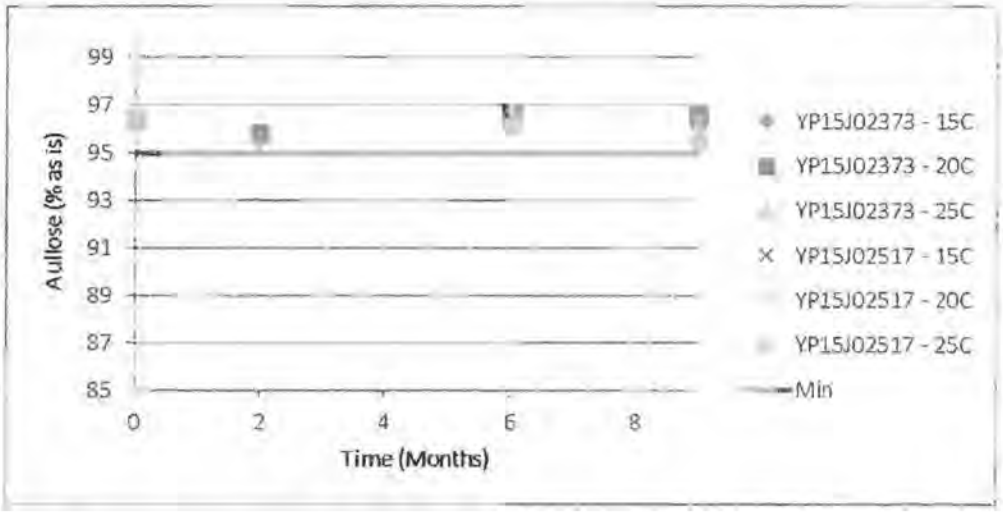
## C. Composition Stability of DOLCIA PRIMA® LS Allulose Syrup

The main component of DOLCIA PRIMA® LS Allulose Syrup is allulose. The allulose did not change significantly during the 9 month storage (Figure 4).

Figure 4. Composition Stability of DOLCIA PRIMA® Allulose Syrup

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## D. Microbial Stability of DOLCIA PRIMA® Allulose Syrup

The DOLCIA PRIMA® Allulose Syrup tested has a water activity of approximately 0.66 which is very similar to other corn syrups and HFCS products. Microbial growth is not supported in these products due to the low water activity as demonstrated in Table 1. In addition, Tate & Lyle has conducted a challenge study on DOLCIA PRIMA® Allulose Syrup with Salmonella and E. Coli which showed that these microorganisms died off after 1 day at room temperature.

Table 1. Microbial Stability of DOLCIA PRIMA® Allulose Syrup

| Temp ( °C ) | Month | E Coli | Salmonella | Total Plate Count | Mold | Yeast |
|---|---|---|---|---|---|---|
| 4 | 0 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| | 3 | NEGATIVE | NEGATIVE | 20 | <10 | <10 |
| | 6 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| | 9 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| 25 | 0 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| | 3 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| | 6 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| | 9 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| 35 | 0 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |
| | 3 | NEGATIVE | NEGATIVE | 20 | <10 | <10 |
| | 6 | NEGATIVE | NEGATIVE | <10 | <10 | <10 |

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## E. Stability of DOLCIA PRIMA® DS Crystalline Allulose

Stability studies on DOLCIA PRIMA® DS Crystalline Allulose are currently underway. Allulose composition and moisture are unchanged after 30 months (2.5 years) when stored in original packaging at the recommended storage conditions of 77 degrees Fahrenheit (25°C) or lower and 50% or less relative humidity. This is similar to other crystalline saccharides such as crystalline fructose or crystalline glucose. DOLCIA PRIMA® DS Crystalline Allulose is an anhydrous crystalline product with moisture <0.5% and therefore does not support microbial growth.

Figure 5. Composition Stability of DOLCIA PRIMA® DS Crystalline Allulose at 25°C

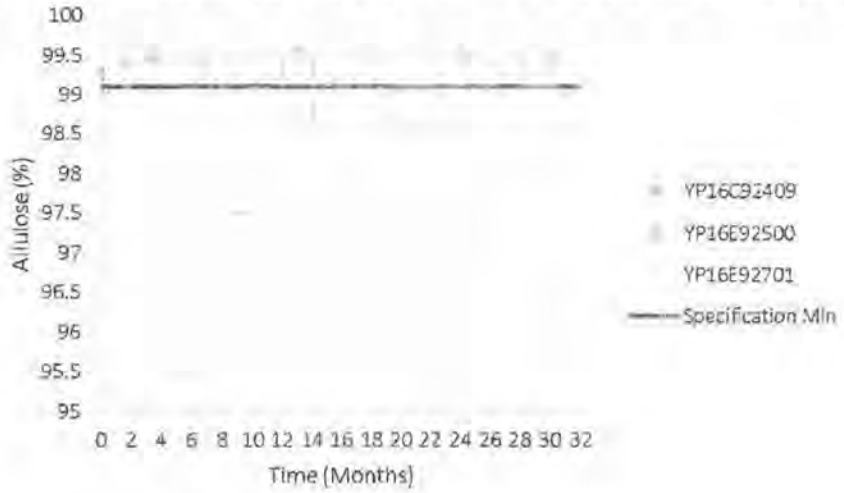


Figure 6. Moisture uptake of DOLCIA PRIMA® DS Crystalline Allulose at 25°C, <50% RH

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[redacted]

Brian Pohrte, Research Chemist

Tate & Lyle 2200 E. Eldorado Street Decatur, IL 62525 Phone: 217/423-4411 Fax: 217/421-2216 www.tateandlyle.com

APPENDIX D

# Intake Assessment Report

Exponent®

*Center for Chemical Regulation and Food Safety*

# ESTIMATED DAILY INTAKE OF ALLULOSE FROM PROPOSED USES

# ESTIMATED DAILY INTAKE OF ALLULOSE FROM PROPOSED USES

Prepared for

Lore Kolberg
Director, Regulatory and Scientific Affairs
Innovation and Commercial Development
Tate & Lyle
222 Walelu Trail
Vonore, TN 37885

Prepared by

Exponent, Inc.
1150 Connecticut Avenue, NW
Suite 1100
Washington, DC 20036

August 30, 2021

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# List of Tables

# List of Acronyms

| | |
|---|---|
| bw | Body weight |
| CEDI | Cumulative Estimated Daily Intake |
| DHHS | Department of Health and Human Services |
| EDI | Estimated Daily Intake |
| FARE® | Foods Analysis and Residue Evaluation® Program |
| FDA | U.S. Food and Drug Administration |
| FNDDS | Food and Nutrient Database for Dietary Studies |
| FPED | Food Patterns Equivalent Database |
| g | gram |
| GRAS | Generally Recognized As Safe |
| GRN | GRAS Notice |
| kg | kilogram |
| NA | Not applicable |
| NCHS | National Center for Health Statistics |
| NFS | Not-further-specified |
| NHANES | National Health and Nutrition Examination Survey |
| RTE | Ready-to-eat |
| U.S. | United States |
| USDA | United States Department of Agriculture |
| WWEIA | What We Eat in America |

# Introduction

At the request of Tate & Lyle, Exponent, Inc. (Exponent) conducted an intake assessment to estimate the estimated daily intake (EDI) of allulose among the United States (U.S.) population from proposed uses in a total of ten food types. The background intake of allulose was also assessed based on existing Generally Recognized As Safe (GRAS) uses in several food and beverage types in order to derive the cumulative estimated daily intake (CEDI) from the combined background and proposed new uses.

The EDI of allulose were generated from dietary recalls collected as part of the *What We Eat in America* (WWEIA) component of the combined 2015-2018 National Health and Nutrition Examination Surveys (NHANES) data files (NCHS 2018, 2020). Exponent developed allulose EDIs on a per capita and per user basis for the U.S. population ages 2 years (y) and older and the following five subpopulations: (1) infants and young children <2 y, (2) children 2-12 y, (3) adolescents 13-18 y, (4) adult females 19 y and older, and (5) adult males 19 y and older. Estimates were generated in units of grams allulose per day (g/day) and grams allulose per kilogram body weight per day (g/kg-bw/day). The sections below summarize the data, methods, and results.

# Data and Methods

## Background Use

Background dietary intake of allulose was determined based on the existing food uses and use levels of allulose as described in U.S. GRAS Notices (GRNs) 400 (CJ Cheiljedang, 2011), 498 (Matsutani Chemical Industry Company, Ltd 2013), 693 (Samyang Corporation, 2017), and 828 (Samyang Corporation, 2018). These uses of allulose are summarized in Table 1 by food category and corresponding use levels. For the purpose of estimating background allulose intake from existing food uses, the maximum use level from all GRNs for a given food type was used in the assessment. The existing food uses and corresponding use level of allulose from each of the four GRNs (i.e., GRNs 400, 498, 693, and 828) to which the U.S. Food and Drug Administration (FDA) issued a no questions letter (FDA 2012, 2014, 2017, 2020) are summarized and presented in Appendix A.

## Proposed Use

Allulose is proposed for use in ten food types including (1) nutritional beverages intended for the general population; (2) nutritional beverages intended for children (i.e., PediaSure); (3) sweetened alcoholic malt beverages; (4) alcoholic premixed cocktails; (5) ready-to-eat (RTE) and cooked cereals including regular and low calorie, reduced calorie, and sugar-free RTE and cooked cereals; (6) grain-free, no sugar, high protein RTE cereals; (7) nutrition bars; (8) ketchup and barbecue sauces; (9) dried cranberries; and (10) meat- and poultry-based jerky. The categories of food to which allulose is proposed for use, descriptions of the general types of foods within each category, and the maximum proposed use of allulose are also summarized in Table 1.

Table 1. Maximum allulose use levels by types of foods and beverages

| | Food Category | Description of Foods Selected for Analysis | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | | | Proposed New Uses | Existing GRAS Uses* | Combined existing GRAS and proposed uses ** |
| 1 | Baked products (bread, muffin, cake and cookies, pastries), dietetic, low calorie, reduced calorie, sugar-free | Sweetened bread/rolls, muffin, and cakes and cookies – all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 10 | 10 |
| 2 | Beverages | | | | |
| 2a | Non-alcoholic beverages, low calorie, reduced calorie, sugar-free | Sweetened coffees, teas, soft drinks, energy drinks, juice drinks, fruit drinks, fruit flavored drinks, flavored/carbonated waters, and enhanced/fortified waters – all identified as low calorie, reduced calorie, or sugar-free. | NA | 3.5 | 3.5 |
| 2b | Nutritional beverages | Nutritional beverages within the "nutritional beverages" and "protein and nutritional powders" WWEIA categories not included as part of the existing GRAS uses in medical foods | 2.5 | NA | 2.5 |
| 2c | Nutritional beverages intended for children (i.e., PediaSure) | PediaSure | 3.5 | NA | 3.5 |
| 2d | Alcoholic malt beverage, sweetened | Sweetened alcoholic malt beverage (food code 93106000), which includes products such as hard lemonade, hard punch, hard tea, etc. | 3.5 | NA | 3.5 |
| 2e | Alcoholic premixed cocktails | All cocktails with added sugar | 3.0 | NA | 3.0 |
| 3 | Candy, hard and soft | | | | |
| 3a | Hard candy (includes pressed candy and mints), low calorie, reduced calorie, sugar-free | Hard candy – low calorie, reduced calorie, sugar-free, or NFS†. | NA | 70 | 70 |
| 3b | Soft candy, low calorie, reduced calorie, sugar-free | Soft candy – low calorie, reduced calorie, sugar-free. | NA | 25 | 25 |

| | Food Category | Description of Foods Selected for Analysis | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | | | Proposed New Uses | Existing GRAS Uses* | Combined existing GRAS and proposed uses ** |
| 4 | Chewing gum | Regular and sugar-free chewing gum. | NA | 50 | 50 |
| 5 | Cereals, ready-to-eat (RTE) and cooked | | | | |
| 5a | RTE and cooked, regular | RTE and cooked cereals identified as containing added sugar. | 12 | 2 | 12 |
| 5b | RTE and cooked, low calorie, reduced calorie, sugar-free | RTE and cooked cereals identified as low calorie, reduced sugar, or sugar-free. | 12 | 5 | 12 |
| 5c | RTE cereals with <5% sugar | RTE cereals with <5% added sugar excluding cereals with no added sugar. | NA | 10 | 10 |
| 5d | Grain-free, no sugar, high protein RTE cereal | No grain-free, no sugar, high protein RTE cereals were reported consumed, hence, zero-sugar added RTE cereals were selected as surrogates. | 20 | NA | 20 |
| 6 | Coffee mix | Sweetened non-reconstituted coffee mixes. | NA | 30 | 30 |
| 7 | Confections & Frostings | Frostings and icings and marshmallows. | NA | 5 | 5 |
| 8 | Dressings for salads | Salad dressings including mayonnaise. | NA | 5 | 5 |
| 9 | Frozen dairy (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free | Desserts including ice cream, soft serve, sorbet - all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 5 | 5 |
| 10 | Gelatins, pudding & fillings | | | | |
| 10a | Gelatins, pudding & fillings, low calorie, reduced calorie, sugar-free | Gelatins and puddings - all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 10 | 10 |
| 10b | Fat-based cream (used in modified fat/calorie cookies, cakes, pastries, pie) | Fat-based cream filling in cookies, cakes, pastries, pies. | NA | 10 | 10 |
| 11 | Nutrition bars | Meal replacement bars, protein bars, energy bars, etc. | 25 | NA | 25 |
| 12 | Jams & Jellies | Jams, jellies, and pastes, all types. | NA | 10 | 10 |

| | | | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | **Food Category** | **Description of Foods Selected for Analysis** | **Proposed New Uses** | **Existing GRAS Uses*** | **Combined existing GRAS and proposed uses **** |
| 13 | Sugar | Sugar added in home preparations including white sugar, brown sugar, cinnamon sugar, raw sugar, honey, molasses, and not specified. | NA | 10 | 10 |
| 14 | Sugar substitutes | Sugar substitutes. | NA | 100 | 100 |
| 15 | Sweet sauces & syrups, low calorie, reduced calorie, sugar-free | Sweet sauces & syrups - all identified as low calorie, reduced calorie, sugar-free, dietetic or NFS†. | NA | 10 | 10 |
| 16 | Ketchup and barbecue sauces | Ketchup and barbecue sauces. | 10 | NA | 10 |
| 17 | Yogurt and frozen yogurt, low calorie, reduced calorie, sugar-free | Yogurt and frozen yogurt - all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 5 | 5 |
| 18 | Medical foods | Nutritional drinks such as Boost, Ensure, and Glucerna to provide a surrogate for medical foods. | NA | 15 | 15 |
| 19 | Cranberries, dried | Dried cranberries (i.e., Craisins). | 25 | NA | 25 |
| 20 | Jerky (meat or poultry based) | Jerky (meat or poultry based). | 15 | NA | 15 |

* Based on current food uses and use levels of allulose as described in U.S. GRNs 400 (CJ Cheiljedang, 2011), 498 (Matsutani Chemical Industry Company, Ltd 2013), 693 (Samyang Corporation, 2017), and 828 (Samyang Corporation, 2018).

† NFS refers to food codes described as "not-further-specified;" providing a generic description to the food reported consumed (i.e., dietetic topping).

NA: Not applicable.

** Maximum use levels applied in estimating cumulative intake from proposed and existing GRAS uses

## Food Consumption Data

Estimated food intakes of allulose were based on food consumption records collected in the WWEIA component of NHANES conducted in 2015-2016 and 2017-2018 (NHANES 2015-2018). This continuous survey uses a complex multistage probability sample designed to be representative of the civilian U.S. population (NCHS 2018, 2020). The NHANES datasets provide nationally representative nutrition and health data and prevalence estimates for nutrition and health status measures in the U.S. Statistical weights are provided by the National Center for Health Statistics (NCHS) to adjust for the differential probabilities of selection.

As part of the examination, trained dietary interviewers collected detailed information on all foods and beverages consumed by respondents in the previous 24-hour time period (midnight to midnight). A second dietary recall was administered by telephone three to ten days after the first dietary interview, but not on the same day of the week as the first interview. The dietary component of the survey is conducted as a partnership between the U.S. Department of Agriculture (USDA) and the U.S. Department of Health and Human Services (DHHS). DHHS is responsible for the sample design and data collection, and USDA is responsible for the survey's dietary data collection methodology, maintenance of the databases used to code and process the data, and data review and processing. A total of 13,666 individuals in the survey period 2015-2018 provided 2 complete days of dietary recalls.

## Selection of Representative Food Codes

Food codes corresponding to each of the food categories to which allulose can currently be added to or is proposed to be added to were identified in the WWEIA, NHANES 2015-2018. Foods in which only a component is of interest for the addition of allulose (e.g., dressing as part of a salad, jelly in a sandwich, icing on a cake) were also identified. Food descriptions and the "additional description" details provided for some food codes were reviewed as part of the process to select representative foods and food mixtures to include in the analysis.

For relevant food mixtures, the proportion of the food code (as a percentage of total weight) corresponding to the component of interest was identified and only this portion of the food weight was used to determine the amount of allulose that may be added. Exponent used USDA's Food and Nutrient Database for Dietary Studies (FNDDS) 2017-2018 (USDA, 2018) to translate the food as consumed into its corresponding

ingredients based on percent weight. Additional details on the identification of the portion of food mixtures assumed to contain allulose are presented in sections below. The list of the food codes included in the analysis is provided in Appendix B.

**Confection & Frosting and Gelatins, Pudding & Fillings**

The average proportion of frosting/icing in baked goods was assumed to be 30% for cakes/cupcakes, 25% for brownies, 30% for cookies, and 20% for pastries. Likewise, the average filling proportion was assumed to be 30% for cookies and 15% for pastries. These proportions were based on frosting/icing or filling contribution between baked goods with and without icing/frosting or filling using portion weight information from the FNDDS.

**Sugar and Sugar Substitutes**

Food codes for sugar and sugar substitutes were identified and assigned the maximum use levels of allulose as specified in Table 1. The WWEIA food codes also include food mixtures that may contain a sweetener added during home preparation. To capture these potential existing uses of allulose as a sugar substitute assumed to occur at the consumer level, food descriptions containing "homemade", "home recipe", "prepared with", "made with", "made from", "with sugar", "sugar added", "sweetened", or "presweetened" were identified and reviewed. When the food was assumed to represent a home preparation, the sugar or sugar substitute portion of the mixture was identified and included in the analysis. The Food Patterns Equivalent Database (FPED) was used to identify the concentration of added sugars in these mixtures (USDA, 2020). For example, sugar portions of the food codes for "Cornbread, made from home recipe" and "Apple, dried, cooked, with sugar" were assumed to contain allulose in the analysis.

For beverage food codes identified as presumably sweetened by the consumer, Exponent used USDA's FPED database to determine the proportion of sugar in the beverage mixtures. This proportion was included in the analysis for the sugar and sugar substitute existing uses.

# Analysis

For each WWEIA NHANES respondent on each day of dietary recall, intake of allulose was calculated as the amount of the select food or food ingredient (g) corresponding to either background existing GRAS uses or proposed uses, and multiplied by the maximum allulose use level of that food as shown in Table 1. Contributions from all foods consumed during the two days of recall were summed and the resulting value was divided by two to result in an estimate of 2-day average allulose intake for each respondent. Intakes of allulose derived on a body weight (bw) basis were calculated using each participant's measured body weight.

Summaries of the estimated allulose intake by the population ages 2 y and older and subpopulations of infants and children <2 y, children 2-12 y, adolescents 13-18 y, adult females 19 y and older, and adult males 19 y and older were derived from the allulose intakes calculated for each respondent. Estimates of intake for the population groups were calculated on a *per user* basis and a *per capita* basis, in units of gram allulose per day (g/day) and gram allulose per kilogram body weight per day (g/kg-bw/day). In this analysis, a "user" is anyone who reported consuming a food with allulose added on either of the survey days. The resulting values represent estimates of allulose intake assuming the maximum use level of allulose.

The 2-day average intakes by each individual were estimated using Exponent's Foods Analysis and Residue Evaluation Program (FARE® version 14.06) software, which uses the statistically weighted values from the survey in its analyses. The statistical weights compensate for variable probabilities of selection, adjust for non-response, and provide intake estimates that are representative of the U.S. population.

## Cumulative EDI (CEDI)

To estimate the CEDI for allulose, food uses of allulose from background food uses and proposed uses together were considered. Specifically, intake of allulose was calculated as the amount of the select food or food ingredient (in grams) from either background existing GRAS and/or proposed uses, and multiplied by the maximum allulose level associated with the combined GRAS and proposed uses of that food as shown in Table 1.

# Results

The two-day average intake estimates of allulose at the mean and 90th percentile of intake was derived using dietary records from NHANES 2015-2018 for the U.S. population 2+ y and subpopulations of infants and young children, children, adolescents, adult females, and adult males. The EDI of allulose from background and proposed uses are summarized in Tables 2 and 3, respectively. The allulose CEDI from the combined background and proposed uses are summarized in Table 4.

## Background EDI

Among the U.S. population 2+ y, 92% consumed one or more foods containing allulose from background uses (i.e., GRAS uses from GRNs 400, 498, 693, and 828; Table 2). The estimated daily intake of allulose from background uses at the per user mean and 90th percentile of intake among this population is 6.69 g/day (0.09 g/kg-bw/day) and 16.39 g/day (0.23 g/kg-bw/day), respectively. Per user mean intake of allulose from background uses ranged from 1.50 g/day among infants <2 y to 8.68 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.14 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 3.63 g/day among infants <2 y to 22.71 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2 y at 0.34 g/kg-bw/day allulose.

The total per user mean and 90th percentile intake estimates of allulose based on NHANES data and reported for the U.S. population by GRNs 400, 498, 693 and 828 ranged from 9-12.55 g/day and 24.8-30 g/day, respectively. The per user mean and 90th percentile intake estimates in the present analysis are approximately 26% and 34% lower, respectively, than those estimates in the GRNs. In order to understand the downward shift of allulose intake observed in the more recent NHANES data, Exponent generated and compared two sets of allulose intake estimates using NHANES 2015-2018 and NHANES 2007-2010 for the food uses reported in GRN 498 (see Appendix C). Lower allulose intake estimates in the present analysis appear to be due to a shift in dietary patterns of non-alcoholic low calorie, reduced calorie, sugar-free beverages. Specifically, the percent users and intake of non-alcoholic beverages (low calorie, reduced calorie, sugar-free) have decreased from 32% in NHANES 2007-2010 to 21% in NHANES 2015-2018 with a decreased amount intake among consumers of non-alcoholic beverages in NHANES 2015-2018. A trend analysis conducted by Bleich et al. (2018) similarly reported an observed decline in beverage and sugar-sweetened beverage consumption for children and adults from 2003 to 2014. There was also a

reduction in intake of regular cereal contributing to lower allulose intakes, i.e., a decrease in percent users (46% in NHANES 2007-2010 versus 33% in NHANES 2015-2018) and lower intake amounts in NHANES 2015-2018. This reduction, however, did not result from changes in dietary patterns but instead was due to differences in the food selection methodology between GRN 498 and the current assessment. The food selection of regular cereals in the present analysis was limited to cereals with added sugar since allulose would not be added to cereals with no added sugar, whereas all cereals excluding low calorie, reduced calorie, and sugar-free cereals were included in the assessment for GRN 498 under regular cereals. The estimated allulose intake from existing background uses in this analysis relies on the most currently available dietary data from NHANES (2015-2018) and shows a lower allulose intake as compared to previously reported allulose EDIs from GRNs 400, 498, 693, and 828.

Table 2. Two-day average EDI of allulose from background uses by the U.S. population 2+ y and subpopulations

| | | | Per Capita | | Per User | |
|---|---|---|---|---|---|---|
| | N* | % User | Mean | 90th Percentile | Mean | 90th Percentile |
| Background Allulose EDIs (g/day) | | | | | | |
| U.S. 2+ y | 11650 | 92 | 6.18 | 15.15 | 6.69 | 16.39 |
| Infants <2 y | 391 | 48 | 0.72 | 1.94 | 1.50 | 3.63 |
| Children 2-12 y | 2566 | 95 | 2.89 | 6.71 | 3.04 | 6.98 |
| Adolescents 13-18 y | 1257 | 88 | 3.27 | 7.62 | 3.70 | 8.33 |
| Males 19+ y | 3696 | 92 | 7.97 | 20.70 | 8.68 | 22.71 |
| Females 19+ y | 4131 | 93 | 6.30 | 16.44 | 6.79 | 17.45 |
| Background Allulose EDIs (g/kg-bw/day) | | | | | | |
| U.S. 2+ y | 11650 | 92 | 0.09 | 0.22 | 0.09 | 0.23 |
| Infants <2 y | 391 | 48 | 0.07 | 0.16 | 0.14 | 0.34 |
| Children 2-12 y | 2566 | 95 | 0.11 | 0.27 | 0.12 | 0.28 |
| Adolescents 13-18 y | 1257 | 88 | 0.05 | 0.12 | 0.06 | 0.14 |
| Males 19+ y | 3696 | 92 | 0.09 | 0.23 | 0.10 | 0.25 |
| Females 19+ y | 4131 | 93 | 0.08 | 0.21 | 0.09 | 0.22 |

* Unweighted number of users; % user, *per capita*, and *per user* estimates were based on NHANES 2015-2018 and derived using the statistical weights provided by the NCHS.

## Proposed Uses EDI

Among the U.S. population 2+ y, 64% consumed one or more foods containing allulose from proposed uses (Table 3). The estimated daily intake of allulose from proposed uses at the per user mean and 90th percentile of intake among this population is 5.92 g/day (0.10 g/kg-bw/day) and 13.47 g/day (0.22 g/kg-bw/day), respectively. Per user mean intake of allulose from proposed uses ranged from 3.61 g/day among infants < 2 y

to 6.94 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.32 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 7.74 g/day among infants <2 y to 16.34 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2 y at 0.66 g/kg-bw/day allulose.

Table 3. Two-day average EDI of allulose from all intended uses by the U.S. population 2+ y and subpopulations

| | | | Per Capita | | Per User | |
|---|---|---|---|---|---|---|
| | N* | % User | Mean | 90th Percentile | Mean | 90th Percentile |
| Allulose EDIs from Proposed Uses (g/day) | | | | | | |
| U.S. 2+ y | 7831 | 64 | 3.78 | 10.35 | 5.92 | 13.47 |
| Infants <2 y | 252 | 31 | 1.13 | 2.64 | 3.61 | 7.74 |
| Children 2-12 y | 2078 | 75 | 3.16 | 7.88 | 4.20 | 8.58 |
| Adolescents 13-18 y | 942 | 67 | 3.40 | 9.58 | 5.09 | 11.00 |
| Males 19+ y | 2316 | 63 | 4.37 | 12.39 | 6.94 | 16.34 |
| Females 19+ y | 2495 | 60 | 3.54 | 10.33 | 5.89 | 13.91 |
| Allulose EDIs from Proposed Uses (g/kg-bw/day) | | | | | | |
| U.S. 2+ y | 7831 | 64 | 0.06 | 0.17 | 0.10 | 0.22 |
| Infants <2 y | 252 | 31 | 0.10 | 0.23 | 0.32 | 0.66 |
| Children 2-12 y | 2078 | 75 | 0.13 | 0.30 | 0.17 | 0.34 |
| Adolescents 13-18 y | 942 | 67 | 0.05 | 0.15 | 0.08 | 0.17 |
| Males 19+ y | 2316 | 63 | 0.05 | 0.14 | 0.08 | 0.19 |
| Females 19+ y | 2495 | 60 | 0.05 | 0.15 | 0.08 | 0.19 |

* Unweighted number of users; % user, *per capita*, and *per user* estimates were based on NHANES 2015-2018 and derived using the statistical weights provided by the NCHS.

## Cumulative EDI (CEDI)

Among the U.S. population 2+ y, 95% consumed one or more foods containing allulose from background uses and/or proposed uses. The allulose CEDI at the per user mean and 90th percentile of intake among this population is 10.09 g/day (0.15 g/kg-bw/day) and 23.53 g/day (0.35 g/kg-bw/day), respectively (Table 4). Per user mean allulose CEDI ranged from 3.33 g/day among infants <2 y to 12.61 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.30 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 7.18 g/day among infants <2 y to 29.86 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2 y at 0.65 g/kg-bw/day allulose.

Table 4. Two-day average CEDI of allulose from background uses and all proposed uses combined by the U.S. population 2+ y and subpopulations

| | | | Per Capita | | Per User | |
|---|---|---|---|---|---|---|
| | N* | % User | Mean | 90th Percentile | Mean | 90th Percentile |
| Allulose CEDIs (g/day) | | | | | | |
| U.S. 2+ y | 12017 | 95 | 9.60 | 22.65 | 10.09 | 23.53 |
| Infants <2 y | 409 | 50 | 1.66 | 4.75 | 3.33 | 7.18 |
| Children 2-12 y | 2632 | 97 | 5.63 | 12.04 | 5.83 | 12.36 |
| Adolescents 13-18 y | 1320 | 92 | 6.28 | 13.39 | 6.79 | 13.55 |
| Males 19+ y | 3828 | 95 | 12.00 | 28.84 | 12.61 | 29.86 |
| Females 19+ y | 4237 | 95 | 9.48 | 23.27 | 9.99 | 24.05 |
| Allulose CEDIs (g/kg-bw/day) | | | | | | |
| U.S. 2+ y | 12017 | 95 | 0.14 | 0.34 | 0.15 | 0.35 |
| Infants <2 y | 409 | 50 | 0.15 | 0.40 | 0.30 | 0.65 |
| Children 2-12 y | 2632 | 97 | 0.22 | 0.48 | 0.23 | 0.49 |
| Adolescents 13-18 y | 1320 | 92 | 0.10 | 0.22 | 0.11 | 0.22 |
| Males 19+ y | 3828 | 95 | 0.13 | 0.32 | 0.14 | 0.33 |
| Females 19+ y | 4237 | 95 | 0.13 | 0.30 | 0.14 | 0.32 |

* Unweighted number of users; % user, *per capita*, and *per user* estimates were based on NHANES 2015-2018 and derived using the statistical weights provided by the NCHS

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# Appendix A. Existing Food Uses of Allulose

| Food Category | Allulose Use Level (%) | | | | |
|---|---|---|---|---|---|
| | **Maximum use level from existing GRAS uses** | **GRN 828 (Samyang Corporation, 2018)** | **GRN 693 (Samyang Corporation, 2017)** | **GRN 498 (Matsutani Chemical Industry Company Ltd, 2013)** | **GRN 400 (CJ Cheiljedang, 2011)** |
| Baked products (bread, muffin, cake/cookies, pastries, dietetic, low calorie, reduced calorie, sugar-free | **10** | 10 | 10 | - | 10 |
| Beverages, non-alcoholic, low calorie, red calorie, sugar free | **3.5** | 3.5 | 3.5 | 3.5 | 2.1 |
| Candy, hard & soft | | | | | |
| (a) Hard candy includes pressed candy and mints, low calorie, reduced calorie, sugar-free | **70** | 50 | 50 | 50 | 70 |
| (b) Soft candy, low calorie, reduced calorie, sugar-free | **25** | 25 | 25 | 25 | 25 |
| Chewing gum | **50** | 50 | 50 | 50 | 50 |
| Cereals, ready to eat and cooked | | | | | |
| (a) RTE and cooked, regular | **2** | 2 | 2 | 2 | - |
| (b) RTE and cooked, low calorie, reduced calorie, sugar-free | **5** | 5 | 5 | 5 | - |
| (c) RTE cereals with <5% sugar | **10** | - | - | - | 10 |
| Coffee mix | **30** | - | - | - | 30 |
| Confections & Frostings | **5** | 5 | 5 | 5 | - |
| Dressing for salads | **5** | 5 | 5 | 5 | - |
| Frozen dairy (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free | **5** | 5 | 5 | 5 | 5 |
| Gelatins, pudding & fillings | | | | | |
| (a) Gelatins, pudding & fillings, low calorie, reduced calorie, sugar-free | **10** | 10 | 10 | 10 | - |
| (b) Fat-based cream (used in modified fat/calorie cookies, cakes, pastries, pie) | **10** | 5 | 5 | - | 10 |
| Jams & Jellies | **10** | 10 | 10 | 10 | - |

| Food Category | Allulose Use Level (%) | | | | |
|---|---|---|---|---|---|
| | **Maximum use level from existing GRAS uses** | **GRN 828 (Samyang Corporation, 2018)** | **GRN 693 (Samyang Corporation, 2017)** | **GRN 498 (Matsutani Chemical Industry Company Ltd, 2013)** | **GRN 400 (CJ Cheiljedang, 2011)** |
| Sugar | **10** | 10 | 10 | 10 | - |
| Sugar Substitutes | **100** | 100 | 100 | 100 | 100 |
| Sweet sauces & syrups, low calorie, reduced calorie, sugar-free | **10** | 10 | 10 | 10 | - |
| Yogurt and frozen yogurt, low calorie, reduced calorie, sugar-free | **5** | 5 | 5 | 5 | 5 |
| Medical foods | **15** | - | - | - | 15 |

# Appendix B. Food Codes Included In Analysis

Food Category

1 Baked products (bread, muffin, cake and cookies, pastries), dietetic, low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 51121015 | Garlic bread, NFS |
| 51122000 | Bread, reduced calorie and/or high fiber, white or NFS |
| 51122100 | Bread, reduced calorie and/or high fiber, white or NFS, with fruit and/or nuts |
| 51122110 | Bread, reduced calorie and/or high fiber, white or NFS, with fruit and/or nuts, toasted |
| 51183990 | Breadsticks, NFS |
| 51184200 | Breadsticks, soft, NFS |
| 51301510 | Bread, wheat or cracked wheat, reduced calorie and/or high fiber |
| 51602020 | Bread, multigrain, reduced calorie and/or high fiber, toasted |
| 53109220 | Snack cake, not chocolate, with icing or filling, reduced fat and calories |
| 53201000 | Cookie, NFS |
| 53260030 | Cookie, chocolate chip, sugar free |
| 53260200 | Cookie, oatmeal, sugar free |
| 53260300 | Cookie, sandwich, sugar free |
| 53260400 | Cookie, sugar or plain, sugar free |
| 53260500 | Cookie, sugar wafer, sugar free |
| 53260600 | Cookie, peanut butter, sugar free |

2 Beverages

2a Non-alcoholic beverages, low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 64134100 | Fruit smoothie, light |
| 92101901 | Coffee, Latte, nonfat |
| 92101911 | Coffee, Latte, decaffeinated, nonfat |
| 92101921 | Frozen coffee drink, nonfat |
| 92101926 | Frozen coffee drink, nonfat, with whipped cream |
| 92102010 | Frozen mocha coffee drink, nonfat |
| 92102040 | Frozen mocha coffee drink, nonfat, with whipped cream |
| 92102501 | Coffee, Iced Latte, nonfat |
| 92130005 | Coffee, pre-lightened and pre-sweetened with low calorie sweetener |
| 92130010 | Coffee, pre-lightened |
| 92130011 | Coffee, decaffeinated, pre-lightened |
| 92130030 | Coffee, pre-sweetened with low calorie sweetener |
| 92130031 | Coffee, decaffeinated, pre-sweetened with low calorie sweetener |
| 92171010 | Coffee, bottled/canned, light |
| 92305090 | Tea, iced, instant, black, pre-sweetened with low calorie sweetener |
| 92305110 | Tea, iced, instant, black, decaffeinated, pre-sweetened with low calorie sweetener |
| 92305920 | Tea, iced, instant, green, pre-sweetened with low calorie sweetener |
| 92307510 | Iced Tea / Lemonade juice drink, light |
| 92307520 | Iced Tea / Lemonade juice drink, diet |
| 92308010 | Tea, iced, brewed, black, pre-sweetened with low calorie sweetener |
| 92308040 | Tea, iced, brewed, black, decaffeinated, pre-sweetened with low calorie sweetener |
| 92308510 | Tea, iced, brewed, green, pre-sweetened with low calorie sweetener |
| 92308540 | Tea, iced, brewed, green, decaffeinated, pre-sweetened with low calorie sweetener |
| 92309020 | Tea, iced, bottled, black, diet |

| | |
|---|---|
| 92309030 | Tea, iced, bottled, black, decaffeinated, diet |
| 92309510 | Tea, iced, bottled, green, diet |
| 92400100 | Soft drink, NFS, diet |
| 92410250 | Carbonated water, sweetened, with low-calorie or no-calorie sweetener |
| 92410315 | Soft drink, cola, reduced sugar |
| 92410320 | Soft drink, cola, diet |
| 92410350 | Soft drink, cola, decaffeinated, diet |
| 92410370 | Soft drink, pepper type, diet |
| 92410400 | Soft drink, pepper type, decaffeinated, diet |
| 92410420 | Soft drink, cream soda, diet |
| 92410520 | Soft drink, fruit flavored, diet, caffeine free |
| 92410560 | Soft drink, fruit flavored, caffeine containing, diet |
| 92410620 | Soft drink, ginger ale, diet |
| 92410720 | Soft drink, root beer, diet |
| 92411610 | Soft drink, cola, fruit or vanilla flavored, diet |
| 92513010 | Slush frozen drink, no sugar added |
| 92550030 | Fruit juice drink, with high vitamin C, light |
| 92550035 | Fruit juice drink, light |
| 92550040 | Fruit juice drink, diet |
| 92550110 | Cranberry juice drink, with high vitamin C, light |
| 92550200 | Grape juice drink, light |
| 92550350 | Orange juice beverage, 40-50% juice, light |
| 92550360 | Apple juice beverage, 40-50% juice, light |
| 92550370 | Lemonade, fruit juice drink, light |
| 92550380 | Pomegranate juice beverage, 40-50% juice, light |
| 92550400 | Vegetable and fruit juice drink, with high vitamin C, diet |
| 92550405 | Vegetable and fruit juice drink, with high vitamin C, light |
| 92550610 | Fruit flavored drink, with high vitamin C, diet |
| 92550620 | Fruit flavored drink, diet |
| 92552000 | Fruit flavored drink, with high vitamin C, powdered, reconstituted, diet |
| 92552010 | Fruit flavored drink, powdered, reconstituted, diet |
| 92552020 | Fruit juice drink, reduced sugar (Sunny D) |
| 92552030 | Fruit juice drink (Capri Sun) |
| 92900200 | Fruit flavored drink, powdered, not reconstituted, diet** |
| 93301183 | Whiskey and diet cola* |
| 93301191 | Rum and diet cola* |
| 93301215 | Vodka and diet cola* |
| 94100200 | Water, bottled, sweetened, with low calorie sweetener |
| 94220215 | Water, bottled, flavored, sugar free (Glaceau Vitamin Water) |
| 94220310 | Water, bottled, flavored, sugar free (SoBe) |
| 95312400 | Energy drink, low calorie (Monster) |
| 95312410 | Energy drink, sugar free (Monster) |
| 95312600 | Energy drink, sugar-free (Red Bull) |
| 95312700 | Energy drink, sugar free (Rockstar) |
| 95313200 | Energy drink, sugar free |
| 95322200 | Sports drink, low calorie (Gatorade G2) |
| 95322500 | Sports drink, low calorie (Powerade Zero) |
| 95323000 | Sports drink, low calorie |

2b Nutritional beverages

| Food code | Food description*,** |
|---|---|
| 11553120 | Fruit smoothie, with whole fruit and dairy, added protein*,** |

| | |
|---|---|
| 64134020 | Fruit smoothie, with whole fruit, no dairy, added protein*,** |
| 78101110 | Fruit and vegetable smoothie, added protein*,** |
| 78101118 | Fruit and vegetable smoothie, non-dairy, added protein*,** |
| 95102000 | Nutritional drink or shake, ready-to-drink (Carnation Instant Breakfast) |
| 95105000 | Nutritional drink or shake, ready-to-drink (Kellogg's Special K Protein) |
| 95106000 | Nutritional drink or shake, ready-to-drink (Muscle Milk) |
| 95106010 | Nutritional drink or shake, ready-to-drink, light (Muscle Milk) |
| 95110000 | Nutritional drink or shake, ready-to-drink (Slim Fast) |
| 95110010 | Nutritional drink or shake, ready-to-drink, sugar free (Slim Fast) |
| 95110020 | Nutritional drink or shake, high protein, ready-to-drink (Slim Fast) |
| 95120000 | Nutritional drink or shake, ready-to-drink, NFS |
| 95120010 | Nutritional drink or shake, high protein, ready-to-drink, NFS |
| 95120020 | Nutritional drink or shake, high protein, light, ready-to-drink, NFS |
| 95201000 | Nutritional powder mix (Carnation Instant Breakfast)** |
| 95201010 | Nutritional powder mix, sugar free (Carnation Instant Breakfast)** |
| 95201200 | Nutritional powder mix (EAS Whey Protein Powder) ** |
| 95201300 | Nutritional powder mix (EAS Soy Protein Powder)** |
| 95201500 | Nutritional powder mix, high protein (Herbalife)** |
| 95201600 | Nutritional powder mix (Isopure)** |
| 95201700 | Nutritional powder mix (Kellogg's Special K20 Protein Water)** |
| 95202000 | Nutritional powder mix (Muscle Milk)** |
| 95210000 | Nutritional powder mix (Slim Fast)** |
| 95210020 | Nutritional powder mix, high protein (Slim Fast)** |
| 95220000 | Nutritional powder mix, NFS** |
| 95220010 | Nutritional powder mix, high protein, NFS** |
| 95230000 | Nutritional powder mix, whey based, NFS** |
| 95230010 | Nutritional powder mix, protein, soy based, NFS** |
| 95230020 | Nutritional powder mix, protein, light, NFS** |
| 95230030 | Nutritional powder mix, protein, NFS** |

2c Nutritional beverages intended for children (i.e., PediaSure)

| Food code | Food description |
|---|---|
| 11710800 | Infant formula, NS as to form (PediaSure) |
| 11710801 | Infant formula, ready-to-feed (PediaSure) |
| 11710806 | Infant formula, with fiber, ready-to-feed (PediaSure Fiber) |

2d Alcoholic malt beverage, sweetened

| Food code | Food description |
|---|---|
| 93106000 | Alcoholic malt beverage, sweetened |

2e Alcoholic premixed cocktails

| Food code | Food description |
|---|---|
| 93301000 | Cocktail, NFS |
| 93301010 | Alexander |
| 93301020 | Bacardi cocktail |
| 93301032 | Cape Cod |
| 93301040 | Daiquiri |
| 93301050 | Gimlet |
| 93301060 | Gin and Tonic |
| 93301083 | Jagerbomb |
| 93301085 | Kamikaze |
| 93301100 | Margarita |
| 93301111 | Martini, flavored |
| 93301125 | Mojito |

| | |
|---|---|
| 93301130 | Old fashioned |
| 93301132 | Orange Blossom |
| 93301141 | Seabreeze |
| 93301142 | Seven and Seven |
| 93301150 | Tom Collins |
| 93301160 | Whiskey sour |
| 93301170 | Whiskey and soda |
| 93301182 | Whiskey and cola |
| 93301183 | Whiskey and diet cola |
| 93301184 | Whiskey and ginger ale |
| 93301190 | Rum and cola |
| 93301191 | Rum and diet cola |
| 93301200 | Pina Colada |
| 93301205 | Brandy and cola |
| 93301211 | Vodka and soda |
| 93301213 | Vodka and lemonade |
| 93301214 | Vodka and cola |
| 93301215 | Vodka and diet cola |
| 93301216 | Vodka and energy drink |
| 93301218 | Vodka and tonic |
| 93301240 | Black Russian |
| 93301250 | White Russian |
| 93301270 | Fruit punch, alcoholic |
| 93301310 | Mai Tai |
| 93301320 | Tequila Sunrise |
| 93301360 | Long Island iced tea |
| 93301400 | Irish Coffee |
| 93301450 | Liqueur with cream |
| 93301500 | Frozen daiquiri |
| 93301510 | Frozen margarita |
| 93301550 | Eggnog, alcoholic |
| 93404000 | Wine cooler |
| 93504100 | Rum cooler |

3 Candy, hard and soft

3a Hard Candy (includes pressed candy and mints), low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 91700010 | Candy, NFS |
| 91770020 | Dietetic or low calorie hard candy |

3b Soft Candy, low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 91770010 | Dietetic or low calorie gumdrops |
| 91770030 | Dietetic or low calorie candy, chocolate covered |

4 Chewing gum

| Food code | Food description |
|---|---|
| 91800100 | Chewing gum, NFS |
| 91801000 | Chewing gum, regular |
| 91802000 | Chewing gum, sugar free |

5 Cereals, ready-to-eat (RTE) and cooked

5a RTE and cooked, regular

| Food code | Food description |
|---|---|
| 56201360 | Grits, instant, made with non-dairy milk, fat added |

| | |
|---|---|
| 56201540 | Cornmeal, Puerto Rican Style |
| 56202905 | Oatmeal, from fast food, maple flavored |
| 56202910 | Oatmeal, from fast food, fruit flavored |
| 56202920 | Oatmeal, from fast food, other flavors |
| 56203075 | Oatmeal, regular or quick, made with non-dairy milk, NS as to fat |
| 56203076 | Oatmeal, regular or quick, made with non-dairy milk, no added fat |
| 56203077 | Oatmeal, regular or quick, made with non-dairy milk, fat added |
| 56203106 | Oatmeal, instant, plain, made with non-dairy milk, no added fat |
| 56203125 | Oatmeal, instant, maple flavored, NS as to fat |
| 56203130 | Oatmeal, instant, maple flavored, no added fat |
| 56203135 | Oatmeal, instant, maple flavored, fat added |
| 56203150 | Oatmeal, instant, fruit flavored, NS as to fat |
| 56203155 | Oatmeal, instant, fruit flavored, no added fat |
| 56203160 | Oatmeal, instant, fruit flavored, fat added |
| 56203175 | Oatmeal, instant, other flavors, no added fat |
| 56203180 | Oatmeal, instant, other flavors, fat added |
| 56205080 | Rice, creamed, made with milk and sugar, Puerto Rican style |
| 56207027 | Cream of wheat, regular or quick, made with non-dairy milk, fat added |
| 56207030 | Cream of wheat, instant, made with water, no added fat |
| 56207060 | Cream of wheat, instant, made with water, fat added |
| 56207094 | Cream of wheat, instant, made with milk, fat added |
| 56207095 | Cream of wheat, instant, made with milk, no added fat |
| 56207102 | Cream of wheat, instant, made with non-dairy milk, no added fat |
| 57100100 | Cereal, ready-to-eat, NFS |
| 57101000 | Cereal (Kellogg's All-Bran) |
| 57103000 | Cereal (Post Alpha-Bits) |
| 57103100 | Cereal (General Mills Cheerios Apple Cinnamon) |
| 57104000 | Cereal (Kellogg's Apple Jacks) |
| 57106050 | Cereal (Post Great Grains Banana Nut Crunch) |
| 57106060 | Cereal (General Mills Cheerios Banana Nut) |
| 57106100 | Cereal (General Mills Basic 4) |
| 57106250 | Cereal (General Mills Kix Berry Berry) |
| 57106260 | Cereal (General Mills Cheerios Berry Burst) |
| 57107000 | Cereal (General Mills Boo Berry) |
| 57110000 | Cereal (Kellogg's All-Bran Bran Buds) |
| 57117000 | Cereal (Quaker Cap'n Crunch) |
| 57117500 | Cereal (Quaker Christmas Crunch) |
| 57119000 | Cereal (Quaker Cap'n Crunch's Crunchberries) |
| 57120000 | Cereal (Quaker Cap'n Crunch's Peanut Butter Crunch) |
| 57124030 | Cereal (General Mills Chex Chocolate) |
| 57124050 | Cereal (General Mills Chex Cinnamon) |
| 57124100 | Cereal (General Mills Cheerios Chocolate) |
| 57124200 | Cereal, chocolate flavored, frosted, puffed corn |
| 57124300 | Cereal (General Mills Lucky Charms Chocolate) |
| 57125000 | Cereal (General Mills Cinnamon Toast Crunch) |
| 57125900 | Cereal (General Mills Honey Nut Clusters) |
| 57126000 | Cereal (Kellogg's Cocoa Krispies) |
| 57127000 | Cereal (Post Cocoa Pebbles) |
| 57128000 | Cereal (General Mills Cocoa Puffs) |
| 57130000 | Cereal (General Mills Cookie Crisp) |
| 57132000 | Cereal (General Mills Chex Corn) |

57134000 Cereal, corn flakes
57135000 Cereal (Kellogg's Corn Flakes)
57137000 Cereal, corn puffs
57139000 Cereal (General Mills Count Chocula)
57143000 Cereal (Kellogg's Cracklin' Oat Bran)
57143500 Cereal (Post Great Grains, Cranberry Almond Crunch)
57148000 Cereal (Kellogg's Crispix)
57148500 Cereal, crispy brown rice
57151000 Cereal, crispy rice
57201900 Cereal (General Mills Dora The Explorer)
57206710 Cereal (General Mills Fiber One Honey Clusters)
57206715 Cereal (General Mills Fiber One Raisin Bran Clusters)
57207000 Cereal, bran flakes
57208000 Cereal (Kellogg's All-Bran Complete Wheat Flakes)
57209000 Cereal (Post Bran Flakes)
57211000 Cereal (General Mills Frankenberry)
57213000 Cereal (Kellogg's Froot Loops)
57213010 Cereal (Kellogg's Froot Loops Marshmallow)
57213850 Cereal (General Mills Cheerios Frosted)
57214000 Cereal (Kellogg's Frosted Mini-Wheats)
57218000 Cereal (Kellogg's Frosted Krispies)
57221700 Cereal, fruit rings
57221810 Cereal (General Mills Cheerios Fruity)
57223000 Cereal (Post Fruity Pebbles)
57224000 Cereal (General Mills Golden Grahams)
57227000 Cereal, granola
57228000 Granola, homemade
57229000 Cereal (Kellogg's Low Fat Granola)
57229500 Cereal (Kellogg's Low Fat Granola with Raisins)
57231000 Cereal (Post Grape-Nuts Flakes)
57231200 Cereal (Post Great Grains Raisins, Dates, and Pecans)
57231250 Cereal (Post Great Grains Double Pecan Whole Grain Cereal)
57237100 Cereal (Post Honey Bunches of Oats Honey Roasted)
57237200 Cereal (Post Honey Bunches of Oats with Vanilla Bunches)
57237300 Cereal (Post Honey Bunches of Oats with Almonds)
57237900 Cereal (Post Honey Bunches of Oats Just Bunches)
57238000 Cereal (Post Honeycomb)
57240100 Cereal (General Mills Chex Honey Nut)
57241000 Cereal (General Mills Cheerios Honey Nut)
57241200 Cereal (Post Shredded Wheat Honey Nut)
57243000 Cereal (Kellogg's Honey Smacks)
57301505 Cereal (Kashi Autumn Wheat)
57301510 Cereal (Kashi GOLEAN)
57301511 Cereal (Kashi GOLEAN Crunch)
57301512 Cereal (Kashi GOLEAN Crunch Honey Almond Flax)
57301530 Cereal (Kashi Heart to Heart Honey Toasted Oat)
57303100 Cereal (General Mills Kix)
57303105 Cereal (General Mills Honey Kix)
57303200 Cereal (Kellogg's Krave)
57304100 Cereal (Quaker Life)
57305100 Cereal (General Mills Lucky Charms)

| | |
|---|---|
| 57305150 | Cereal, frosted oat cereal with marshmallows |
| 57305160 | Cereal (Malt-O-Meal Blueberry Muffin Tops) |
| 57305165 | Cereal (Malt-O-Meal Cinnamon Toasters) |
| 57305170 | Cereal (Malt-O-Meal Coco-Roos) |
| 57305174 | Cereal (Malt-O-Meal Colossal Crunch) |
| 57305175 | Cereal (Malt-O-Meal Cocoa Dyno-Bites) |
| 57305180 | Cereal (Malt-O-Meal Corn Bursts) |
| 57305200 | Cereal (Malt-O-Meal Crispy Rice) |
| 57305210 | Cereal (Malt-O-Meal Frosted Flakes) |
| 57305215 | Cereal (Malt-O-Meal Frosted Mini Spooners) |
| 57305300 | Cereal (Malt-O-Meal Fruity Dyno-Bites) |
| 57305400 | Cereal (Malt-O-Meal Honey Graham Squares) |
| 57305500 | Cereal (Malt-O-Meal Honey Nut Toasty O's) |
| 57305600 | Cereal (Malt-O-Meal Marshmallow Mateys) |
| 57306130 | Cereal (Malt-O-Meal Raisin Bran) |
| 57306500 | Cereal (Malt-O-Meal Golden Puffs) |
| 57306800 | Cereal (Malt-O-Meal Tootie Fruities) |
| 57308190 | Cereal, muesli |
| 57308400 | Cereal (General Mills Cheerios Multigrain) |
| 57309100 | Cereal (Nature Valley Granola) |
| 57316300 | Cereal (Health Valley Oat Bran Flakes) |
| 57316380 | Cereal (General Mills Cheerios Oat Cluster Crunch) |
| 57316385 | Cereal (General Mills Cheerios Protein) |
| 57316450 | Cereal (General Mills Oatmeal Crisp with Almonds) |
| 57316710 | Cereal (Quaker Honey Graham Oh's) |
| 57320500 | Cereal (Quaker Granola with Oats, Honey, and Raisins) |
| 57321900 | Cereal (Nature's Path Organic Flax Plus) |
| 57326000 | Cereal (Barbara's Puffins) |
| 57327450 | Cereal (Quaker Toasted Oat Bran) |
| 57327500 | Cereal (Quaker Oatmeal Squares) |
| 57329000 | Cereal, raisin bran |
| 57330000 | Cereal (Kellogg's Raisin Bran) |
| 57330010 | Cereal (Kellogg's Raisin Bran Crunch) |
| 57331000 | Cereal (Post Raisin Bran) |
| 57332050 | Cereal (General Mills Total Raisin Bran) |
| 57332100 | Cereal (General Mills Raisin Nut Bran) |
| 57335550 | Cereal (General Mills Reese's Puffs) |
| 57336000 | Cereal (General Mills Chex Rice) |
| 57337000 | Cereal, rice flakes |
| 57339000 | Cereal (Kellogg's Rice Krispies) |
| 57339500 | Cereal (Kellogg's Rice Krispies Treats Cereal) |
| 57341200 | Cereal (Kellogg's Smart Start Strong) |
| 57341300 | Cereal (Kellogg's Smorz) |
| 57344000 | Cereal (Kellogg's Special K) |
| 57344001 | Cereal (Kellogg's Special K Blueberry) |
| 57344005 | Cereal (Kellogg's Special K Chocolatey Delight) |
| 57344007 | Cereal (Kellogg's Special K Low Fat Granola) |
| 57344010 | Cereal (Kellogg's Special K Red Berries) |
| 57344015 | Cereal (Kellogg's Special K Fruit & Yogurt) |
| 57344020 | Cereal (Kellogg's Special K Vanilla Almond) |
| 57344025 | Cereal (Kellogg's Special K Cinnamon Pecan) |

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| | 57347000 | Cereal (Kellogg's Corn Pops) |
| | 57348000 | Cereal, frosted corn flakes |
| | 57349000 | Cereal (Kellogg's Frosted Flakes) |
| | 57355000 | Cereal (Post Golden Crisp) |
| | 57406100 | Cereal (General Mills Total) |
| | 57407100 | Cereal (General Mills Trix) |
| | 57411000 | Cereal (General Mills Chex Wheat) |
| | 57416010 | Cereal, puffed wheat, sweetened |
| | 57418000 | Cereal (General Mills Wheaties) |

5b RTE and cooked, low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 56203510 | Oatmeal, reduced sugar, plain, no added fat |
| 56203550 | Oatmeal, reduced sugar, flavored, NS as to fat |
| 56203555 | Oatmeal, reduced sugar, flavored, no added fat |
| 56203560 | Oatmeal, reduced sugar, flavored, fat added |
| 57125010 | Cereal (General Mills 25% Less Sugar Cinnamon Toast Crunch) |
| 57128005 | Cereal (General Mills 25% Less Sugar Cocoa Puffs) |
| 57407110 | Cereal (General Mills 25% Less Sugar Trix) |

5c RTE cereals with <5% sugar

| Food code | Food description |
|---|---|
| 57000100 | Cereal, oat, NFS |
| 57123000 | Cereal (General Mills Cheerios) |
| 57306700 | Cereal (Malt-O-Meal Toasted Oat Cereal) |
| 57401100 | Cereal, toasted oat |
| 57410000 | Cereal (Weetabix Whole Grain) |

5d Grain-free, no sugar, high protein RTE cereal

| Food code | Food description |
|---|---|
| 57206700 | Cereal (General Mills Fiber One) |
| 57230000 | Cereal (Post Grape-Nuts) |
| 57301500 | Cereal (Kashi 7 Whole Grain Puffs) |
| 57307500 | Cereal, millet, puffed |
| 57340000 | Cereal, puffed rice |
| 57341000 | Cereal (Post Shredded Wheat'n Bran) |
| 57408100 | Cereal (Uncle Sam) |
| 57416000 | Cereal, puffed wheat, plain |
| 57417000 | Cereal (Post Shredded Wheat) |

6 Coffee mix

| Food code | Food description |
|---|---|
| 92121000 | Coffee, instant, pre-lightened and pre-sweetened with sugar, reconstituted* |
| 92121001 | Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, reconsitituted* |
| 92121010 | Coffee, instant, pre-sweetened with sugar, reconstituted* |
| 92121020 | Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, reconstituted* |
| 92121030 | Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted* |
| 92121040 | Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted* |
| 92121041 | Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted* |
| 92191400 | Coffee, instant, pre-sweetened with sugar, not reconstituted |
| 92193000 | Coffee, instant, pre-lightened and pre-sweetened with sugar, not reconstituted |

7 Confections & Frostings

| Food code | Food description |
|---|---|
| 51160110 | Roll, sweet, cinnamon bun, frosted* |
| 51161020 | Roll, sweet, with fruit, frosted* |
| 51161050 | Roll, sweet, frosted* |
| 51161270 | Pan Dulce, with sugar topping* |
| 51161280 | Pan Dulce, with raisins and icing* |
| 51165000 | Coffee cake, yeast type* |
| 53100100 | Cake or cupcake, NS as to type* |
| 53101200 | Cake, angel food, with icing or filling* |
| 53101250 | Cake, angel food, with fruit and icing or filling* |
| 53102200 | Cake or cupcake, applesauce, with icing or filling* |
| 53102700 | Cake or cupcake, banana, with icing or filling* |
| 53102800 | Cake or cupcake, Black Forest* |
| 53104260 | Cake or cupcake, carrot, with icing or filling* |
| 53104400 | Cake or cupcake, coconut, with icing or filling* |
| 53105270 | Cake or cupcake, chocolate, devil's food or fudge, with icing or filling* |
| 53105300 | Cake or cupcake, German chocolate, with icing or filling* |
| 53108200 | Snack cake, chocolate, with icing or filling* |
| 53109200 | Snack cake, not chocolate, with icing or filling* |
| 53111000 | Cake or cupcake, gingerbread* |
| 53114100 | Cake or cupcake, lemon, with icing or filling* |
| 53115200 | Cake or cupcake, marble, with icing or filling* |
| 53115320 | Cake or cupcake, nut, with icing or filling* |
| 53115410 | Cake or cupcake, oatmeal* |
| 53115450 | Cake or cupcake, peanut butter* |
| 53116020 | Cake, pound, with icing or filling* |
| 53116270 | Cake, pound, chocolate* |
| 53116510 | Cake or cupcake, pumpkin, with icing or filling* |
| 53117200 | Cake or cupcake, spice, with icing or filling* |
| 53118200 | Cake, sponge, with icing or filling* |
| 53118300 | Cake, sponge, chocolate* |
| 53118500 | Cake, torte* |
| 53118550 | Cake, tres leche* |
| 53120270 | Cake or cupcake, white, with icing or filling* |
| 53121270 | Cake or cupcake, yellow, with icing or filling* |
| 53124110 | Cake or cupcake, zucchini* |
| 53204000 | Cookie, brownie, NS as to icing* |
| 53204100 | Cookie, brownie, with icing or filling* |
| 53204840 | Cookie, brownie, reduced fat, NS as to icing* |
| 53204860 | Cookie, brownie, fat free, NS as to icing* |
| 53206100 | Cookie, chocolate chip sandwich* |
| 53208000 | Cookie, marshmallow, chocolate-covered* |
| 53208200 | Cookie, marshmallow pie, chocolate covered* |
| 53209005 | Cookie, chocolate, with icing or coating* |
| 53210900 | Cookie, graham cracker with chocolate and marshmallow* |
| 53226000 | Cookie, marshmallow, with coconut* |
| 53226500 | Cookie, marshmallow, with rice cereal, no bake* |
| 53226550 | Cookie, marshmallow, with rice cereal and chocolate chips* |
| 53226600 | Cookie, marshmallow and peanut butter, with oat cereal, no bake* |
| 53233000 | Cookie, oatmeal* |

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| 53233010 | Cookie, oatmeal, with raisins* |
| 53234100 | Cookie, peanut butter, with chocolate* |
| 53238000 | Cookie, sandwich-type, not chocolate or vanilla* |
| 53239050 | Cookie, shortbread, with icing or filling* |
| 53240010 | Cookie, animal, with frosting or icing* |
| 53243000 | Cookie, vanilla sandwich* |
| 53243050 | Cookie, vanilla sandwich, reduced fat* |
| 53244010 | Cookie, butter or sugar, with chocolate icing or filling* |
| 53244020 | Cookie, butter or sugar, with icing or filling other than chocolate* |
| 53420000 | Cream puff, eclair, custard or cream filled, NS as to icing* |
| 53420200 | Cream puff, eclair, custard or cream filled, iced* |
| 53452420 | Pastry, puff, custard or cream filled, iced or not iced* |
| 53510000 | Danish pastry, plain or spice* |
| 53510100 | Danish pastry, with fruit* |
| 53520110 | Doughnut, cake type* |
| 53520120 | Doughnut, chocolate* |
| 53520135 | Doughnut, cake type, with icing* |
| 53520140 | Doughnut, cake type, chocolate icing* |
| 53520160 | Doughnut, chocolate, with chocolate icing* |
| 53520170 | Doughnut holes* |
| 53521100 | Doughnut, chocolate, raised or yeast, with chocolate icing* |
| 53521110 | Doughnut, yeast type* |
| 53521120 | Doughnut, chocolate, raised or yeast* |
| 53521130 | Doughnut, yeast type, with chocolate icing* |
| 53521230 | Doughnut, custard-filled, with icing* |
| 53530000 | Breakfast tart* |
| 53610100 | Coffee cake, crumb or quick-bread type* |
| 63402980 | Fruit salad, excluding citrus fruits, with marshmallows* |
| 63403040 | Fruit salad, including citrus fruits, with marshmallows* |
| 91304040 | Topping, marshmallow |
| 91305010 | Icing, chocolate |
| 91305020 | Icing, white |
| 91723000 | Marshmallow |

8 Dressings for salads

| Food code | Food description |
|---|---|
| 11440010 | Chipotle dip, yogurt based* |
| 11440020 | Dill dip, yogurt based* |
| 11440040 | Ranch dip, yogurt based* |
| 11440050 | Spinach dip, yogurt based* |
| 11440070 | Vegetable dip, yogurt based* |
| 12350010 | Dip, NFS* |
| 12350200 | Chipotle dip, regular* |
| 12350210 | Dill dip, regular* |
| 12350220 | Onion dip, regular* |
| 12350225 | Onion dip, light* |
| 12350230 | Ranch dip, regular* |
| 12350235 | Ranch dip, light* |
| 12350240 | Spinach dip, regular* |
| 12350245 | Spinach dip, light* |
| 12350250 | Vegetable dip, regular* |
| 12350255 | Vegetable dip, light* |

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| 14620110 | Artichoke dip* |
| 14620115 | Spinach and artichoke dip* |
| 14620130 | Seafood dip* |
| 14640026 | Cheese sandwich, American cheese, on white bread, with mayonnaise* |
| 14640028 | Cheese sandwich, American cheese, on wheat bread, with mayonnaise* |
| 14640030 | Cheese sandwich, American cheese, on whole wheat bread, with mayonnaise* |
| 14640032 | Cheese sandwich, Cheddar cheese, on white bread, with mayonnaise* |
| 14640034 | Cheese sandwich, Cheddar cheese, on wheat bread, with mayonnaise* |
| 14640036 | Cheese sandwich, Cheddar cheese, on whole wheat bread, with mayonnaise* |
| 14640042 | Cheese sandwich, reduced fat American cheese, on whole wheat bread, with mayonnaise* |
| 14640046 | Cheese sandwich, reduced fat Cheddar cheese, on wheat bread, with mayonnaise* |
| 14640048 | Cheese sandwich, reduced fat Cheddar cheese, on whole wheat bread, with mayonnaise* |
| 14670000 | Mozzarella cheese, tomato, and basil, with oil and vinegar dressing* |
| 27220080 | Ham croquette* |
| 27246300 | Chicken or turkey cake, patty, or croquette* |
| 27250040 | Crab cake* |
| 27250070 | Salmon cake or patty* |
| 27250160 | Tuna cake or patty* |
| 27250400 | Shrimp cake or patty* |
| 27416250 | Beef salad* |
| 27420020 | Ham or pork salad* |
| 27446200 | Chicken or turkey salad, made with mayonnaise* |
| 27446205 | Chicken or turkey salad with nuts and/or fruits* |
| 27446220 | Chicken or turkey salad with egg* |
| 27446225 | Chicken or turkey salad, made with light mayonnaise* |
| 27446230 | Chicken or turkey salad, made with mayonnaise-type salad dressing* |
| 27446235 | Chicken or turkey salad, made with light mayonnaise-type salad dressing* |
| 27446240 | Chicken or turkey salad, made with creamy dressing* |
| 27446245 | Chicken or turkey salad, made with light creamy dressing* |
| 27446260 | Chicken or turkey salad, made with any type of fat free dressing* |
| 27450010 | Crab salad* |
| 27450020 | Lobster salad* |
| 27450060 | Tuna salad, made with mayonnaise* |
| 27450061 | Tuna salad, made with light mayonnaise* |
| 27450062 | Tuna salad, made with mayonnaise-type salad dressing* |
| 27450063 | Tuna salad, made with light mayonnaise-type salad dressing* |
| 27450064 | Tuna salad, made with creamy dressing* |
| 27450066 | Tuna salad, made with Italian dressing* |
| 27450068 | Tuna salad, made with any type of fat free dressing* |
| 27450070 | Shrimp salad* |
| 27450080 | Seafood salad* |
| 27450090 | Tuna salad with cheese* |
| 27450100 | Tuna salad with egg* |
| 27450130 | Crab salad made with imitation crab* |
| 27500050 | Sandwich, NFS* |
| 27500100 | Meat sandwich, NFS* |
| 27510000 | Beef sandwich, NFS* |
| 27510145 | Cheeseburger, 1 miniature patty, with condiments, on miniature bun, from fast food / restaurant* |

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| 27510165 | Cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| 27510171 | Whopper Jr with cheese (Burger King)* |
| 27510175 | Cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant (Wendy's Jr. Cheeseburger Deluxe)* |
| 27510205 | Cheeseburger, 1 small patty, with condiments, on white bun* |
| 27510206 | Cheeseburger, 1 small patty, with condiments, on wheat bun* |
| 27510207 | Cheeseburger, 1 small patty, with condiments, on whole wheat bun* |
| 27510225 | Cheeseburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| 27510251 | Cheeseburger, 1 medium patty, with condiments, on white bun* |
| 27510252 | Cheeseburger, 1 medium patty, with condiments, on wheat bun* |
| 27510253 | Cheeseburger, 1 medium patty, with condiments, on whole wheat bun* |
| 27510266 | Cheeseburger, 1 large patty, with condiments, on bun, from fast food / restaurant* |
| 27510276 | Bacon cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| 27510312 | Bacon cheeseburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| 27510341 | Bacon cheeseburger, 1 medium patty, with condiments, on white bun* |
| 27510342 | Bacon cheeseburger, 1 medium patty, with condiments, on wheat bun* |
| 27510343 | Bacon cheeseburger, 1 medium patty, with condiments, on whole wheat bun* |
| 27510346 | Bacon cheeseburger, 1 large patty, with condiments, on bun, from fast food / restaurant* |
| 27510376 | Double cheeseburger, 2 small patties, with condiments, on bun, from fast food / restaurant* |
| 27510406 | Double cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510431 | Double bacon cheeseburger, 2 small patties, with condiments, on bun, from fast food / restaurant (Burger King Bacon Double Cheeseburger)* |
| 27510451 | Double bacon cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510465 | Double bacon cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Wendy's Baconator)* |
| 27510475 | Double bacon cheeseburger, 2 large patties, with condiments, on bun, from fast food / restaurant* |
| 27510486 | Triple cheeseburger, 3 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510506 | Hamburger, 1 miniature patty, with condiments, on miniature bun, from fast food / restaurant* |
| 27510511 | Hamburger, 1 miniature patty, on miniature bun, from school* |
| 27510536 | Hamburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| 27510552 | Whopper Jr (Burger King)* |
| 27510555 | Hamburger, 1 small patty, with condiments, on bun, from fast food / restaurant (Wendy's Jr. Hamburger)* |
| 27510565 | Hamburger, from school cafeteria* |
| 27510585 | Hamburger, 1 small patty, with condiments, on white bun* |
| 27510587 | Hamburger, 1 small patty, with condiments, on whole wheat bun* |
| 27510606 | Hamburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| 27510641 | Hamburger, 1 medium patty, with condiments, on white bun* |
| 27510642 | Hamburger, 1 medium patty, with condiments, on wheat bun* |
| 27510643 | Hamburger, 1 medium patty, with condiments, on whole wheat bun* |
| 27510667 | Double hamburger, 2 small patties, with condiments, on bun, from fast food / restaurant* |

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| 27510676 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510681 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Burger King Double WHOPPER)* |
| 27510682 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Wendy's 1/2 lb Double)* |
| 27510950 | Reuben sandwich, corned beef sandwich with sauerkraut and cheese, with spread* |
| 27513040 | Roast beef submarine sandwich, with lettuce, tomato and spread* |
| 27513041 | Roast beef submarine sandwich, with cheese, lettuce, tomato and spread* |
| 27520150 | Bacon, lettuce, and tomato sandwich with spread* |
| 27520155 | Bacon, lettuce, and tomato submarine sandwich, with spread* |
| 27520156 | Bacon, lettuce, tomato, and cheese submarine sandwich, with spread* |
| 27520160 | Bacon, chicken, and tomato club sandwich, on multigrain roll with lettuce and spread* |
| 27520166 | Bacon, breaded fried chicken fillet, and tomato club sandwich with cheese, lettuce and spread* |
| 27520310 | Ham sandwich with lettuce and spread* |
| 27520320 | Ham and cheese sandwich, with lettuce and spread* |
| 27520350 | Ham and cheese sandwich, with spread, grilled* |
| 27520370 | Hot ham and cheese sandwich, on bun* |
| 27540110 | Sliced chicken sandwich, with spread* |
| 27540111 | Sliced chicken sandwich, with cheese and spread* |
| 27540120 | Chicken salad or chicken spread sandwich* |
| 27540170 | Chicken patty sandwich, miniature, with spread* |
| 27540240 | Chicken fillet, broiled, sandwich, on whole wheat roll, with lettuce, tomato and spread* |
| 27540295 | Buffalo chicken submarine sandwich* |
| 27540296 | Buffalo chicken submarine sandwich with cheese* |
| 27540310 | Turkey sandwich, with spread* |
| 27540360 | Turkey and bacon submarine sandwich, with lettuce, tomato and spread* |
| 27540361 | Turkey and bacon submarine sandwich, with cheese, lettuce, tomato and spread* |
| 27541000 | Turkey, ham, and roast beef club sandwich, with lettuce, tomato and spread* |
| 27545010 | Turkey or chicken burger, with condiments, on bun, from fast food / restaurant* |
| 27545200 | Turkey or chicken burger, with condiments, on white bun* |
| 27545210 | Turkey or chicken burger, with condiments, on wheat bun* |
| 27545220 | Turkey or chicken burger, with condiments, on whole wheat bun* |
| 27550110 | Crab cake sandwich* |
| 27550120 | Salmon cake sandwich* |
| 27550720 | Tuna salad sandwich, on bread* |
| 27550730 | Tuna salad sandwich, on bread, with cheese* |
| 27550740 | Tuna salad sandwich, on bun* |
| 27550745 | Tuna salad sandwich, on bun, with cheese* |
| 27550750 | Tuna salad submarine sandwich, with lettuce and tomato* |
| 27550751 | Tuna salad submarine sandwich, with cheese, lettuce and tomato* |
| 27550755 | Tuna salad wrap sandwich* |
| 27550800 | Seafood salad sandwich* |
| 27560120 | Bologna and cheese sandwich, with spread* |
| 27560500 | Pepperoni and salami submarine sandwich, with lettuce, tomato and spread* |
| 32102000 | Egg, deviled* |
| 32103000 | Egg salad, made with mayonnaise* |
| 32103015 | Egg salad, made with light mayonnaise* |
| 32103020 | Egg salad, made with mayonnaise-type salad dressing* |
| 32103025 | Egg salad, made with light mayonnaise-type salad dressing* |

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| 32103050 | Egg Salad, made with any type of fat free dressing* |
| 32202025 | Egg, cheese and ham on bagel* |
| 41203030 | Black bean salad* |
| 41420100 | Miso sauce* |
| 58127500 | Vegetable submarine sandwich, with fat free spread* |
| 58134640 | Tortellini, cheese-filled, meatless, with vinaigrette dressing* |
| 58148110 | Macaroni or pasta salad, made with mayonnaise* |
| 58148111 | Macaroni or pasta salad, made with light mayonnaise* |
| 58148112 | Macaroni or pasta salad, made with mayonnaise-type salad dressing* |
| 58148114 | Macaroni or pasta salad, made with Italian dressing* |
| 58148117 | Macaroni or pasta salad, made with light creamy dressing* |
| 58148118 | Macaroni or pasta salad, made with any type of fat free dressing* |
| 58148120 | Macaroni or pasta salad with egg* |
| 58148130 | Macaroni or pasta salad with tuna* |
| 58148150 | Macaroni or pasta salad with shrimp* |
| 58148160 | Macaroni or pasta salad with tuna and egg* |
| 58148170 | Macaroni or pasta salad with chicken* |
| 58148180 | Macaroni or pasta salad with cheese* |
| 58148550 | Macaroni or pasta salad with meat* |
| 63401010 | Apple salad with dressing* |
| 63402950 | Fruit salad, excluding citrus fruits, with salad dressing or mayonnaise* |
| 63402980 | Fruit salad, excluding citrus fruits, with marshmallows* |
| 63403040 | Fruit salad, including citrus fruits, with marshmallows* |
| 71600950 | Potato salad with egg, from restaurant* |
| 71601010 | Potato salad with egg, made with mayonnaise* |
| 71601015 | Potato salad with egg, made with light mayonnaise* |
| 71601020 | Potato salad with egg, made with mayonnaise-type salad dressing* |
| 71601025 | Potato salad with egg, made with light mayonnaise-type salad dressing* |
| 71601035 | Potato salad with egg, made with light creamy dressing* |
| 71601050 | Potato salad with egg, made with any type of fat free dressing* |
| 71602010 | Potato salad, German style* |
| 71602950 | Potato salad, from restaurant* |
| 71603010 | Potato salad, made with mayonnaise* |
| 71603015 | Potato salad, made with light mayonnaise* |
| 71603020 | Potato salad, made with mayonnaise-type salad dressing* |
| 71603050 | Potato salad, made with any type of fat free dressing* |
| 73101110 | Carrots, raw, salad* |
| 73101210 | Carrots, raw, salad with apples* |
| 74701000 | Tomato sandwich* |
| 75140500 | Broccoli salad with cauliflower, cheese, bacon bits, and dressing* |
| 75140510 | Broccoli slaw salad* |
| 75140990 | Cabbage salad or coleslaw, from fast food / restaurant* |
| 75141000 | Cabbage salad or coleslaw, made with coleslaw dressing* |
| 75141005 | Cabbage salad or coleslaw, made with light coleslaw dressing* |
| 75141020 | Cabbage salad or coleslaw, made with Italian dressing* |
| 75141025 | Cabbage salad or coleslaw, made with light Italian dressing* |
| 75141030 | Cabbage salad or coleslaw, made with creamy dressing* |
| 75141035 | Cabbage salad or coleslaw, made with light creamy dressing* |
| 75141040 | Cabbage salad or coleslaw, made with any type of fat free dressing* |
| 75141100 | Cabbage salad or coleslaw with apples and/or raisins, with dressing* |
| 75141200 | Cabbage salad or coleslaw with pineapple, with dressing* |

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| 75142500 | Cucumber salad, made with sour cream dressing* |
| 75142550 | Cucumber salad, made with Italian dressing* |
| 75142600 | Cucumber salad made with cucumber and vinegar* |
| 75302080 | Bean salad, yellow and/or green string beans* |
| 75416600 | Pea salad with cheese* |
| 81308100 | Fry sauce* |
| 83100100 | Salad dressing, NFS, for salads |
| 83100200 | Salad dressing, NFS, for sandwiches |
| 83101000 | Blue or roquefort cheese dressing |
| 83102000 | Caesar dressing |
| 83103000 | Coleslaw dressing |
| 83104000 | French or Catalina dressing |
| 83105500 | Honey mustard dressing |
| 83106000 | Italian dressing, made with vinegar and oil |
| 83107000 | Mayonnaise, regular |
| 83108000 | Vegan mayonnaise |
| 83109000 | Russian dressing |
| 83110000 | Mayonnaise-type salad dressing |
| 83112000 | Avocado dressing |
| 83112500 | Creamy dressing |
| 83112950 | Poppy seed dressing |
| 83112990 | Sesame dressing |
| 83114000 | Thousand Island dressing |
| 83115000 | Yogurt dressing |
| 83200100 | Salad dressing, light, NFS |
| 83201000 | Blue or roquefort cheese dressing, light |
| 83202020 | French or Catalina dressing, light |
| 83203000 | Caesar dressing, light |
| 83204000 | Mayonnaise, light |
| 83204030 | Mayonnaise, reduced fat, with olive oil |
| 83204050 | Mayonnaise-type salad dressing, light |
| 83204500 | Honey mustard dressing, light |
| 83205450 | Italian dressing, light |
| 83206500 | Sesame dressing, light |
| 83207000 | Thousand Island dressing, light |
| 83210100 | Creamy dressing, light |
| 83300100 | Blue or roquefort cheese dressing, fat free |
| 83300200 | Caesar dressing, fat free |
| 83300300 | Creamy dressing, fat free |
| 83300400 | French or Catalina dressing, fat free |
| 83300500 | Honey mustard dressing, fat free |
| 83300600 | Italian dressing, fat free |
| 83300700 | Mayonnaise, fat free |
| 83300900 | Salad dressing, fat free, NFS |
| 83301000 | Thousand Island dressing, fat free |

9 Frozen dairy (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 13110000 | Ice cream, NFS |
| 13110320 | Ice cream, no sugar added, flavors other than chocolate |
| 13110330 | Ice cream, no sugar added, chocolate |
| 13120740 | Ice cream cone, NFS |

| | |
|---|---|
| 13121000 | Ice cream sundae, NFS |
| 13130300 | Light ice cream, vanilla |
| 13130310 | Light ice cream, chocolate |
| 13130320 | Light ice cream, no sugar added, NS as to flavor |
| 13130330 | Light ice cream, no sugar added, flavors other than chocolate |
| 13130340 | Light ice cream, no sugar added, chocolate |
| 13135000 | Light ice cream sandwich, vanilla |
| 13135010 | Light ice cream sandwich, chocolate |
| 13136000 | Ice cream sandwich, made with light, no sugar added ice cream |
| 13140000 | Light ice cream bar, vanilla |
| 13140100 | Light ice cream bar, vanilla, chocolate coated |
| 13140115 | Light ice cream bar, chocolate |
| 13140575 | Light ice cream, no sugar added, cone, flavors other than chocolate |
| 13140580 | Light ice cream, no sugar added, cone, chocolate |
| 13142100 | Light ice cream cone, vanilla, prepackaged |
| 13142110 | Light ice cream cone, chocolate, prepackaged |
| 13160160 | Fat free ice cream, no sugar added, flavors other than chocolate |
| 13161600 | Fudgesicle, light |
| 13161630 | Light ice cream, bar or stick, with low-calorie sweetener, chocolate coated |

10 Gelatins, pudding & fillings

10a Gelatins, pudding & fillings, low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 13200110 | Pudding, chocolate, NFS |
| 13210250 | Pudding, chocolate, low calorie, containing artificial sweetener, NS as to from dry mix or ready-to-eat |
| 13210280 | Pudding, flavors other than chocolate, NFS |
| 13210290 | Pudding, flavors other than chocolate, low calorie, containing artificial sweetener, NS as to from dry mix or ready-to-eat |
| 13210520 | Pudding, tapioca, made from dry mix |
| 13220210 | Pudding, flavors other than chocolate, made from dry mix, sugar free |
| 13220220 | Pudding, chocolate, made from dry mix, sugar free |
| 13230120 | Pudding, flavors other than chocolate, ready-to-eat, sugar free |
| 13230140 | Pudding, chocolate, ready-to-eat, sugar free |
| 13230500 | Pudding, tapioca, ready-to-eat |
| 91511010 | Gelatin dessert, sugar free |
| 91511020 | Gelatin dessert, sugar free, with fruit* |
| 91511030 | Gelatin dessert, dietetic, with whipped topping, sweetened with low calorie sweetener* |
| 91511060 | Gelatin dessert, dietetic, with sour cream, sweetened with low calorie sweetener* |

10b Fat-based cream (used in modified fat/calorie cookies, cakes, pastries, pie)

| Food code | Food description |
|---|---|
| 53209010 | Cookie, sugar wafer, chocolate-covered* |
| 53209015 | Cookie, chocolate sandwich* |
| 53209020 | Cookie, chocolate sandwich, reduced fat* |
| 53209100 | Cookie, chocolate, sandwich, with extra filling* |
| 53209500 | Cookie, chocolate and vanilla sandwich* |
| 53210000 | Cookie, chocolate wafer* |
| 53233050 | Cookie, oatmeal sandwich, with creme filling* |
| 53237010 | Cookie, raisin sandwich, cream-filled* |
| 53242000 | Cookie, sugar wafer* |
| 53344200 | Mixed fruit tart filled with custard or cream cheese* |
| 53420000 | Cream puff, eclair, custard or cream filled, NS as to icing* |

| | |
|---|---|
| 53420100 | Cream puff, eclair, custard or cream filled, not iced* |
| 53420200 | Cream puff, eclair, custard or cream filled, iced* |
| 53430000 | Crepe, NS as to filling* |
| 53430100 | Crepe, chocolate filled* |
| 53452420 | Pastry, puff, custard or cream filled, iced or not iced* |
| 53521210 | Doughnut, custard-filled* |
| 53521230 | Doughnut, custard-filled, with icing* |
| 54102200 | Graham crackers, sandwich, with filling* |

11 Nutrition bars

| Food code | Food description |
|---|---|
| 53710800 | Cereal or granola bar (Kashi Chewy) |
| 53710802 | Cereal or granola bar (Kashi Crunchy) |
| 53720100 | Nutrition bar (Balance Original Bar) |
| 53720200 | Nutrition bar (Clif Bar) |
| 53720210 | Nutrition bar (Clif Kids Organic Zbar) |
| 53720300 | Nutrition bar (PowerBar) |
| 53720400 | Nutrition bar (Slim Fast Original Meal Bar) |
| 53720500 | Nutrition bar (Snickers Marathon Protein Bar) |
| 53720600 | Nutrition bar (South Beach Living Meal Bar) |
| 53720610 | Nutrition bar (South Beach Living High Protein Bar) |
| 53720700 | Nutrition bar (Tiger's Milk) |
| 53720800 | Nutrition bar (Zone Perfect Classic Crunch) |
| 53729000 | Nutrition bar or meal replacement bar, NFS |

12 Jams & Jellies

| Food code | Food description |
|---|---|
| 42203000 | Peanut butter and jelly* |
| 42302010 | Peanut butter and jelly sandwich, NFS* |
| 42302015 | Peanut butter and jelly sandwich, with regular peanut butter, regular jelly, on white bread* |
| 42302020 | Peanut butter and jelly sandwich, with regular peanut butter, regular jelly, on wheat bread* |
| 42302025 | Peanut butter and jelly sandwich, with regular peanut butter, regular jelly, on whole wheat bread* |
| 42302055 | Peanut butter and jelly sandwich, with reduced fat peanut butter, regular jelly, on white bread* |
| 42302060 | Peanut butter and jelly sandwich, with reduced fat peanut butter, regular jelly, on wheat bread* |
| 42302065 | Peanut butter and jelly sandwich, with reduced fat peanut butter, regular jelly, on whole wheat bread* |
| 42302105 | Peanut butter and jelly sandwich, with regular peanut butter, reduced sugar jelly, on white bread* |
| 42302110 | Peanut butter and jelly sandwich, with regular peanut butter, reduced sugar jelly, on wheat bread* |
| 42302115 | Peanut butter and jelly sandwich, with regular peanut butter, reduced sugar jelly, on whole wheat bread* |
| 42302155 | Peanut butter and jelly sandwich, with reduced fat peanut butter, reduced sugar jelly, on white bread* |
| 42302160 | Peanut butter and jelly sandwich, with reduced fat peanut butter, reduced sugar jelly, on wheat bread* |
| 42302165 | Peanut butter and jelly sandwich, with reduced fat peanut butter, reduced sugar jelly, on whole wheat bread* |

| | |
|---|---|
| 42303100 | Peanut butter and jelly sandwich, frozen commercial product without crusts* |
| 53233080 | Cookie, oatmeal sandwich, with peanut butter and jelly filling* |
| 53344200 | Mixed fruit tart filled with custard or cream cheese* |
| 53344300 | Dessert pizza* |
| 53521140 | Doughnut, jelly* |
| 58201005 | Jelly sandwich, regular jelly, on white bread* |
| 58201015 | Jelly sandwich, regular jelly, on wheat bread* |
| 58201025 | Jelly sandwich, regular jelly, on whole wheat bread* |
| 58201035 | Jelly sandwich, reduced sugar jelly, on white bread* |
| 58201045 | Jelly sandwich, reduced sugar jelly, on wheat bread* |
| 91401000 | Jelly, all flavors |
| 91402000 | Jam, preserve, all flavors |
| 91403000 | Fruit butter, all flavors |
| 91404000 | Marmalade, all flavors |
| 91405000 | Jelly, sugar free, all flavors |
| 91405500 | Jelly, reduced sugar, all flavors |
| 91406000 | Jam, preserve, marmalade, sugar free, all flavors |
| 91406500 | Jam, preserve, marmalade, sweetened with fruit juice concentrates, all flavors |
| 91406600 | Jam, preserve, marmalade, reduced sugar, all flavors |
| 91407100 | Guava paste |
| 91407120 | Sweet potato paste |
| 91407150 | Bean paste, sweetened |

13 Sugar

| Food code | Food description |
|---|---|
| 11541110 | Milk shake, home recipe, chocolate* |
| 11541120 | Milk shake, home recipe, flavors other than chocolate* |
| 11541130 | Milk shake, home recipe, chocolate, light* |
| 11541135 | Milk shake, home recipe, flavors other than chocolate, light* |
| 13210500 | Pudding, tapioca, made from home recipe, made with milk* |
| 28340310 | Chicken or turkey gumbo soup, home recipe, canned or ready-to-serve* |
| 41601030 | Black bean soup, home recipe, canned or ready-to-serve* |
| 51000180 | Bread, made from home recipe or purchased at a bakery, NS as to major flour* |
| 51101050 | Bread, white, made from home recipe or purchased at a bakery* |
| 51101060 | Bread, white, made from home recipe or purchased at a bakery, toasted* |
| 51161270 | Pan Dulce, with sugar topping* |
| 51300140 | Bread, whole wheat, made from home recipe or purchased at bakery* |
| 51300150 | Bread, whole wheat, made from home recipe or purchased at bakery, toasted* |
| 51301040 | Bread, wheat or cracked wheat, made from home recipe or purchased at bakery* |
| 51301050 | Bread, wheat or cracked wheat, made from home recipe or purchased at bakery, toasted* |
| 52104010 | Biscuit, home recipe* |
| 52202060 | Cornbread, made from home recipe* |
| 52206060 | Cornbread muffin, stick, round, made from home recipe* |
| 53206020 | Cookie, chocolate chip, made from home recipe or purchased at a bakery* |
| 55801000 | Funnel cake with sugar* |
| 55801010 | Funnel cake with sugar and fruit* |
| 58146222 | Pasta with tomato-based sauce, home recipe* |
| 58146302 | Pasta with tomato-based sauce, and added vegetables, home recipe* |
| 58146322 | Pasta with tomato-based sauce and meat, home recipe* |
| 58146332 | Pasta with tomato-based sauce, meat, and added vegetables, home recipe* |
| 58146342 | Pasta with tomato-based sauce and poultry, home recipe* |

| | |
|---|---|
| 58146352 | Pasta with tomato-based sauce, poultry, and added vegetables, home recipe* |
| 58146362 | Pasta with tomato-based sauce and seafood, home recipe* |
| 58146372 | Pasta with tomato-based sauce, seafood, and added vegetables, home recipe* |
| 58146602 | Pasta, whole grain, with tomato-based sauce, home recipe* |
| 58146612 | Pasta, whole grain, with tomato-based sauce and added vegetables, home recipe* |
| 58146622 | Pasta, whole grain, with tomato-based sauce and meat, home recipe* |
| 58146632 | Pasta, whole grain, with tomato-based sauce, meat, and added vegetables, home recipe* |
| 58146642 | Pasta, whole grain, with tomato-based sauce and poultry, home recipe* |
| 58146652 | Pasta, whole grain, with tomato-based sauce, poultry, and added vegetables, home recipe* |
| 58146662 | Pasta, whole grain, with tomato-based sauce and seafood, home recipe* |
| 58146672 | Pasta, whole grain, with tomato-based sauce, seafood, and added vegetables, home recipe* |
| 58401010 | Barley soup, home recipe, canned, or ready-to-serve* |
| 62101230 | Apple, dried, cooked, with sugar* |
| 63101130 | Applesauce, stewed apples, with sugar* |
| 63101330 | Apple, baked, with sugar* |
| 63135630 | Peach, frozen, with sugar* |
| 63147620 | Rhubarb, frozen, with sugar* |
| 63223620 | Strawberries, frozen, with sugar* |
| 91101000 | Sugar, NFS |
| 91101010 | Sugar, white, granulated or lump |
| 91101020 | Sugar, white, confectioner's, powdered |
| 91102010 | Sugar, brown |
| 91104100 | Sugar, cinnamon |
| 91302010 | Honey |
| 91302020 | Agave liquid sweetener |
| 91303000 | Molasses |
| 92101820 | Coffee, macchiato, sweetened* |
| 92101850 | Coffee, cafe con leche* |
| 92101851 | Coffee, cafe con leche, decaffeinated* |
| 92102450 | Iced Coffee, pre-lightened and pre-sweetened* |
| 92130000 | Coffee, pre-lightened and pre-sweetened with sugar* |
| 92130020 | Coffee, pre-sweetened with sugar* |
| 92130021 | Coffee, decaffeinated, pre-sweetened with sugar* |
| 92305040 | Tea, iced, instant, black, pre-sweetened with sugar* |
| 92305050 | Tea, iced, instant, black, decaffeinated, pre-sweetened with sugar* |
| 92305910 | Tea, iced, instant, green, pre-sweetened with sugar* |
| 92307400 | Tea, iced, instant, black, pre-sweetened, dry* |
| 92308000 | Tea, iced, brewed, black, pre-sweetened with sugar* |
| 92308030 | Tea, iced, brewed, black, decaffeinated, pre-sweetened with sugar* |
| 92308500 | Tea, iced, brewed, green, pre-sweetened with sugar* |
| 92308530 | Tea, iced, brewed, green, decaffeinated, pre-sweetened with sugar* |

14 Sugar substitutes

| Food code | Food description |
|---|---|
| 91106010 | Sugar substitute and sugar blend |
| 91107000 | Sugar substitute, sucralose, powder |
| 91108000 | Sugar substitute, stevia, powder |
| 91108010 | Sugar substitute, stevia, liquid |
| 91108020 | Sugar substitute, monk fruit, powder |

| | |
|---|---|
| 91200000 | Sugar substitute, powder, NFS |
| 91200005 | Sugar substitute, liquid, NFS |
| 91200040 | Sugar substitute, saccharin, powder |
| 91200110 | Sugar substitute, saccharin, liquid |
| 91201010 | Sugar substitute, aspartame, powder |

15 Sweet sauces & syrups, low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 11513801 | Chocolate milk, made from light syrup with whole milk* |
| 11513802 | Chocolate milk, made from light syrup with reduced fat milk* |
| 11513803 | Chocolate milk, made from light syrup with low fat milk* |
| 11513804 | Chocolate milk, made from light syrup with fat free milk* |
| 91300010 | Syrup, NFS |
| 91301081 | Chocolate syrup, light |
| 91301082 | Chocolate syrup, thin type, sugar free |
| 91301510 | Pancake syrup, light |
| 91306025 | Caramel dip, light |
| 91351010 | Syrup, dietetic |

16 Ketchup and barbecue sauces

| Food code | Food description |
|---|---|
| 21304210 | Beef, shortribs, barbecued, with sauce, lean and fat eaten* |
| 21304220 | Beef, shortribs, barbecued, with sauce, lean only eaten* |
| 22701030 | Pork, spareribs, barbecued, with sauce, NS as to fat eaten* |
| 22701040 | Pork, spareribs, barbecued, with sauce, lean and fat eaten* |
| 22701050 | Pork, spareribs, barbecued, with sauce, lean only eaten* |
| 24103070 | Chicken, NS as to part, grilled with sauce, NS as to skin eaten* |
| 24103075 | Chicken, NS as to part, grilled with sauce, skin eaten* |
| 24103080 | Chicken, NS as to part, grilled with sauce, skin not eaten* |
| 24123310 | Chicken breast, grilled with sauce, skin eaten* |
| 24123311 | Chicken breast, grilled with sauce, skin not eaten* |
| 24134150 | Chicken leg, drumstick and thigh, grilled with sauce, skin eaten* |
| 24134151 | Chicken leg, drumstick and thigh, grilled with sauce, skin not eaten* |
| 24142510 | Chicken drumstick, grilled with sauce, skin eaten* |
| 24142511 | Chicken drumstick, grilled with sauce, skin not eaten* |
| 24154020 | Chicken thigh, grilled with sauce, skin eaten* |
| 24154021 | Chicken thigh, grilled with sauce, skin not eaten* |
| 24164010 | Chicken wing, grilled with sauce* |
| 24168001 | Chicken "wings" with other sauces or seasoning, from fast food / restaurant* |
| 24168011 | Chicken "wings" with other sauces or seasoning, from precooked* |
| 24168021 | Chicken "wings" with other sauces or seasoning, from other sources* |
| 24168030 | Chicken "wings", boneless, with hot sauce, from fast food / restaurant* |
| 24168031 | Chicken "wings", boneless, with hot sauce, from other sources* |
| 24209000 | Turkey with barbecue sauce, skin eaten* |
| 24209001 | Turkey with barbecue sauce, skin not eaten* |
| 27111500 | Beef sloppy joe, no bun* |
| 27116200 | Beef with barbecue sauce* |
| 27116300 | Beef with sweet and sour sauce* |
| 27120030 | Ham or pork with barbecue sauce* |
| 27120060 | Sweet and sour pork* |
| 27146011 | Chicken, shredded or pulled, with barbecue sauce* |
| 27150170 | Sweet and sour shrimp* |
| 27160010 | Meat with barbecue sauce, NS as to type of meat* |

| | |
|---|---|
| 27315250 | Stuffed cabbage rolls with beef and rice* |
| 27510145 | Cheeseburger, 1 miniature patty, with condiments, on miniature bun, from fast food / restaurant* |
| 27510165 | Cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| 27510170 | Cheeseburger (Burger King)* |
| 27510171 | Whopper Jr with cheese (Burger King)* |
| 27510175 | Cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant (Wendy's Jr. Cheeseburger Deluxe)* |
| 27510205 | Cheeseburger, 1 small patty, with condiments, on white bun* |
| 27510206 | Cheeseburger, 1 small patty, with condiments, on wheat bun* |
| 27510207 | Cheeseburger, 1 small patty, with condiments, on whole wheat bun* |
| 27510225 | Cheeseburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| 27510251 | Cheeseburger, 1 medium patty, with condiments, on white bun* |
| 27510252 | Cheeseburger, 1 medium patty, with condiments, on wheat bun* |
| 27510253 | Cheeseburger, 1 medium patty, with condiments, on whole wheat bun* |
| 27510266 | Cheeseburger, 1 large patty, with condiments, on bun, from fast food / restaurant* |
| 27510276 | Bacon cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| 27510312 | Bacon cheeseburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| 27510341 | Bacon cheeseburger, 1 medium patty, with condiments, on white bun* |
| 27510342 | Bacon cheeseburger, 1 medium patty, with condiments, on wheat bun* |
| 27510343 | Bacon cheeseburger, 1 medium patty, with condiments, on whole wheat bun* |
| 27510346 | Bacon cheeseburger, 1 large patty, with condiments, on bun, from fast food / restaurant* |
| 27510376 | Double cheeseburger, 2 small patties, with condiments, on bun, from fast food / restaurant* |
| 27510386 | Double cheeseburger (Burger King)* |
| 27510406 | Double cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510431 | Double bacon cheeseburger, 2 small patties, with condiments, on bun, from fast food / restaurant (Burger King Bacon Double Cheeseburger)* |
| 27510451 | Double bacon cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510465 | Double bacon cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Wendy's Baconator)* |
| 27510475 | Double bacon cheeseburger, 2 large patties, with condiments, on bun, from fast food / restaurant* |
| 27510486 | Triple cheeseburger, 3 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510506 | Hamburger, 1 miniature patty, with condiments, on miniature bun, from fast food / restaurant* |
| 27510511 | Hamburger, 1 miniature patty, on miniature bun, from school* |
| 27510536 | Hamburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| 27510551 | Hamburger (Burger King)* |
| 27510552 | Whopper Jr (Burger King)* |
| 27510555 | Hamburger, 1 small patty, with condiments, on bun, from fast food / restaurant (Wendy's Jr. Hamburger)* |
| 27510565 | Hamburger, from school cafeteria* |
| 27510585 | Hamburger, 1 small patty, with condiments, on white bun* |
| 27510587 | Hamburger, 1 small patty, with condiments, on whole wheat bun* |

| | |
|---|---|
| 27510606 | Hamburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| 27510641 | Hamburger, 1 medium patty, with condiments, on white bun* |
| 27510642 | Hamburger, 1 medium patty, with condiments, on wheat bun* |
| 27510643 | Hamburger, 1 medium patty, with condiments, on whole wheat bun* |
| 27510667 | Double hamburger, 2 small patties, with condiments, on bun, from fast food / restaurant* |
| 27510676 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| 27510681 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Burger King Double WHOPPER)* |
| 27510682 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Wendy's 1/2 lb Double)* |
| 27520500 | Pork sandwich, on white roll, with onions, dill pickles and barbecue sauce* |
| 27520510 | Pork barbecue sandwich or Sloppy Joe, on bun* |
| 27545010 | Turkey or chicken burger, with condiments, on bun, from fast food / restaurant* |
| 27545200 | Turkey or chicken burger, with condiments, on white bun* |
| 27545210 | Turkey or chicken burger, with condiments, on wheat bun* |
| 27545220 | Turkey or chicken burger, with condiments, on whole wheat bun* |
| 28110620 | Beef short ribs, boneless, with barbecue sauce, potatoes, vegetable, frozen meal* |
| 28160650 | Stuffed green pepper, frozen meal* |
| 74401010 | Ketchup |
| 74406010 | Barbecue sauce |
| 81308100 | Fry sauce* |

17 Yogurt and frozen yogurt, low calorie, reduced calorie, sugar-free

| Food code | Food description |
|---|---|
| 11400000 | Yogurt, NFS |
| 11459990 | Frozen yogurt, NFS |
| 11460400 | Yogurt, frozen, chocolate, nonfat milk, with low-calorie sweetener |
| 11460410 | Yogurt, frozen, flavors other than chocolate, nonfat milk, with low-calorie sweetener |

18 Medical foods

| Food code | Food description |
|---|---|
| 95101000 | Nutritional drink or shake, ready-to-drink (Boost) |
| 95101010 | Nutritional drink or shake, ready-to-drink (Boost Plus) |
| 95103000 | Nutritional drink or shake, ready-to-drink (Ensure) |
| 95103010 | Nutritional drink or shake, ready-to-drink (Ensure Plus) |
| 95104000 | Nutritional drink or shake, ready-to-drink, sugar free (Glucerna) |
| 95120050 | Nutritional drink or shake, liquid, soy-based |

19 Cranberries, dried

| Food code | Food description |
|---|---|
| 42500000 | Trail mix, NFS* |
| 42501000 | Trail mix with nuts and fruit* |
| 42501500 | Trail mix with chocolate* |
| 42502100 | Trail mix with pretzels, cereal, or granola* |
| 53710810 | Cereal or granola bar (KIND Fruit and Nut Bar)* |
| 53713010 | Cereal or granola bar, fruit and nut* |
| 62101000 | Fruit, dried, NFS, uncooked |
| 62101050 | Fruit mixture, dried* |
| 62109100 | Cranberries, dried |

20 Jerky (meat or poultry based)

| Food code | Food description |
|---|---|
| 21602100 | Beef jerky |

22002800 Pork jerky
23321900 Venison/deer jerky

* Only the component of the food (by weight) with existing or proposed use of allulose was included in the analysis
** Non-reconstituted dry powder was adjusted to the reconstituted/prepared amount.

# Appendix C. Allulose Intake Comparison to GRN 498

In the current analysis, a downward shift of allulose intake was observed using the more recent NHANES data (i.e., NHANES 2015-2018) as compared to total allulose intakes reported by GRNs 400, 498, 693, and 828. The total per user mean and 90$^{th}$ percentile intake estimates of allulose based on older NHANES data and reported for the U.S. population by GRNs 400, 498, 693 and 828 ranged from 9-12.55 g/day and 24.8-30 g/day, respectively. Allulose intake estimates from background uses in the present analysis at the per user mean and 90$^{th}$ percentile is 6.69 g/day and 16.39 g/day, respectively. These estimates at the per user mean and 90$^{th}$ percentile is at least 26% and 34% lower, respectively, than those estimates in the GRNs.

In order to understand the downward shift of allulose intake observed using more recent NHANES data, Exponent generated and compared two sets of allulose intake estimates based on NHANES 2015-2018 and NHANES 2007-2010 for the food uses reported in GRN 498 as shown in Table C-1 below. Estimates based on NHANES 2015-2018 account for new food codes that have emerged since NHANES 2007-2010.

Table C-1. Two-day average allulose intake by GRN 498 food use categories from NHANES 2007-2010 and NHANES 2015-2018 for the U.S. population 2+ y

| | | U.S. 2+ y Allulose Intake (g/day) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | NHANES 2007-2010* | | | | | | NHANES 2015-2018 | | | | | |
| | | N- | % | Per Capita | | Per User | | N- | % | Per Capita | | Per User | |
| | Proposed Food Category | user† | User | Mean | 90th | Mean | 90th | user† | User | Mean | 90th | Mean | 90th |
| 1 | Beverages (non-alcoholic), low calorie, reduced calorie, sugar-free | 4,136 | 32 | 5.5 | 18.6 | 17.3 | 39.4 | 2,191 | 21 | 3.3 | 10.3 | 15.8 | 34.8 |
| 2 | Cereals, low calorie, reduced calorie, sugar-free‡ | 15‡ | <1.0 | NA | NA | NA | NA | 57‡ | <1.0 | 0.02 | 0 | 5.5 | 12.1 |
| | Cereals, regular | 7,399 | 46 | 0.6 | 1.8 | 1.3 | 3.2 | 4,389 | 33 | 0.3 | 1.0 | 0.9 | 1.9 |
| 3 | Chewing gum | 662 | 4 | 0.1 | 0.0 | 1.7 | 3.5 | 379 | 3 | <0.05 | 0 | 1.4 | 2.0 |
| 4 | Confections & frostings | 1,655 | 13 | 0.1 | 0.2 | 0.6 | 1.3 | 3,408 | 26 | 0.2 | 0.6 | 0.7 | 1.5 |
| 5 | Frozen dairy desserts (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free | 223 | 1 | <0.05 | 0.0 | 2.6 | 5.5 | 195 | 2 | 0.1 | 0 | 3.7 | 7.2 |
| 6 | Yogurt and frozen yogurt, low calorie, reduced calorie, sugar-free | 487 | 4 | 0.2 | 0.0 | 5.2 | 8.9 | 24‡ | 0 | <0.05 | 0 | 3.0 | 6.1 |
| 7 | Dressings for salads | 4,557 | 36 | 0.4 | 1.2 | 1.0 | 2.0 | 6,100 | 54 | 0.5 | 1.6 | 1.0 | 2.1 |
| 8 | Gelatins, pudding & fillings, low calorie, reduced calorie, sugar-free | 201 | 1 | 0.1 | 0.0 | 7.3 | 12.1 | 126 | 1 | 0.1 | 0 | 8.7 | 13.0 |
| 9 | Hard candy, low calorie, reduced calorie, sugar-free | 11‡ | <1.0 | NA | NA | NA | NA | 35‡ | <1.0 | <0.05 | 0 | 7.8 | 17.4 |
| 10 | Soft candy, low calorie, reduced calorie, sugar-free | 26‡ | <1.0 | <0.05 | 0.0 | 2.0 | 4.5 | 13‡ | <1.0 | <0.05 | 0 | 2.9 | 5.2 |
| 11 | Jams & jellies | 2,083 | 14 | 0.2 | 0.5 | 1.2 | 2.2 | 1,506 | 13 | 0.2 | 0.5 | 1.2 | 2.0 |
| 12 | Sugar | 5,801 | 39 | 0.6 | 1.8 | 1.5 | 3.7 | 5,618 | 43 | 0.7 | 2.0 | 1.6 | 3.7 |
| 13 | Sugar substitutes | 1,660 | 12 | 0.3 | 0.5 | 2.2 | 4.5 | 974 | 8 | 0.2 | 0 | 2.3 | 5.0 |
| 14 | Sweet sauces & syrups, low calorie, reduced calorie, sugar-free | 238 | 2 | <0.05 | 0.0 | 1.7 | 4.0 | 168 | 1 | <0.05 | 0 | 2.4 | 6.0 |

* Estimates reported in GRN 498.

† Unweighted number of users; % user, per capita, and per user estimates were based on statistical weights provided by the National Center for Health Statistics (NCHS).

‡ The estimated per user mean and 90th percentile daily intakes associated with the unweighted number of users are likely not statistically reliable due to small user sample size.

NA Not available, sample sizes too small to provide intake estimates.

APPENDIX E

# Epimerase Enzyme Data/Information

**Conclusion**

We, the members of the Expert Panel, have independently and collectively critically evaluated the information summarized above and conclude that Codexis' CDX-032 D-psicose-3-epimerase enzyme preparation produced by fermentation from recombinant *Escherichia coli* expressing an engineered synthetic epimerase gene, meeting appropriate food-grade specifications and manufactured in accordance with current Good Manufacturing Practice, is safe, suitable, and Generally Recognized as Safe (GRAS) (based on scientific procedures) for its intended use in the production of D-psicose.

It is our opinion that other qualified experts would concur with these conclusions.

[redacted]

29 August 2014

Stanley M. Tarka Ph.D.
The Pennsylvania State University College of Medicine

Date

[redacted]

29 Aug 2014

Michael W. Pariza Ph.D.
Emeritus Professor, Food Science
Emeritus Director, Food Research Institute
University of Wisconsin

Date

[redacted]

29 August 2014

Ashley Roberts Ph.D.
Intertek Health Sciences Consultancy

Date

EXHIBIT 1

# Report of the Expert Panel

# OPINION OF THE GRAS PANEL ON THE SAFETY AND GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF ALLULOSE FOR USE IN FOOD

## Introduction

An independent panel of experts (the GRAS Panel), qualified by scientific training and experience to evaluate the safety of food and food ingredients, was requested by Tate & Lyle to determine the safety and Generally Recognized as Safe (GRAS) status of the use of allulose in select foods for human consumption. The allulose ingredient is proposed for use in nine new food types including (1) nutritional beverages; (2) nutritional beverages intended for children; (3) sweetened alcoholic malt beverages; (4) alcoholic premixed cocktails; (5) grain-free, no sugar, high protein RTE cereals; (6) nutrition bars; (7) ketchup and barbecue sauces; (8) dried cranberries; and (9) meat- and poultry-based jerky, in addition to those foods included in GRNs 400, 498, 693 and 828 (i.e., select low calorie, reduced calorie, or sugar-free foods including bakery products, beverages, cereals, chewing gums, confections and frostings, frozen dairy desserts, yogurt and frozen yogurt, dressings for salads, gelatins, pudding and fillings, hard and soft candies, jams and jellies, sugar, sugar substitutes, sweet sauces and syrups, fat based creams, medical foods and coffee mix). Higher use levels are also proposed for existing categories for ready-to-eat (RTE) and cooked cereals including regular and low calorie, reduced calorie, and sugar-free RTE and cooked cereals. The allulose ingredient is manufactured in accordance with current Good Manufacturing Practice (cGMP) and meets the proposed specifications.

A detailed review based on the existing scientific literature on the safety of allulose was conducted by ToxStrategies, Inc. (ToxStrategies) and is summarized in the attached dossier. The GRAS Panel members independently reviewed the dossier prepared by ToxStrategies and other pertinent information and first convened on October 24, 2019 via teleconference. Based on their independent, critical evaluation of all of the available information and discussions during the October 24, 2019 teleconference and reviews again in May 2020 and September 2021, the GRAS Panel unanimously concluded that the intended uses described herein for Tate & Lyle's allulose ingredient, meeting appropriate food-grade specifications as described in the supporting dossier (**GRAS Determination of Allulose for Use as an Ingredient in Human Food**) and manufactured according to cGMP, are safe, suitable, and GRAS based on scientific procedures. A summary of the basis for the GRAS Panel's conclusion is provided below.

## Summary and Basis for GRAS Determination

## Description

Allulose is a sweetener derived from corn (*Zea mays* L.) glucose by enzymatic epimerization of corn starch in a multi-step process. It contains negligible residual amounts of other related monosaccharides and impurities. Allulose has 70% of the sweetness of sucrose but provides negligible energy, and therefore is an excellent substitute for sucrose to reduce sugar and energy intake.

## Manufacturing Process

The starting material is typical corn (U.S. Grade #2 Dent Corn [dried grain]), and the intermediate products are monosaccharides (glucose and fructose). All enzymes used in the process are safe and suitable for food uses and consistent with enzymes identified in previous GRAS notifications (including their sources). The allulose ingredient is produced in two forms: syrup and crystalline powder. The manufacturing process is conducted under Good Manufacturing Practice (GMP) for both end products and is identical in every step but the last.

Analytical results for the allulose ingredient confirm that the finished product meets the analytical specifications. The results also demonstrate that T&L's manufacturing process results in a consistently reproducible product and confirm the lack of significant levels of impurities and/or contaminants (e.g., heavy metals, microbiological contaminants). In addition, the corn starting material is periodically analyzed for the presence of pesticides and mycotoxins as part of Tate & Lyle's standard Quality Assurance processes. The results of stability testing conducted using liquid allulose, Dolcia Prima® LS brand, at temperatures of 4°C, 25°C, and 35°C demonstrate its stability through the end of the product's shelf-life in the syrup version up to 9 months. Stability studies on Dolcia Prima® DS crystalline allulose show that this material is stable for up to 30 months.

## History of Use

Allulose is naturally present in small quantities in many common foods, such as in dried fruits (e.g., figs, raisins), fried dough, brown sugar and ketchup. Allulose has been added to food as an alternative sweetener and has a history of safe use. Multiple GRAS "no questions" letters have been issued (GRNs 400, 498, 693) regarding the safety of the intended uses and use levels of allulose in foods in which it serves as a sugar replacer/sweetener at levels up to 100% (FDA, 2012, 2014, 2017). Allulose is added to select foods as a sweetener, per previous GRAS notifications, and these foods include bakery products, chewing gum, hard candies, frozen dairy desserts, carbonated beverages, non-carbonated beverages, soft candies, yogurt, ready-to-eat cereals, coffee mix, jams/jellies, frostings, sauces, and many others.

## Intended Use and Intake Assessment

The focus of this GRAS determination is for the use of allulose as a sweetener in select foods that have not been previously identified in any of the publicly available GRN's (GRN 498, GRN 693, and GRN 828).

The following table summarizes current and proposed additional food categories and associated use levels. An intake assessment employing dietary survey data obtained from What We Eat in America (WWEIA), the dietary interview portion of the National Health and Nutrition Examination Survey (NHANES) was conducted to estimate the mean and 90$^{th}$ percentile daily intakes of allulose based on its intended use in foods.

| | | | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | **Food Category** | **Description of Foods Selected for Analysis** | **Proposed New Uses** | **Existing GRAS Uses*** | **Combined existing GRAS and proposed uses **** |
| 1 | Baked products (bread, muffin, cake and cookies, pastries), dietetic, low calorie, reduced calorie, sugar-free | Sweetened bread/rolls, muffin, and cakes and cookies – all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 10 | 10 |
| 2 | Beverages | | | | |
| 2a | Non-alcoholic beverages, low calorie, reduced calorie, sugar-free | Sweetened coffees, teas, soft drinks, energy drinks, juice drinks, fruit drinks, fruit flavored drinks, flavored/carbonated waters, and enhanced/fortified waters – all identified as low calorie, reduced calorie, or sugar-free. | NA | 3.5 | 3.5 |
| 2b | Nutritional beverages | Nutritional beverages within the "nutritional beverages" and "protein and nutritional powders"WWEIA categories not included as part of the existing GRAS uses in medical foods | 2.5 | NA | 2.5 |
| 2c | Nutritional beverages intended for children (i.e., PediaSure) | PediaSure | 3.5 | NA | 3.5 |
| 2d | Alcoholic malt beverage, sweetened | Sweetened alcoholic malt beverage (food code 93106000), which includes products such as hard lemonade, hard punch, hard tea, etc. | 3.5 | NA | 3.5 |
| 2e | Alcoholic premixed cocktails | All cocktails with added sugar | 3.0 | NA | 3.0 |
| 3 | Candy, hard and soft | | | | |
| 3a | Hard candy (includes pressed candy and mints), low calorie, reduced calorie, sugar-free | Hard candy – low calorie, reduced calorie, sugar-free, or NFS†. | NA | 70 | 70 |
| 3b | Soft candy, low calorie, reduced calorie, sugar-free | Soft candy – low calorie, reduced calorie, sugar-free. | NA | 25 | 25 |

| | Food Category | Description of Foods Selected for Analysis | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | | | Proposed New Uses | Existing GRAS Uses* | Combine dexisting GRAS and proposed uses ** |
| 4 | Chewing gum | Regular and sugar-free chewing gum. | NA | 50 | 50 |
| 5 | Cereals, ready-to-eat (RTE) and cooked | | | | |
| 5a | RTE and cooked, regular | RTE and cooked cereals identified as containing added sugar. | 12 | 2 | 12 |
| 5b | RTE and cooked, low calorie, reduced calorie, sugar-free | RTE and cooked cereals identified as low calorie, reduced sugar, or sugar-free. | 12 | 5 | 12 |
| 5c | RTE cereals with <5% sugar | RTE cereals with <5% added sugar excluding cereals with no added sugar. | NA | 10 | 10 |
| 5d | Grain-free, no sugar, high protein RTE cereal | No grain-free, no sugar, high protein RTE cereals were reported consumed, hence, zero-sugar added RTE cereals were selected as surrogates. | 20 | NA | 20 |
| 6 | Coffee mix | Sweetened non-reconstituted coffee mixes. | NA | 30 | 30 |
| 7 | Confections & Frostings | Frostings and icings and marshmallows. | NA | 5 | 5 |
| 8 | Dressings for salads | Salad dressings including mayonnaise. | NA | 5 | 5 |
| 9 | Frozen dairy (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free | Desserts including ice cream, soft serve, sorbet - all identified as low calorie, reduced calorie,sugar-free, or NFS†. | NA | 5 | 5 |
| 10 | Gelatins, pudding & fillings | | | | |
| 10a | Gelatins, pudding & fillings, low calorie, reduced calorie, sugar-free | Gelatins and puddings - all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 10 | 10 |
| 10b | Fat-based cream (used in modified fat/calorie cookies, cakes, pastries, pie) | Fat-based cream filling in cookies, cakes, pastries, pies. | NA | 10 | 10 |
| 11 | Nutrition bars | Meal replacement bars, protein bars, energy bars, etc. | 25 | NA | 25 |
| 12 | Jams & Jellies | Jams, jellies, and pastes, all types. | NA | 10 | 10 |

| | | | Maximum Allulose Use Level, % | | |
|---|---|---|---|---|---|
| | **Food Category** | **Description of Foods Selected for Analysis** | **Proposed New Uses** | **Existing GRAS Uses*** | **Combine dexisting GRAS and proposed uses **** |
| 13 | Sugar | Sugar added in home preparations including white sugar, brown sugar, cinnamon sugar, raw sugar, honey, molasses, and not specified. | NA | 10 | 10 |
| 14 | Sugar substitutes | Sugar substitutes. | NA | 100 | 100 |
| 15 | Sweet sauces & syrups, low calorie, reduced calorie, sugar-free | Sweet sauces & syrups - all identified as low calorie, reduced calorie, sugar-free, dietetic orNFS†. | NA | 10 | 10 |
| 16 | Ketchup and barbecue sauces | Ketchup and barbecue sauces. | 10 | NA | 10 |
| 17 | Yogurt and frozen yogurt, low calorie, reduced calorie, sugar-free | Yogurt and frozen yogurt - all identified as low calorie, reduced calorie, sugar-free, or NFS†. | NA | 5 | 5 |
| 18 | Medical foods | Nutritional drinks such as Boost, Ensure, and Glucerna to provide a surrogate for medical foods. | NA | 15 | 15 |
| 19 | Cranberries, dried | Dried cranberries (i.e., Craisins). | 25 | NA | 25 |
| 20 | Jerky (meat or poultry based) | Jerky (meat or poultry based). | 15 | NA | 15 |

* Based on current food uses and use levels of allulose as described in U.S. GRNs 400 (CJ Cheiljedang, 2011), 498 (Matsutani Chemical Industry Company, Ltd 2013), 693 (Samyang Corporation, 2017), and 828 (Samyang Corporation, 2018).

† NFS refers to food codes described as "not-further-specified;" providing a generic description to the food reported consumed (i.e., dietetic topping).NA: Not applicable.

** Maximum use levels applied in estimating cumulative intake from proposed and existing GRAS uses

The Cumulative Estimated Daily Intake (CEDI) for the extended uses of allulose in grams per day and grams per kilogram body weight per day for the following age groups in the US populations: 2 years and older, 2 to 5 years, 6 to 18 years, and 19 years and older are presented below.

| | | | Per Capita | | Per User | |
|---|---|---|---|---|---|---|
| | N * | % User | Mean | 90th Percentile | Mean | 90th Percentile |
| Allulose CEDIs (g/day) | | | | | | |
| U.S. 2+ y | 12017 | 95 | 9.60 | 22.65 | 10.09 | 23.53 |
| Infants <2 y | 409 | 50 | 1.66 | 4.75 | 3.33 | 7.18 |
| Children 2-12 y | 2632 | 97 | 5.63 | 12.04 | 5.83 | 12.36 |
| Adolescents 13-18 y | 1320 | 92 | 6.28 | 13.39 | 6.79 | 13.55 |
| Males 19+ y | 3828 | 95 | 12.00 | 28.84 | 12.61 | 29.86 |
| Females 19+ y | 4237 | 95 | 9.48 | 23.27 | 9.99 | 24.05 |
| Allulose CEDIs (g/kg-bw/day) | | | | | | |
| U.S. 2+ y | 12017 | 95 | 0.14 | 0.34 | 0.15 | 0.35 |
| Infants <2 y | 409 | 50 | 0.15 | 0.40 | 0.30 | 0.65 |
| Children 2-12 y | 2632 | 97 | 0.22 | 0.48 | 0.23 | 0.49 |
| Adolescents 13-18 y | 1320 | 92 | 0.10 | 0.22 | 0.11 | 0.22 |
| Males 19+ y | 3828 | 95 | 0.13 | 0.32 | 0.14 | 0.33 |
| Females 19+ y | 4237 | 95 | 0.13 | 0.30 | 0.14 | 0.32 |

*Unweighted number of users; % user, *per capita*, and *per user* estimates were based on NHANES 2015-2018 and derived using the statistical weights provided by the NCHS.

In the U.S. population 2+ y, 95% consumed one or more foods containing allulose from background and/or proposed uses. The allulose CEDI at the per user mean and 90th percentile intakes among this population is 10.09 g/day (0.15 g/kg-bw/day) and 23.53 g/day (0.35 g/kg-bw/day), respectively. Per user mean allulose CEDI ranged from 3.33 g/day among infants <2 y to 12.61 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.30 g/kg-bw/day allulose. The per user 90th percentile intake estimates of allulose ranged from 7.18 g/day among infants <2 y to 29.86 g/day among males 19+ y. The highest per user 90th percentile of intake on a body weight basis was among infants <2y at 0.65 g/kg-bw/day allulose.

The total per user mean and 90th percentile intake estimates of allulose based on NHANES data and reported for the U.S. population by GRNs 400, 498, 693 and 828 ranged from 9-12.55 g/day and 24.8-30 g/day, respectively. The per user mean and 90th percentile intake estimates in the present analysis are approximately 26% and 34% lower, respectively, than those estimates in the GRNs. In order to understand the downward shift of allulose intake observed in the more recent NHANES data, Exponent generated and compared two sets of allulose intake estimates using NHANES 2015- 2018 and NHANES 2007-2010 for the food uses reported in GRN 498 (see Appendix C of Exponent Intake Assessment Report; Appendix D of this GRN). Lower allulose intake

estimates in the present analysis appear to be due to a shift in dietary patterns of non-alcoholic low calorie, reduced calorie, sugar-free beverages. Specifically, the percent users and intake of non-alcoholic beverages (low calorie, reduced calorie, sugar-free) have decreased from 32% in NHANES 2007-2010 to 21% in NHANES 2015-2018 with a decreased intake among consumers of non- alcoholic beverages in NHANES 2015-2018. A trend analysis conducted by Bleich et al.(2018) similarly reported an observed decline in beverage and sugar-sweetened beverage consumption for children and adults from 2003 to 2014. There was also a reduction in intake of regular cereal contributing to lower allulose intakes, i.e., a decrease in percent users (46% in NHANES 2007-2010 versus 33% in NHANES 2015-2018) and lower intake amounts in NHANES 2015-2018. This reduction, however, did not result from changes in dietary patterns but instead was due to differences in the food selection methodology between GRN 498 and the current assessment. The food selection of regular cereals in the present analysis was limited to cereals with added sugar since allulose would not be added to cereals with no added sugar, whereas all cereals excluding low calorie, reduced calorie, and sugar-free cereals were included in the assessment for GRN 498 under regular cereals. The estimated allulose intake from existing background uses in this analysis relies on the most currently available dietary data from NHANES (2015-2018) and shows a lower allulose intake as compared to previously reported allulose EDIs from GRNs 400, 498, 693, and 828.

The estimate of the 90$^{th}$ percentile *per user* consumption for the general US population (2+ years of age) of approximately 23.53 g/day, or 0.35 g/kg bw/day is extremely conservative. It is known that a 2-day survey overestimates the actual consumption. Shorter surveys are associated with misclassification of individuals, inaccurate correlation coefficients, reduced power, and overestimation of the percentages of high and low intakes. The effects of survey duration are thought to be due to the within-person and day-to-day variation. In addition, the percentage of respondents who consume a food increases as survey duration increases, because the longer duration begins to incorporate days with no consumption, thus decreasing the mean intakes among consumers over time.

**Safety Data**

Allulose has been added to food as an alternative sweetener and has a history of safe use. Multiple GRAS "no questions" letters have been issued (GRNs 400, 498, 693, 828) with respect to the conclusion regarding the safety of the intended uses and use levels of allulose in foods in which it serves as a sugar replacer/sweetener at levels up to 100% (FDA, 2012, 2014, 2017, 2020). Clinical and preclinical studies with allulose have been conducted to examine its general toxicity and gastrointestinal tolerance.

Regulatory authorities have reviewed the safety of allulose and found it to be safe for use in human food. Numerous studies and publications support the safety of allulose, including *in vitro* studies, *in vivo* animal studies, and clinical studies in humans. A summary of the most relevant studies on allulose absorption, distribution, metabolism, and excretion (ADME), acute and subchronic toxicity, reproductive and developmental toxicity, mutagenicity and genotoxicity, and chronic toxicity in animals along with clinical studies have been summarized and reviewed. The compositional profile of

allulose presents no obvious safety concerns. As a result, allulose has been reviewed and approved in several countries for addition to food for human consumption.

ADME data on allulose are available in both animals and humans, and the results are similar for both. Allulose is rapidly absorbed such that large bolus doses are more likely to have an impact on laxation than smaller cumulative doses. As such, clinical studies have demonstrated that the tolerability of allulose is highly dependent on the mode and timeline of ingestion. Individual tolerance develops with continued ingestion over time. Mild gastrointestinal intolerance (GI intolerance) is considered a physiological response to osmotic loading. It is of no toxicological significance, is generally self-limiting, and is not severe or indicative of toxicity per se. GI intolerance due to allulose is a short-term individual tolerability issue similar to other foods (dried fruit) or food ingredients (fructose), and other sweeteners such as polyols like sorbitol, mannitol, and xylitol.

No adverse effects attributable to allulose were observed in multiple animal studies; in a 90-day study (high dose-2000 mg/kg bw/day) and in a chronic study (approximately 1300 mg/kg bw/day).

Data are available from a number of human studies in both sexes, healthy individuals, and sensitive subpopulations such as diabetics. No effects were observed in multiple human studies, except gastrointestinal intolerance at very high dose levels. Gastrointestinal intolerance is related to the presence of excess indigestible material in the gastrointestinal tract and is temporary and reversible. It is not unique to allulose; similar effects are observed with other sweeteners, such as polyols like sorbitol, mannitol, and xylitol.

Allulose can be considered safe for human consumption at up to 63 g/day, when consumed in portions throughout the day as one would typically, based on multiple meals or snacks throughout the day (Han et al., 2018), and up to 28–42 g (0.4 – 0.6 g/kg/day for a 70 kg individual) can be consumed in one sitting (Han et al., 2018; Iida et al., 2007).

In summary, the published study data, additional unpublished supporting data, and previous reviews by regulatory authorities (e.g., GRN Nos. 400, 498, 693, 828), support the conclusion that Tate & Lyle's allulose ingredient is safe for use as a sweetener, at the proposed use levels in specified foods.

## General Recognition of the Safety of Allulose

The intended use of allulose has been determined to be safe through scientific procedures as set forth in 21 CFR§170.3(b), thus satisfying the so-called "technical" element of the GRAS determination and is based on the following:

- Allulose is manufactured from corn, following current cGMP for food (21 CFR § Part 110). The raw materials and processing aids used in the manufacturing

process are food grade and/or approved for use in food. The allulose ingredient has been characterized appropriately, contains a minimum of 95%–98% alluose (syrup and crystalline forms, respectively), and meets appropriate food-grade specifications.

- There is a body of common knowledge of historical human consumption of allulose from foods containing allulose. Allulose is naturally present in small quantities in many common foods, such as in dried fruits (e.g., figs, raisins, fried dough, brown sugar, and ketchup). The additional intended uses will be in select alcoholic beverages, meat/poultry products (i.e., jerky), grain-based cereal bars, dried cranberries, and presweetened cereal as a sweetener.

- Allulose is rapidly absorbed such that large bolus doses are more likely to have an impact on laxation than smaller cumulative doses. As such, clinical studies have demonstrated that the tolerability of allulose is highly dependent on the mode and timeline of ingestion. Individual tolerance develops with continued ingestion over time. Mild GI intolerance is considered to be a physiological response to osmotic loading and is of no toxicological significance, is generally self-limiting, and not severe or indicative of toxicity per se but is a short-term individual tolerability issue similar to other foods (dried fruit) or food ingredients (fructose), and other sweeteners such as polyols like sorbitol, mannitol, and xylitol.

- Allulose is currently added to food, and multiple GRAS "no-questions" letters have been issued (GRNs 400, 498, 693, 828) that support the safe use of allulose in foods in which it serves as a sugar replacement/sweetener at 90$^{th}$ percentile daily intake levels for ages 2+ of up to approximately 30 g/day. GRN 498 stated the following, "*A potential side effect of D-allulose is gastrointestinal discomfort when ingested in large quantities. It is well-known that this type of side effect is transient. As consumption levels of non-digestible carbohydrates decreased throughout the 20th century, human tolerance levels also decreased. This tolerance and loss of tolerance suggests that the gastrointestinal symptoms associated with high intakes of non-digestible carbohydrates are likely transient and can improve over time. This type of symptom is usually transient and is not considered to be of toxicological significance*".

- The clinical study of Iida et al. (2007) established a dose-response relationship for the onset of diarrhea in humans, showing that in men the maximum tolerated dose was 0.5 g/kg bw, whereas in women, it was 0.6 g/kg bw (above these doses, gastrointestinal effects such as abdominal pain, gas formation, and diarrhea occurred). Thus, it was established that, for humans, the NOAEL for allulose is 0.5 g/kg bw (33.3 g/day) for men and 0.6 g/kg bw (31 g/day) for women (Iida et al., 2007; FDA, 2012, 2014, 2017).

- The allulose CEDI at the per user mean and 90$^{th}$ percentile of intake among this population is 10.09 g/day (0.15 g/kg-bw/day) and 23.53 g/day (0.35 g/kg-bw/day), respectively. Per user mean allulose CEDI ranged from 3.33 g/day

among infants <2 y to 12.61 g/day among males 19+ y. On a per body weight basis, the highest per user mean intake was among infants <2 y at 0.30 g/kg-bw/day allulose. The per user 90 $^{th}$ percentile intake estimates of allulose ranged from 7.18 g/day among infants <2 y to 29.86 g/day among males 19+ y. The highest per user 90 $^{th}$ percentile of intake on a body weight basis was among infants <2y at 0.65 g/kg-bw/day allulose.

- Allulose can be considered safe for human consumption up to 24–36 g (0.4 – 0.6 g/kg/day for a 60 kg individual) when consumed in one sitting. As summarized above, the 90$^{th}$ percentile estimated total daily intake for the US population, ages 2+ is 23.53 g/day; this is likely an overestimate of intake as it assumes allulose is used in all intended foods at the maximum intended use level. The 90$^{th}$ percentile daily intake is at the lower end of the range of intake considered safe for human consumption in one sitting.

- No safety/toxicity concerns related to consumption of allulose are evident, beyond that of gastrointestinal intolerance at high bolus doses. The 90$^{th}$ percentile estimated total daily intake for the US population, ages 2+ of 23.53 g/day is conservative, and as such, tolerability should be of limited concern even at the 90$^{th}$ percentile total daily intake for the US population, ages 2+ of 23.53 g/day.

- Regulatory authorities have reviewed the extensive safety study database for allulose and found no issues of concern with respect to its use in human food at the proposed use levels. Numerous studies have been conducted and published in support of the safety of allulose, including *in vitro* studies and *in vivo* animal studies (i.e., acute and subchronic toxicity, mutagenicity and genotoxicity, chronic toxicity), as well as clinical studies in adults. No adverse effects attributable to allulose were observed in multiple animal studies; in 90-day studies (1670 - 2000 mg/kg bw/day) and in a chronic study (approximately 1300 mg/kg bw/day).
- The body of publicly available scientific literature on the consumption and safety of allulose is sufficient to support the safety and GRAS status of the proposed new uses of the allulose ingredient.

**Conclusions of the GRAS Panel**

We, the undersigned independent qualified members of the GRAS Panel, have individually and collectively, critically reviewed the published and ancillary information pertinent to the identification, use, and safety of Tate & Lyle's allulose ingredient. We unanimously conclude that the intended use of the allulose ingredient produced consistent with good manufacturing practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier ["**GRAS Determination of Allulose for Use as an Ingredient in Human Food**"] is safe.

We the members of the GRAS Panel, further unanimously conclude that the intended use of Tate & Lyle's allulose ingredient, produced consistent with good manufacturing practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier is Generally Recognized as Safe (GRAS) based on scientific procedures under the conditions of intended use in conventional foods and alcoholic beverages specified herein.

It is our professional opinion that other qualified experts critically evaluating the same information, would concur with this conclusion.

_____ _____

Michael Carakostas, DVM, PhD
Consultant
MC Scientific Consulting LLC

Date

_____ _____

Stanley M. Tarka, Jr., Ph.D., F.A.T.S.
Consultant
Tarka Group, Inc.

Date

_____ _____

Thomas A. Vollmuth, Ph.D.
Consultant
Vollmuth and Associates, LLC

Date

**Conclusions of the GRAS Panel**

We, the undersigned independent qualified members of the GRAS Panel, have individually and collectively, critically reviewed the published and ancillary information pertinent to the identification, use, and safety of Tate & Lyle's allulose ingredient. We unanimously conclude that the intended use of the allulose ingredient produced consistent with good manufacturing practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier ["**GRAS Determination of Allulose for Use as an Ingredient in Human Food**"] is safe.

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It is our professional opinion that other qualified experts critically evaluating the same information, would concur with this conclusion.

[redacted]

Michael Carakostas, DVM, PhD
Consultant
MC Scientific Consulting LLC

7-30-2021
Date

Stanley M. Tarka, Jr., Ph.D., F.A.T.S.
Consultant
Tarka Group, Inc.

Date

Thomas A. Vollmuth, Ph.D.
Consultant
Vollmuth and Associates, LLC

Date

**Conclusions of the GRAS Panel**

We, the undersigned independent qualified members of the GRAS Panel, have individually and collectively, critically reviewed the published and ancillary information pertinent to the identification, use, and safety of Tate & Lyle's allulose ingredient. We unanimously conclude that the intended use of the allulose ingredient produced consistent with good manufacturing practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier ["**GRAS Determination of Allulose for Use as an Ingredient in Human Food**"] is safe.

We the members of the GRAS Panel, further unanimously conclude that the intended use of Tate & Lyle's allulose ingredient, produced consistent with good manufacturing practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier is Generally Recognized as Safe (GRAS) based on scientific procedures under the conditions of intended use in conventional foods and alcoholic beverages specified herein.

It is our professional opinion that other qualified experts critically evaluating the same information, would concur with this conclusion.

Michael Carakostas, DVM, PhD
Consultant
MC Scientific Consulting LLC

Date

[redacted]

29 September 2021

Stanley M. Tarka, Jr., Ph.D., F.A.T.S.
Consultant
Tarka Group, Inc.

Date

Thomas A. Vollmuth, Ph.D.
Consultant
Vollmuth and Associates, LLC

Date

**Conclusions of the GRAS Panel**

We, the undersigned independent qualified members of the GRAS Panel, have individually and collectively, critically reviewed the published and ancillary information pertinent to the identification, use, and safety of Tate & Lyle's allulose ingredient. We unanimously conclude that the intended use of the allulose ingredient produced consistent with good manufacturing practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier ["**GRAS Determination of Allulose for Use as an Ingredient in Human Food**"] is safe.

We the members of the GRAS Panel, further unanimously conclude that the intended use of Tate & Lyle's allulose ingredient, produced consistent with good manufacturing practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier is Generally Recognized as Safe (GRAS) based on scientific procedures under the conditions of intended use in conventional foods and alcoholic beverages specified herein.

It is our professional opinion that other qualified experts critically evaluating the same information, would concur with this conclusion.

Michael Carakostas, DVM, PhD
Consultant
MC Scientific Consulting LLC

Date

Stanley M. Tarka, Jr., Ph.D., F.A.T.S.
Consultant
Tarka Group, Inc.

Date

Thomas A. Vollmuth, Ph.D.
Consultant
Vollmuth and Associates, LLC

30 Sept 2024
Date

**References**

FDA. 2012. GRAS Notification No. 400. D-psicose. http://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices&id=400.

FDA. 2014. GRAS Notification No. 498. D-psicose. http://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices&id=498.

FDA 2017. GRAS Notification No. 693. D-psicose http://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices&id=693.

FDA 2020. GRAS Notification No. 828. D-psicose https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=GRASNotices&id=828&sort=GRN_No&order=DESC&startrow=1&type=basic&search=828

Han Y, Choi BR, Kim SY. 2018. Gastrointestinal tolerance of d-allulose in healthy and young adults. a non-randomized controlled trial. Nutrition 10(12), 2010-2021.

Iida T, Kishimoto Y, Yoshikawa Y, Okuma K, Yagi K, Matsuo T, Izumori K. 2007. Estimation of maximum non-effective level of D-psicose in causing diarrhea in human subjects. J Advanced Food Ingred 10(1):15–19.

EXHIBIT 2

# USDA/FSIS Data Package

| | |
|---|---|
| **From:** | Nga Tran |
| **To:** | Hice, Stephanie |
| **Subject:** | [EXTERNAL] GRN 001057 |
| **Date:** | Friday, July 15, 2022 9:31:01 AM |
| **Attachments:** | Confidentail -Tate+Lyle_Allulose_NHANES2015-2018_FILE4FDA.xlsx |



Dear Stiffy,

At the request of the submitter of GRN 001057, I am providing you with our excel file with NHANES food codes and the corresponding adjusted use levels for allulose that were used for the cumulative dietary exposure estimate from background sources, current and intended uses for allulose.

Please do not hesitate to let me know if you need further details or explanation.

Best,

**Nga Tran, Dr.PH, MPH**
Principal Scientist
**Exponent**
1150 Connecticut Ave., NW
Suite 1100
Washington, DC 20036
Direct +1-202-772-4915 • Email ntran@exponent.com
www.exponent.com

**From:** Don Schmitt
**To:** Hice, Stephanie
**Subject:** [EXTERNAL] Re: GRN 001057 - Request for Clarifying Information
**Date:** Monday, July 11, 2022 1:31:15 PM
**Attachments:** image001.png
image002.png
image003.png
image004.png
image005.png
image006.png
image007.png
image008.png
image009.png
image010.png

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Hi Stephanie,

Just heard back from Tate & Lyle and they have spoken with Nga Tran at Exponent. She indicated that Exponent (probably Nga) will send the requested data directly to you. The reason for this is that there is some proprietary information involved, so Exponent is unable to share it with Tate & Lyle and/or ToxStrategies.

Let me know if you need anything else after receiving the information from Exponent.

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

14 YEARS ESTABLISHED 2008

ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com

**From:** "Donald Schmitt, MPH" <dschmitt@toxstrategies.com>
**Date:** Monday, July 11, 2022 at 8:26 AM
**To:** "Hice, Stephanie" <Stephanie.Hice@fda.hhs.gov>
**Subject:** Re: GRN 001057 - Request for Clarifying Information

Good morning Stephanie,

I will get the requested information ASAP. I know several individuals are at the IFT Meeting this week, but hopefully I can provide it by the end of the week.

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

14 YEARS ESTABLISHED 2008 ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com



---

**From:** "Hice, Stephanie" <Stephanie.Hice@fda.hhs.gov>
**Date:** Monday, July 11, 2022 at 8:22 AM
**To:** "Donald Schmitt, MPH" <dschmitt@toxstrategies.com>
**Subject:** GRN 001057 - Request for Clarifying Information



Dear Mr. Schmitt,

Please find below a request for clarifying information needed to continue our evaluation of GRN 001057:

The notifier used USDA's Food and Nutrient Database for Dietary Studies (FNDDS) to convert the food as consumed into its corresponding ingredients based on percent weight. The notifier provided the list of the National Health and Nutrition Examination Survey (NHANES) food codes included in their analysis in Appendix D, but did not provide additional details on the adjustment of the use levels based on the FNDDS data. This information is necessary to confirm their refined exposure estimate. We ask that the notifier please provide a file with NHANES food codes and the corresponding adjusted use levels for allulose that were used for the cumulative dietary exposure estimate from background sources, current and intended uses.

Please do not include any confidential information in your response.

If you have questions or need further clarification, please feel free to contact me.

Thank you for your attention to this request.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)


**From:** Don Schmitt
**To:** Hice, Stephanie
**Cc:** Kolberg, Lore
**Subject:** [EXTERNAL] Re: GRN 001057 - USDA/FSIS Questions for Notifier
**Date:** Friday, September 1, 2023 1:09:57 PM
**Attachments:** image001.png
image002.png
image003.png
image004.png
image005.png
image006.png
image007.png
image008.png
GRN 1057 USDA FSIS responses 083123.pdf

---



Hi Stephanie,

Attached are Tate & Lyle's responses to the questions from USDA FSIS.

Sincerely,

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

15 YEARS ESTABLISHED 2008

ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com

**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Date:** Tuesday, August 22, 2023 at 10:13 AM
**To:** Don Schmitt <dschmitt@toxstrategies.com>
**Subject:** GRN 001057 - USDA/FSIS Questions for Notifier



Dear Mr. Schmitt,

During USDA/FSIS' evaluation of GRAS Notice No. 001057, they noted questions that need to be addressed and are attached to this email.

We respectfully request a response within **10 business days**. If you are unable to complete the response within that time frame, please contact me to discuss further options. Please do not include any confidential information in your response. **Please provide responses to these questions in a separate PDF from the questions asked by FDA.**

If you have questions or need further clarification, please feel free to contact me. Thank you in advance for your attention to USDA/FSIS' comments.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)

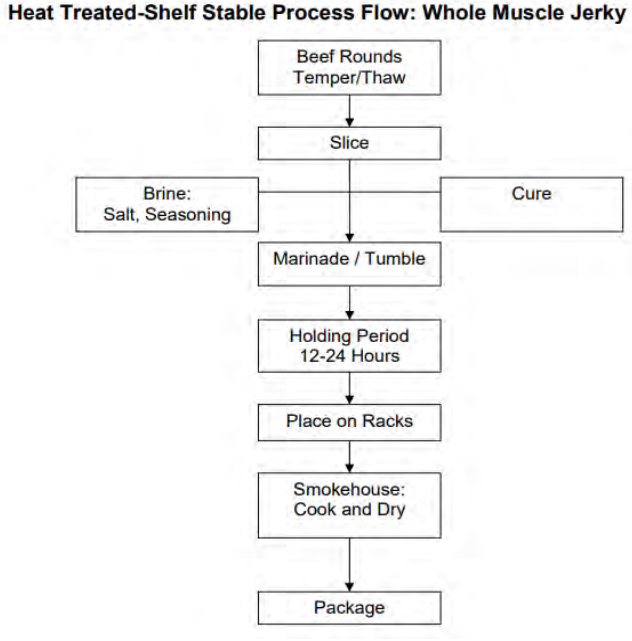
FDA U.S. FOOD & DRUG ADMINISTRATION

**GRN 1057 Items for Clarification from USDA FSIS**

1. Please provide an SDS for the substance and a typical protocol of how the substance will be used when it is formulated into a product.

   **Response:** Please see the attached SDS documents for both the crystalline and liquid allulose products. A typical protocol for use is as follows: allulose incorporation would follow typical, approved production methods where sugars and/or sugar syrups have been incorporated into seasonings, brines or marinades used in the preparation of chunked or ground, or chopped and formed, or whole muscle pieces soaked or vacuum tumbled, as may be common in industrial processing. These products would then be cured or uncured, smoked or unsmoked, as well as air dried or oven dried. The jerky products would meet USDA Food Standards and Labelling Policy requirements and would have been dried to a moisture-to-protein ratio (MPR) of 0.75:1.0 or less and allulose in finished products, as consumed, would comply to maximum permitted use levels (15% max by weight, as consumed).

   An example of the whole muscle beef jerky process would consist first of slicing, then preparing the brine solution (containing allulose), curing, followed by marination/tumbling, and smokehouse processing (cooking and drying) prior to finished product packaging. The following is a flow diagram of the process:




   (Reference: FSIS USDA RTE-SS Process Familiarization 11-29-16)

2. On page 21 the notifier lists the maximum use level at 15% in USDA regulated products (i.e., jerky (meat or poultry based), while the maximum use level in some FDA regulated products is up to 25%. Please confirm whether 15% is the maximum use level in jerky (meat or poultry based).

   **Response:** Tate & Lyle requests a maximum use level of 15% in jerky (meat or poultry based).

**From:** Don Schmitt
**To:** Hice, Stephanie
**Cc:** Kolberg, Lore
**Subject:** Re: [EXTERNAL] Re: GRN 001057 - USDA/FSIS Questions for Notifier
**Date:** Tuesday, September 5, 2023 1:49:31 PM
**Attachments:** image001.png
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image003.png
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DOLCIA PRIMA DS_SDS_LOU_20230224.PDF
DOLCIA PRIMA LS ALLULOSE SYRUP_SDS_LOU_TLP_20230224.PDF

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Stephanie,

My apologies. Please see the attached SDS documents for both the crystalline and liquid allulose products.

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

15 YEARS ESTABLISHED 2008

ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com

**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Date:** Tuesday, September 5, 2023 at 12:37 PM
**To:** Don Schmitt <dschmitt@toxstrategies.com>
**Cc:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Subject:** RE: [EXTERNAL] Re: GRN 001057 - USDA/FSIS Questions for Notifier



Good afternoon, Don –

Thank you for your responses to USDA's comments. In the amendment you provided, the response to question 1 notes that the SDS is attached; however, I do not see the SDS. Would you please provide a copy of the SDS?

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)

FDA U.S. FOOD & DRUG ADMINISTRATION

**From:** Don Schmitt <dschmitt@toxstrategies.com>
**Sent:** Friday, September 1, 2023 1:09 PM
**To:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Cc:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Subject:** [EXTERNAL] Re: GRN 001057 - USDA/FSIS Questions for Notifier



Hi Stephanie,

Attached are Tate & Lyle's responses to the questions from USDA FSIS.

Sincerely,

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com



---

**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Date:** Tuesday, August 22, 2023 at 10:13 AM
**To:** Don Schmitt <dschmitt@toxstrategies.com>
**Subject:** GRN 001057 - USDA/FSIS Questions for Notifier



Dear Mr. Schmitt,

During USDA/FSIS' evaluation of GRAS Notice No. 001057, they noted questions that need to be addressed and are attached to this email.

We respectfully request a response within **10 business days**. If you are unable to complete the response within that time frame, please contact me to discuss further options. Please do not include any confidential information in your response. **Please provide responses to these questions in a separate PDF from the questions asked by FDA.**

If you have questions or need further clarification, please feel free to contact me. Thank you in advance for your attention to USDA/FSIS' comments.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)


*Safety Data Sheet*

# DOLCIA PRIMA® LS ALLULOSE SYRUP

## SECTION 1:IDENTIFICATION OF THE SUBSTANCE/ MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1 PRODUCT IDENTIFIER

| | |
|---|---|
| - Chemical name | Allulose |
| - CAS number | 551-68-8 |

1.2 RELEVANT IDENTIFIED USES OF THE SUBSTANCE AND USES ADVISED AGAINST
Liquid food ingredient.

1.3 DETAILS OF THE SUPPLIER

- Company identification

Americas:
Tate & Lyle Solutions USA LLC
5450 Prairie Stone Pkwy
Hoffman Estates, IL 60192
USA

Europe:
Tate & Lyle Slovakia s.r.o.
Boleraz 114
919 08 boleraz
Slovakia

Asia-Pacific:
Tate & Lyle
3 Biopolis Drive, #05-11 Synapse
Singapore 138623

1.4 EMERGENCY PHONE NR.

CHEMTREC
Toll-Free: 1-800-424-9300 (USA and Canada)
Non Toll-Free +1-703-527-3887 (Global)

## SECTION 2: HAZARDS IDENTIFICATION

2.1. CLASSIFICATION OF THE SUBSTANCE OR MIXTURE
According with the version of the Globally Harmonized System of Classification and labeling adopted in the United States and Regulation 1272/2008/EC [CLP]: Not classified

2.2. LABEL ELEMENTS

SIGNAL WORD:
Not applicable

HAZARD STATEMENTS:
Not applicable

SYMBOL:
Not applicable

PRECAUTIONARY STATEMENTS:
Not applicable

2.3. OTHER HAZARDS
This product is not considered hazardous as defined in the OSHA hazard Communication Standard (29 CFR 1910.1200)product is a liquid food ingredient.

FIRE AND EXPLOSION HAZARD:
Liquid product will not burn.

POTENTIAL ACUTE HEALTH EFFECTS FROM OCCUPATIONAL EXPOSURE:
Inhalation: No effects known or anticipated.
Skin contact: No effects known or anticipated.
Eye contact: No effects known or anticipated.
Ingestion: No effects known or anticipated.

## SECTION 3:COMPOSITION/INFORMATION OF INGREDIENTS

| | |
|---|---|
| - Chemical name | Allulose |
| - CAS number | 551-68-8 |
| - EINECS number | 208-999-7 |

## SECTION 4:FIRST AID MEASURES

4.1 DESCRIPTION OF FIRST AID MEASURES

| | |
|---|---|
| - General advice | Seek medical attention if irritation develops after first aid application |
| - Inhalation | No special treatment under normal circumstances. |
| - Skin contact | No special treatment under normal circumstances. Clean with soap and water. |
| - Eye contact | No special treatment under normal circumstances. Rinse with |

| | |
|---|---|
| | eye wash solution or clean water. If symptoms develop, obtain medical attention. |
| - Ingestion | No special treatment under normal circumstances. |

4.2 MOST IMPORTANT SYMPTOMS AND EFFECTS, BOTH ACUTE AND DELAYED
None Anticipated

4.3 INDICATION OF ANY IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT NEEDED.
None Anticipated

## SECTION 5: FIRE-FIGHTING MEASURES

5.1 EXTINGUISHING MEDIA
Use media appropriate for surrounding fire.

5.2 SPECIFIC HAZARDS
FIRE AND EXPLOSION HAZARD:
None, liquid product will not burn.

5.3 SPECIFIC PROTECTIVE EQUIPMENT AND PRECAUTIONS FOR FIRE-FIGHTERS
Wear self-contained breathing apparatus and full protective gear. Use water spray to cool fire exposed containers.

FLAMMABILITY CLASS (OSHA)
Not applicable

HAZARDOUS COMBUSTION PRODUCTS
Carbon dioxide and carbon monoxide

## SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1 PERSONAL PRECAUTIONS
None under normal conditions.

6.2 ENVIRONMENTAL PRECAUTIONS
Prevent further leakage or spillage if safe to do so. No special environmental precautions

required

6.3 METHODS FOR CLEANING UP
OCCUPATIONAL SPILL:
No specific cleaning procedure is necessary. If washing down spilled area is necessary, use copious amounts of water and control runoff. Follow local, state and federal regulations for product disposal.

6.4 REFERENCE TO OTHER SECTIONS
See Section 7 for information on safe handling
See Section 8 for information on personal protection equipment
See Section 13 for disposal information

## SECTION 7: HANDLING AND STORAGE

7.1 PRECAUTIONS FOR SAFE HANDLING
No specific handling is necessary.

7.2 CONDITIONS OF SAFE STORAGE, INCLUDING ANY INCOMPATIBILITIES
Follow the storage conditions as described in the specification sheet.

7.3 SPECIFIC END USE(S)
Not applicable

## SECTION 8: EXPOSURE CONTROLS / PERSONAL PROTECTION

8.1 CONTROL PARAMETERS
Not hazardous as defined in OSHA 29 CFR 1910.1200. Product is a liquid food ingredient.
Exposure limits: Not applicable

8.2 EXPOSURE CONTROLS
APPROPRIATE ENGINEERING CONTROLS:
Ventilation: Normal industrial hygiene measures should be sufficient.

APPROPRIATE PERSONAL PROTECTIVE EQUIPMENT:
Eye protection: Safety glasses are recommended.
Emergency wash facilities: Eye wash is recommended for conditions where splashing is likely.
Special protective clothing: Not normally required.

Gloves: Not normally required.
Respirator: Not normally required.

FOR FIREFIGHTING AND OTHER IMMEDIATELY DANGEROUS TO LIFE OR HEALTH CONDITIONS:
See section 5

## SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1 INFORMATION ON BASIC PHYSICAL AND CHEMICAL PROPERTIES

| | |
|---|---|
| - Physical form | Syrup |
| - Color | Transparent water like to light yellow |
| - Odor | Bland |
| - pH (concentration) | Data on specification sheet if available. |
| - Boiling point | No data |
| - Flash point | No data |
| - Melting/freezing point | No data |
| - Decomposition temperature | No data |
| - Auto-ignition temperature | No data |
| - Explosion properties | No data |
| - Oxidising properties | No data |
| - Vapour pressure | No data |
| - Vapor density | No data |
| - Relative density | No data |
| - Bulk density | No data |
| - Specific gravity | No data |
| - Viscosity | Data on specification sheet if available. |
| - Water solubility | Soluble |
| - Solubility (non aqueous) | No data |
| - Partition coefficient | No data |
| - Dissociation constant | No data |
| - Evaporation rate | No data |

9.2 OTHER INFORMATION

## SECTION 10: STABILITY AND REACTIVITY

10.1 REACTIVITY
Stable

10.2 CHEMICAL STABILITY
Stable under normal conditions.

Polymerization will not occur.

10.3 POSSIBILITY OF HAZARDOUS REACTIONS
Not applicable

10.4 CONDITIONS TO AVOID
Avoid contact with strong oxidizers.

10.5 INCOMPATIBLE MATERIALS
Oxidizing agents, strong acids

10.6 HAZARDOUS DECOMPOSITION PRODUCTS
Nothing unusual

## SECTION 11: TOXICOLOGICAL INFORMATION

11.1 INFORMATION ON TOXICOLOGICAL EFFECTS
This (these) product(s) is(are) food ingredients.

ACUTE HEALTH EFFECTS:
Inhalation: No effects known or anticipated.
Skin contact: No effects known or anticipated.
Eye contact: No effects known or anticipated.
Ingestion: No effects known or anticipated.

CHRONIC HEALTH EFFECTS: None known or anticipated.

CARCINOGEN STATUS:
OSHA: Not listed.
NTP: Not listed.
IARC: Not listed.

## SECTION 12: ECOLOGICAL INFORMATION

12.1 TOXICITY
No data
12.2 PERSISTENCE/DEGRADABILITY
Readily biodegradable

12.3 BIOACCUMULATIVE POTENTIAL

Food and feed ingredient, not relevant.

12.4 MOBILITY IN SOIL
Not applicable

12.5 BPT, vPvB
The substance does not meet the criteria for PBT or vPvB.

12.6 OTHER ADVERSE EFFECTS
None known

## SECTION 13: DISPOSAL CONSIDERATIONS

13.1 WASTE TREATMENT METHODS
Follow local, state and federal regulations for product disposal. Not a hazardous waste unless contaminated with hazardous products.

## SECTION 14: TRANSPORTATION INFORMATION

International regulations (RID/ADR; RTMDR; IMDG; IATA/OACI): Not classified as dangerous for transport.
DOT shipping label: Non-hazardous

## SECTION 15: REGULATORY INFORMATION

15.1 SAFETY, HEALTH AND ENVIRONMENTAL REGULATIONS
According with the version of the Globally Harmonized System of Classification and labeling adopted in the United States and Regulation 1272/2008/EC(CLP): Not classified

15.2 CHEMICAL SAFETY ASSESSMENT
US FEDERAL REGULATIONS:
Clean Air Act:
ODS: Not applicable.
TSCA Status: Not applicable.
SARA (EPCRA) Section 313 (40 C.F.R. § 372.65): Not applicable.

STATE REPORTING REQUIREMENTS:
California Proposition 65: Not applicable.

## SECTION 16: OTHER INFORMATION

DISCLAIMER OF LIABILITY

The information in this SDS is collected from reliable sources. However, the information is provided without any warranty, expressed or implied. The conditions or methods of handling, storage, use or disposal of the product might be beyond our control and knowledge. For the avoidance of doubt, we shall in no such circumstances be under any liability in respect of loss, damage or expenses arising from handling, storage, use or disposal of the product by your company and/or your subcontractors. This SDS is only applicable for the product mentioned in the identification chapter and title. If the product is used as a component in another product, this SDS may not be applicable on the composite material.

*Safety Data Sheet*

# DOLCIA PRIMA® DS CRYSTALLINE ALLULOSE

## SECTION 1:IDENTIFICATION OF THE SUBSTANCE/ MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1 PRODUCT IDENTIFIER

| | |
|---|---|
| - Chemical name | Allulose |
| - CAS number | 551-68-8 |

1.2 RELEVANT IDENTIFIED USES OF THE SUBSTANCE AND USES ADVISED AGAINST
Dry food ingredient.

1.3 DETAILS OF THE SUPPLIER

- Company identification

Americas:
Tate & Lyle Solutions USA LLC
5450 Prairie Stone Pkwy
Hoffman Estates, IL 60192
USA

Europe:
Tate & Lyle Slovakia s.r.o.
Boleraz 114
919 08 boleraz
Slovakia

Asia-Pacific:
Tate & Lyle
3 Biopolis Drive, #05-11 Synapse
Singapore 138623

1.4 EMERGENCY PHONE NR.

CHEMTREC
Toll-Free: 1-800-424-9300 (USA and Canada)
Non Toll-Free +1-703-527-3887 (Global)

## SECTION 2: HAZARDS IDENTIFICATION

2.1. CLASSIFICATION OF THE SUBSTANCE OR MIXTURE
According with the version of the Globally Harmonized System of Classification and labeling adopted in the United States and Regulation 1272/2008/EC [CLP]: Not classified

2.2. LABEL ELEMENTS

SIGNAL WORD:
Not applicable

HAZARD STATEMENTS:
Not applicable

SYMBOL:
Not applicable

PRECAUTIONARY STATEMENTS:
Not applicable

2.3. OTHER HAZARDS
FIRE AND EXPLOSION HAZARD:
May form combustible dust concentrations in air. Possibility of dust explosion. it is recommended that all dust control equipment and material transport systems involved are engineered to prevent conditions contributing to dust explosions. Do not allow dust to accumulate on flat surfaces, on rafters or building structural components. Keep away from all ignition sources including heat, sparks and flame.

POTENTIAL ACUTE HEALTH EFFECTS FROM OCCUPATIONAL EXPOSURE:
Inhalation: Exposure to high airborne concentrations may cause mild respiratory irritation due to drying effects of dust.
Skin contact: Sustained exposure in a dusty manufacturing environment may result in mechanical irritation in the creases of the skin, particularly at the fingers.
No health effects known or anticipated.
Eye contact: May cause slight mechanical irritation from acute exposure.
Ingestion: No effects known or anticipated.

## SECTION 3:COMPOSITION/INFORMATION OF INGREDIENTS

| | |
|---|---|
| - Chemical name | Allulose |
| - CAS number | 551-68-8 |
| - EINECS number | 208-999-7 |

## SECTION 4:FIRST AID MEASURES

4.1 DESCRIPTION OF FIRST AID MEASURES

| | |
|---|---|
| - General advice | Seek medical attention if irritation develops after first aid application |
| - Inhalation | Move people from the exposure to fresh air. |

| | |
|---|---|
| - Skin contact | Wash skin with soap and water. |
| - Eye contact | Remove particulates by irrigating with eye wash solution or clean water, holding eyelids apart. |
| - Ingestion | Wash mouth and flush throat upto the stomach. |

4.2 MOST IMPORTANT SYMPTOMS AND EFFECTS, BOTH ACUTE AND DELAYED
None Anticipated

4.3 INDICATION OF ANY IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT NEEDED.
None Anticipated

## SECTION 5: FIRE-FIGHTING MEASURES

5.1 EXTINGUISHING MEDIA
Water spray, dry powder, carbon dioxide or media appropriate for surrounding fire. Use of water jet may cause explosive dust conditions.

5.2 SPECIFIC HAZARDS
FIRE AND EXPLOSION HAZARD: Possibility of dust explosion. It is recommended that all dust control equipment and material transport systems involved are engineered to prevent conditions contributing to dust explosions. Do not allow dust to accumulate on flat surfaces, on rafters or building structural components. Use of water jet may cause explosive dust conditions.
SEE NFPA 61, Standard for the prevention of Fire and Dust Explosions in Agricultural and Food Processing Facilities, 2008 or later Edition, and other related standards.

5.3 SPECIFIC PROTECTIVE EQUIPMENT AND PRECAUTIONS FOR FIRE-FIGHTERS
Wear self-contained breathing apparatus and full protective gear. Use water spray to cool fire exposed containers.

FLAMMABILITY CLASS (OSHA)
Not applicable

HAZARDOUS COMBUSTION PRODUCTS
Carbon dioxide and carbon monoxide

## SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1 PERSONAL PRECAUTIONS

None under normal conditions. Avoid prolonged inhalation of dust.

6.2 ENVIRONMENTAL PRECAUTIONS
Prevent further leakage or spillage if safe to do so. No special environmental precautions required

6.3 METHODS FOR CLEANING UP
Vacuum or sweep spills. Minimize dust generation.
If washing down spilled area is necessary, use copious amounts of water and control runoff.
Follow local, state and federal regulations for product disposal

6.4 REFERENCE TO OTHER SECTIONS
See Section 7 for information on safe handling
See Section 8 for information on personal protection equipment
See Section 13 for disposal information

## SECTION 7: HANDLING AND STORAGE

7.1 PRECAUTIONS FOR SAFE HANDLING
See NFPA 61, Standard for the Prevention of Fire and Dust Explosions in Agricultural and Food Processing Facilities, 2008 Edition, and other related standards. Use with adequate ventilation. Minimize dust generation and accumulation; dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are disturbed.

All dust control equipment and material transport systems involved are engineered to prevent conditions contributing to dust explosions and may require explosion relief vents or an explosion suppression system or an oxygen-deficient environment. Bonding and grounding systems may be required.

Dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) should be designed to limit or prevent leakage of dust into the work area.

Do not allow dust to accumulate on flat surfaces, on rafters or building structural components. Routine housekeeping should be instituted to reduce dust accumulation. Use Avoid dispersal of dust in the air; use vacuum or wet sweeping methods. Do not use compressed air to clean surfaces.

Keep away from all ignition sources including heat, sparks, and flame. Where dust accumulations occur use non-sparking tools.

7.2 CONDITIONS OF SAFE STORAGE, INCLUDING ANY INCOMPATIBILITIES
Store in a cool dry place. Store in a tightly closed container/bag.
The packaging material should have reasonable moisture and air barriers and comply with food regulations.

7.3 SPECIFIC END USE(S)
Not applicable

## SECTION 8: EXPOSURE CONTROLS / PERSONAL PROTECTION

8.1 CONTROL PARAMETERS
Exposure limits: Nuisance dust (also called particulate not otherwise regulated (PNOR)).
OSHA PEL: 15 mg/m3 Total dust
5 mg/m3 Respirable dust
ACGIH TLV: 10 mg/m3 Inhalable dust
5 mg/m3 Respirable dust
15 mg/m3 Total dust

8.2 EXPOSURE CONTROLS
APPROPRIATE ENGINEERING CONTROLS:
Ventilation: See NFPA 61, Standard for the Prevention of Fire and Dust Explosions in Agricultural and Food Processing Facilities, 2008 Edition, and National Fire Protection Association 650, Standard for Pneumatic Conveying Systems for Handling Combustible Materials, 1997 Edition and other related standards. Normal industrial hygiene measures should be sufficient for protection of employees from exposure to dusts. Local and mechanical exhaust is desirable when dumping bags.

APPROPRIATE PERSONAL PROTECTIVE EQUIPMENT:
Eye protection: Safety glasses are recommended. Safety goggles are desirable when dumping bags.
Emergency wash facilities: Eye wash is recommended for conditions where dust generation is likely.
Special protective clothing: Not normally required.
Gloves: Not normally required. Use ordinary work gloves if dust dries skin.
Respirator: NIOSH approved N-95 dust respirator if working in situations that could generate large amounts of airborne dust.

FOR FIREFIGHTING AND OTHER IMMEDIATELY DANGEROUS TO LIFE OR HEALTH CONDITIONS:
See section 5.

## SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1 INFORMATION ON BASIC PHYSICAL AND CHEMICAL PROPERTIES

| | |
|---|---|
| - Physical form | Crystalline |
| - Color | White to off-white |
| - Odor | Odorless |
| - pH (concentration) | Data on specification sheet if available. |
| - Boiling point | No data |
| - Flash point | No data |
| - Melting/freezing point | No data |
| - Decomposition temperature | No data |
| - Auto-ignition temperature | No data |
| - Explosion properties | No data |
| - Oxidising properties | No data |
| - Vapour pressure | No data |
| - Vapor density | No data |
| - Relative density | No data |
| - Bulk density | No data |
| - Specific gravity | No data |
| - Viscosity | No data |
| - Water solubility | Soluble |
| - Solubility (non aqueous) | No data |
| - Partition coefficient | No data |
| - Dissociation constant | No data |
| - Evaporation rate | No data |

9.2 OTHER INFORMATION

## SECTION 10: STABILITY AND REACTIVITY

10.1 REACTIVITY
Stable

10.2 CHEMICAL STABILITY
Stable under normal conditions.
Polymerization will not occur.

10.3 POSSIBILITY OF HAZARDOUS REACTIONS
Not applicable

10.4 CONDITIONS TO AVOID
Practices which produce dust or disperse finely divided dust in air.
See NFPA 61. Standard for the Prevention of Fire and Dust Explosions in Agricultural and Food Processing Facilities, 2008 Edition, and other related standards.

10.5 INCOMPATIBLE MATERIALS
Oxidizing agents, strong acids

10.6 HAZARDOUS DECOMPOSITION PRODUCTS
Nothing unusual

## SECTION 11: TOXICOLOGICAL INFORMATION

11.1 INFORMATION ON TOXICOLOGICAL EFFECTS

| | |
|---|---|
| - Inhalation | Exposure to high airborne concentrations may cause mild respiratory irritation due to drying effects of dust. |
| - Ingestion | No effects known or anticipated. |
| - Skin irritation / corrosion | Sustained exposure in a dusty manufacturing environment may result in mechanical irritation in the creases of the skin, particularly at the fingers, or other drying effects. No health effects known or anticipated. |
| - Eye irritation | May cause slight mechanical irritation from acute exposure. |
| - Skin sensitisation | Not sensitizing |
| - Chronic toxicity | Not known or anticipated |
| - Genetic toxicity | Not known or anticipated |
| - Carcinogenicity | Not classifiable as Carcinogen. |
| - Reprotoxicity | Not known or anticipated |
| - Specific effects | Not applicable |

## SECTION 12: ECOLOGICAL INFORMATION

12.1 TOXICITY
Starch and its breakdown products are not known to be toxic to plant and animal life.
12.2 PERSISTENCE/DEGRADABILITY
Readily biodegradable

12.3 BIOACCUMULATIVE POTENTIAL

Starch and its breakdown products are not fat-soluble, and do not accumulate in plant or animal tissue.

12.4 MOBILITY IN SOIL
Not applicable

12.5 BPT, vPvB
The substance does not meet the criteria for PBT or vPvB.

12.6 OTHER ADVERSE EFFECTS
None known

## SECTION 13: DISPOSAL CONSIDERATIONS

13.1 WASTE TREATMENT METHODS
Follow local, state and federal regulations for product disposal. Not a hazardous waste unless contaminated with hazardous products.

## SECTION 14: TRANSPORTATION INFORMATION

International regulations (RID/ADR; RTMDR; IMDG; IATA/OACI): Not classified as dangerous for transport.
DOT shipping label: Non-hazardous

## SECTION 15: REGULATORY INFORMATION

15.1 SAFETY, HEALTH AND ENVIRONMENTAL REGULATIONS
According with the version of the Globally Harmonized System of Classification and labeling adopted in the United States and Regulation 1272/2008/EC(CLP): Not classified

15.2 CHEMICAL SAFETY ASSESSMENT
US FEDERAL REGULATIONS:
Clean Air Act:
ODS: Not applicable.
TSCA Status: Not applicable.
SARA (EPCRA) Section 313 (40 C.F.R. § 372.65): Not applicable.

STATE REPORTING REQUIREMENTS:
California Proposition 65: Not applicable.

## SECTION 16: OTHER INFORMATION

See Hazard Communication Guidance for Combustible Dusts, OSHA 3371-08 2009, U.S. Occupational Safety and Health Administration, https://www.osha.gov/Publications/3371combustible-dust.html (accessed 10/8/14)

NFPA 654, Standard for the Prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids, for general safe handling and design guidance.

Safety Data Sheet according to Commission Regulation (EU) No 2020/878 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

DISCLAIMER OF LIABILITY

The information in this SDS is collected from reliable sources. However, the information is provided without any warranty, expressed or implied. The conditions or methods of handling, storage, use or disposal of the product might be beyond our control and knowledge. For the avoidance of doubt, we shall in no such circumstances be under any liability in respect of loss, damage or expenses arising from handling, storage, use or disposal of the product by your company and/or your subcontractors. This SDS is only applicable for the product mentioned in the identification chapter and title. If the product is used as a component in another product, this SDS may not be applicable on the composite material.

**From:** Don Schmitt
**To:** Hice, Stephanie
**Cc:** Kolberg, Lore
**Subject:** Re: [EXTERNAL] Re: GRN 001057 - Questions for Notifier
**Date:** Friday, September 15, 2023 4:53:17 PM
**Attachments:** image001.png
image002.png
image003.png
image004.png
image005.png
image006.png
image007.png
image008.png
image009.png
image010.png
GRN 1057 Items for Clarification and Responses 091523.pdf

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Hi Stephanie,

Attached are Tate & Lyle's responses to FDA's questions regarding GRN 1057.

Sincerely,

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

15 YEARS ESTABLISHED 2008

ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com

**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Date:** Wednesday, August 23, 2023 at 1:07 PM
**To:** Don Schmitt <dschmitt@toxstrategies.com>
**Cc:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Subject:** RE: [EXTERNAL] Re: GRN 001057 - Questions for Notifier



Dear Mr. Schmitt,

Thank you for the update. Yes, an extension until September 15, 2023, is fine.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)


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**From:** Don Schmitt <dschmitt@toxstrategies.com>
**Sent:** Wednesday, August 23, 2023 12:59 PM
**To:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Cc:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Subject:** [EXTERNAL] Re: GRN 001057 - Questions for Notifier



Hi Stephanie,

We are working on responses to the list of questions you provided on August 14. One of the questions requires that the intake assessment be revised and this will take Exponent a few weeks to

complete, given their previous commitments. Therefore, Tate & Lyle is requesting a 3-week extension of the time to reply to all 12 questions. That would be Friday, September 15.

Thank you for considering this extension request.

Best regards,

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist

15 YEARS ESTABLISHED 2008

ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com



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**From:** Don Schmitt <dschmitt@toxstrategies.com>
**Date:** Monday, August 14, 2023 at 9:46 AM
**To:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Subject:** Re: GRN 001057 - Questions for Notifier

Hi Stephanie,

I will speak with Tate & Lyle and be back in touch shortly.

Don

Donald F. Schmitt, M.P.H.

Senior Managing Scientist


ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com



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**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Date:** Monday, August 14, 2023 at 8:07 AM
**To:** Don Schmitt <dschmitt@toxstrategies.com>
**Subject:** GRN 001057 - Questions for Notifier



Dear Mr. Schmitt,

During our evaluation of GRAS Notice No. 001057, we noted questions that need to be addressed and are attached to this email.

We respectfully request a response within **10 business days**. If you are unable to complete the response within that time frame, please contact me to discuss further options. Please do not include any confidential information in your response.

If you have questions or need further clarification, please feel free to contact me. Thank you in advance for your attention to our comments.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)


**GRN 1057 Items for Clarification**

1. On page 6, and in places throughout the notice, the notifier states that the intended use of D-psicose is substitutional for the intended uses described in GRNs 000400, 000498, 000693, and 000828, including medical foods, which were included in the list of intended uses described in GRN 000400. Since issuing the response letter for GRN 000400, FDA published a guidance document, entitled "Guidance for Industry: Frequently Asked Questions About Medical Foods". This guidance states FDA's view that the definition of medical foods constrains the types of products that fit within that category (notice of availability published on May 9, 2016, 81 FR 29867).

   On page 21 of GRN 001057, the notifier includes the following in the description of medical foods: "Nutritional drinks such as Boost, Ensure, and Glucerna to provide a surrogate for medical foods". In our guidance referenced above, FDA states, "Medical foods are distinguished from the broader category of foods for special dietary use by the requirement that medical foods be intended to meet distinctive nutritional requirements of a disease or condition, used under medical supervision, and intended for the specific dietary management of a disease or condition. Medical foods are not those simply recommended by a physician as part of an overall diet to manage the symptoms or reduce the risk of a disease or condition. Not all foods fed to patients with a disease, including diseases that require dietary management, are medical foods. Instead, medical foods are foods that are specially formulated and processed (as opposed to a naturally occurring foodstuff used in a natural state) for a patient who requires use of the product as a major component of a disease or condition's specific dietary management."

   Based on this definition, we do not believe that the foods included in this category on page 21 of GRN 001057 meet the definition of medical foods and instead fall under the "nutritional beverages" category. For the administrative record, please provide a revised copy of Table 9 reflecting this change.

   **Response:** See the following revised Table 9 as prepared by Exponent in revised intake assessment (September 8, 2023) and attached to this document (Question #11 attachment).

*Table 9. Maximum allulose use levels by food type of foods and beverages*

| No.* | Food category | Description of Foods Selected for Analysis | Tate and Lyle's proposed new uses (%) |
|---|---|---|---|
| 2b | Nutritional beverages | All nutritional drinks such as Carnation Instant Breakfast, Muscle Milk, Slim Fast, and all other nutritional drinks or shakes | 2.5 |
| 2c | PediaSure | PediaSure | 3.5 |
| 5a | RTE and cooked, regular | RTE and cooked cereals identified as containing added sugar | 12** |
| 5b | RTE and cooked, low calorie, reduced calorie, sugar-free | RTE and cooked cereals identified as low calorie, reduced sugar, or sugar-free | 12** |
| 5d | Grain-free, no sugar, high protein RTE cereal | No grain-free, no sugar, high protein RTE cereals were reported consumed, hence, zero-sugar added RTE cereals were selected as surrogates. | 20 |
| 9 | Frozen dairy (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free | Desserts including ice cream, soft serve, sorbet - all identified as low calorie, reduced calorie, sugar-free, or NFS‡ | 8** |
| 11 | Nutrition bars | Meal replacement bars, protein bars, energy bars, etc. | 15 |
| 16 | Ketchup and barbecue sauces | Ketchup and barbecue sauces | 10 |
| 19 | Cranberries, dried | Dried cranberries (i.e., Craisins) | 25 |
| 20 | Jerky (meat or poultry based) | Jerky (meat or poultry based) | 15 |

* Numbering in Table 9. Maximum allulose use levels by types of foods and beverages, in Exponent's March 28, 2022 report.
** Existing Use levels from previous GRNs are below Tate & Lyle's proposed levels

2. In Table 3 (pages 11-12), the notifier lists the processing aids used during the manufacture of D-psicose and provides corresponding CAS numbers. The provided CAS number for the glucoisomerase included in the table corresponds to polyoxyl stearyl ether. For the administrative record, please provide the correct CAS number for the glucoisomerase included in Table 3.

   **Response:** The correct CAS No. is 9055-00-9.

3. The notifier states that the enzyme glucoisomerase is used to convert D-glucose to D- fructose (page 12). The notifier states that this enzyme is obtained from a genetically engineered strain of *Streptomyces rubiginosus* strain "DP-Pzn37". Please indicate if this enzyme is purchased or if it is prepared by the notifier. In addition, please indicate if this enzyme is removed from the final product or if it is expected to be present in the final product. We note that this enzyme, while the subject of 21 CFR 184.1372, is not listed as being obtained from a genetically engineered strain of *S. rubiginosus*, as such please describe the genetic construction of strain "DP-Pzn37". We recommend that the notifier submit a GRAS notice for the intended use of the enzyme.

**Response:** On August 16, 2023, Tate & Lyle requested a clarification of FDA's needs regarding question 3, "specifically what FDA is looking for when you say, 'please describe the genetic construction of strain dP-Pzn37'? The DNA sequence is the most sensitive IP for enzyme suppliers, and they are typically reticent to provide it to their customers, in this case Tate & Lyle."

The agency responded on August 17: "In response to that portion of the question, we would be looking for a description of the production strain for this enzyme (e.g., statements of pathogenicity, toxigenicity) and a general description of the construction of the production strain (e.g., which genes are inserted/excised). We would not be looking for you to supply the full genome, including any gene sequences."

The glucoisomerase enzyme is not prepared by T&L, the notifier. The enzyme is produced by IFF (formerly Danisco) and it is purchased by Primient, the producer of fructose syrup, which T&L purchases as an intermediate material for further processing to produce d-psicose (allulose). Attached are three documents regarding the glucoisomerase enzyme and the production strain. They include a Certificate of Source and GRAS statement from IFF as well as a safety evaluation of the enzyme xylose isomerase (another name for glucoisomerase) from the genetically modified *Streptomyces rubiginosus* strain DP-Pzn37 (EFSA, 2020).

The manufacturer of the enzyme (Danisco, now IFF) submitted a dossier on their enzyme for safety evaluation by EFSA (2020) and they directed Tate & Lyle to that safety evaluation for the information and data requested by FDA in question 3. Based on the 2020 EFSA review (see attachment), the strain was considered non-toxigenic and non-pathogenic. Information regarding the construction of the production strain can also be found in the EFSA safety evaluation document. In conclusion, EFSA (2020) found both the enzyme and production strain safe for use in the production of high fructose syrups in the EU.

*Streptomyces rubiginosus* is a bacterial species of the genus *Streptomyces* and isolated from soil. As stated in the EFSA safety evaluation, the glucoisomerase enzyme is produced with a genetically modified bacterium *S. rubiginosus* strain DP- Pzn37, which is deposited at the Westerdijk Fungal Biodiversity Institute (The Netherlands). The whole genome sequence of the production strain has been analyzed for the presence of antimicrobial resistance genes. Genetic stability has been demonstrated. In addition, similarity of the amino acid sequence to those of known allergens was searched and no matches were found (EFSA, 2020).

Most importantly, glucoisomerase is not expected to be present in the final product. Not only is the enzyme used in an immobilized form in the production of high-fructose corn syrup, but the purification steps applied during the production of fructose have been shown to effectively remove the food enzyme (EFSA, 2020). Based on information from the enzyme supplier, the glucoisomerase enzyme from the genetically modified *Streptomyces rubiginosus* strain DP-Pzn37 has a history of use in the U.S. in the production of high-fructose corn syrup.

As suggested by the agency, Tate & Lyle has communicated to the enzyme supplier FDA's recommendation to submit a GRAS notification for the intended use of the enzyme.

4. For the administrative record, please state whether any of the raw materials used in the production of D-psicose are allergens or are derived from allergenic sources.

**Response:** None of the raw materials used in the production of D-psicose are allergens or are derived from allergenic sources.

5. The content of total non-allulose saccharides in crystalline D-psicose is listed as <2%, dry basis, in Table 2 (page 9) and <0.9%, dry basis, in Table 4 (page 13). Please clarify whether the level for total non-allulose saccharides in crystalline D-psicose is <2% or <0.9%.

   **Response:** Table 2 is incorrect. The level for total non-allulose saccharides in crystalline D-psicose is 0.9% as stated in Tables 4 and 6.

6. In Table 4 (page 13), the provided specification limit for sulfur dioxide is <10 mg/kg. We note that sulfur dioxide is not listed as a processing aid used in the manufacture of D- psicose in Table 3 (page 11). Please clarify if the sulfur dioxide is the chemical residue from corn processing and specify a technical effect for sulfur dioxide in the processing of corn.

   **Response:** Sulfur dioxide is a chemical residue from corn processing. Sulfur dioxide is typically used in corn processing to control undesirable bacterial growth, increase corn hull permeability, and promote swelling and softening of the dense corn kernel.

7. In Table 7 (page 14), the notifier lists the following specifications:

   a. *Escherichia coli* "not detected (CFU/10 g)". For the administrative record, please clarify the limit of detection for this specification.

      **Response:** The limit of detection is 1 CFU/10g sample.

   b. *Salmonella* serovars "Negative (CFU/25 g)". For the administrative record, please confirm whether this refers to a specification of "negative/25g".

      **Response:** Yes, this refers to a specification of negative/25g.

8. On page 15, the notifier states, "The method employed for analysis of *E. coli* is TN10512L, is an internal method, which references ISO21528-1:2017. The method TN10512L is validated for the intended use. The method employed for analysis of *Salmonella* is TN10547, is an internal validated method for the intended use that references ISO6579-1:2017"; however, on page 58, the referenced methods for *E. coli* and *Salmonella* serovars are listed as TN 10412L and TN 10510, respectively. For the administrative record, please clarify this discrepancy.

   **Response:** The correct methods are in the COAs – TN10412L for *E. coli* and TN 10510 for *Salmonella*.

9. On pages 58-60, the listed microbiological specifications and units do not align with those provided in Table 7 (page 14). For example (but not limited to), the specification and units for total plate count is listed as ≤200 CFU/10 g on page 14 but is listed as ≤200 CFU/g on page 58. For the administrative record, please provide revised copies of the certificates of analyses presented on pages 58-60, with the corrected specifications and units.

**Response:** See new Tables 5 and 6 which align with the COAs in Appendix B.

***Table 5. Analytical results for three non-consecutive lots of allulose syrup***

| Specification | | Lot No. YP19DO3774 | Lot No. YP19G01863 | Lot No. YP18D03177 |
|---|---|---|---|---|
| Allulose (%, dry basis) | >95 | 96.2 | 96.3 | 96.3 |
| Total non-allulose saccharides (%) | <5 | 2.6 | 2.9 | 2.4 |
| Dry solids (%) | 70-78 | 70.8 | 70.5 | 71.0 |
| pH | 3.0 – 4.5 | 4.2 | 3.9 | 4.3 |
| Sulfur dioxide (ppm) | <10 | <10 | <10 | <10 |
| Total plate count | ≤200 cfu/10g | <10 | <10 | <10 |
| Yeast | ≤10 cfu/10g | <10 | <10 | <10 |
| Mold | ≤10 cfu/10g | <10 | <10 | <10 |
| Arsenic (ppm) | <0.1 | 0.016 | 0.011 | 0.024 |
| Cadmium (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Lead (ppm) | <0.1 | <0.005 | <0.005 | 0.006 |
| Mercury (ppm) | <0.01 | <0.005 | <0.005 | <0.005 |

***Table 6. Analytical results for three non-consecutive lots of crystalline allulose***

| Specification | | Lot No. LO18J90596 | Lot No. LO19F90351 | Lot No. LO18J90294 |
|---|---|---|---|---|
| Allulose (%, dry basis) | >99.1 | 99.4 | 99.8 | 99.2 |
| Total non-allulose saccharides (%) | <0.9 | 0.27 | 0.06 | 0.29 |
| Moisture (%) | <0.5 | 0.14 | 0.12 | 0.10 |
| Ash (%) | <0.5 | <0.1 | <0.1 | <0.1 |
| Sulfur dioxide (ppm) | <10 | <10 | <10 | <10 |
| Total plate count | ≤200 cfu/g | <10 | 10 | 10 |
| Yeast | ≤10 cfu/g | <10 | 10 | <10 |
| Mold | ≤10 cfu/g | <10 | 10 | <10 |
| Arsenic (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Cadmium (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Lead (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Mercury (ppm) | <0.01 | <0.005 | <0.005 | <0.005 |

10. In Table 9 (page 19), the proposed maximum use level of D-psicose in frozen dairy products, such as ice cream and sorbets, is listed as "NA". However, we note that the use level of 8% for D-psicose was used for the cumulative dietary exposure estimate (amendment dated July 15, 2022). Please clarify if the notifier is proposing a use level of 8% in frozen dairy products, which is higher than the current use level of 5% for frozen dairy products, or if the use level of 8% is a result of an error.

**Response:** The use level of 8% in the amendment dated July 15, 2022 is correct.

11. In Part 3, the notifier provides dietary exposure estimates from background uses of D- psicose (i.e., GRNs 000400, 000498, 000693, and 000828) (Table 10, page 25) as well as cumulative dietary exposure estimates (background and proposed uses of D-psicose) (Table 12, page 27).

    - Considering that GRNs 001024 and 001029 submitted for the use of D-psicose recently received "no questions" letters from FDA, we request that the notifier update the dietary exposure estimates provided in Tables 10 and 12 to account for the recently notified additional uses of D-psicose.

    - Specifically, GRN 001024 includes the use of D-psicose in "Alcoholic beverages (pre-mixed cocktails, wine coolers, and malt beverages, low/reduced calorie)" that the notifier should consider including in the updated background and cumulative dietary exposure estimates.

    - We note that we consider the cumulative dietary exposure to D-psicose that was estimated in GRN 001024 to be 22.9 g/person (p)/d at the $90^{th}$ percentile for the US population aged 2 years and older as the current dietary exposure to D-psicose. When revising the notifier's dietary exposures, the dietary exposure presented in GRN 001024 could be used to represent the background dietary exposure to D- psicose.

    - Based on human tolerance studies discussed in GRN 001057, conservative safe limits of allulose consumption are shown to be 0.5 g/kg bw/d for men and 0.6 g/kg bw/d for women. Since FDA considers 60 kg body weight as average of both males and females, the g/kg bw/d numbers translate to 30 and 36 g/person/day for males and females, respectively. The 30 g/person/day exposure appears to be safe for both males and females. Therefore, please provide a revised exposure estimate that satisfies the above conditions of safe consumption at the 90th percentile, that is, an exposure around 30 g/p/d or less.

      **Response:** Please see the attached revised intake assessment conducted by Exponent (dated, September 8, 2023).

      As per FDA's comment, the use of allulose in alcoholic beverages (pre-mixed cocktails, wine coolers, and malt beverages, low/reduced calorie) were included in GRN 001024 and should be considered part of the background exposure and CEDI. As such, Tate and Lyle excluded alcoholic beverages from its proposed uses. Tate and Lyle also reduced the proposed use level in nutrition bars to 15% (previously 25%).

Revised estimated daily intake (EDI) for allulose from the proposed uses were based on food consumption records collected in the WWEIA component of NHANES conducted in 2017-2018 (NHANES 2017-2018). In the previous intake assessment report, Exponent used two NHANES survey cycles (NHANES 2015-2018). However, NHANES 2017-2018 was used in this update in order to be consistent with GRN 001024. The updated results from Tate and Lyle's proposed new uses of allulose are provided in **Table 2** of the attached report.

The resulting revised per user cumulative estimated daily intake of allulose is as follows:

| Sub-population | Background EDI (g/day) (GRN 001024) | | EDI (g/day) from Proposed Uses | Cumulative Estimated Daily Intake (g/day) | | |
|---|---|---|---|---|---|---|
| | % Users | Mean per capita | Mean per capita | Mean per capita | Mean per user* | Pseudo 90th** Per user |
| US 2+ y | 77.0 | 7.8 | 3.4 | 11.2 | 14.5 | 29.0 |
| 2-12 y | 70.5 | 4.2 | 3.3 | 7.5 | 10.6 | 21.2 |
| 13-18 y | 62.9 | 3.6 | 3.3 | 6.9 | 10.9 | 21.8 |
| 19+ y | 81.2 | 8.9 | 3.4 | 12.3 | 15.1 | 30.2 |

* Mean per capita divided by % users to derive mean per user
* Pseudo 90th is derived based on 2 x mean (FDA 2006 guidance)[2]

As stated in question 11, based on human tolerance studies discussed in GRN 001057, conservative safe limits of allulose consumption are shown to be 0.5 g/kg bw/d for men and 0.6 g/kg bw/d for women. Since FDA considers 60 kg body weight as average of both males and females, the g/kg bw/d numbers translate to 30 and 36 g/person/day for males and females, respectively. The 30 g/person/day exposure appears to be safe for both males and females. Therefore, please provide a revised exposure estimate that satisfies the above conditions of safe consumption at the 90th percentile, that is, an exposure around 30 grams/day or less.

As shown in the above table, the CEDI for the per user US population 2+ years of age is 29.0 gram/day; below the 30 gram/day level. Only the 19+ age group intake of 30.2 grams/day is slightly above the 30 g/day level and considered not of significance.

12. Please provide an updated literature search that discusses the safety of D-psicose, including the date (month and year) the literature search was performed and discuss whether there are any study results that may be contradictory to a GRAS conclusion.

**Response: Per request,** please see the attached updated literature search (January 2020 – August 2023). Search terms employed are also provided. There are no study results that contradict the conclusions regarding the safety and GRAS status of allulose.

No pivotal studies that would contradict the conclusions that the proposed uses and use levels of allulose are both safe and GRAS were found. Allulose (d-psicose) has a long

history of safe use in food for consumption in the US as supported by the four GRNs summarized in Table 13 as well as the more recent GRNs 1024 and 1029 (all received letters on no objection).

GRNs 1024 and 1029 included several more recent studies not cited in GRN 1057 and are referenced here for completeness. They include the following: Teysseire et al. (2022); Tanaka et al. (2021); Ahmed et al. (2022); Daniel et al. (2021).

We agree with the summary of the An et al. (2019) preclinical study and the conclusions of the submitters of GRN 1029 provided in the attachments to the GRN. An et al. conducted a 90-day oral toxicity study in rats and determined a NOAEL for d-allulose was 5,000 mg/kg bw/day.

As for the paper by Daniel et al. (2021) that questioned the safety of allulose because it may enhance the intestinal colonization of *Klebsiella pneumonia,* we agree with the submitters of GRN 1029. This continues to be an area of some research, but there is no conclusive evidence that this poses a safety concern to humans consuming allulose. Again, allulose (d-psicose) has a long history of safe use in food for human consumption in the US.

A few recent preclinical study publications are summarized below:

Sa et al. (2022) evaluated the teratogenicity of d-allulose in rats (modified OECD guidelines test number 414). Pregnant SD female rats received repeat doses of 1250, 2500, or 5000 mg/kg bw/day of d-allulose, or a vehicle control by gavage on gestation days 6–15. On gestation day 20, pregnant rats were weighed, anesthetized, and a laparectomy performed to remove the uterus, after which the contents were weighed. Fetuses were examined macroscopically for any soft tissue or skeletal changes. Parameters evaluated included general observations, body weight, food consumption, mortality, corpora lutea, numbers of embryonic or fetal deaths, and viable fetuses including live birth rate, fetal resorption rate, and stillbirth rate, as well as sex, body weights, and skeletal and soft tissue alterations of fetuses. No treatment-related abnormalities were observed in prenatal developmental toxicity and fetal malformation parameters. The NOAEL of d-allulose for teratogenicity was estimated to be 5000 mg/kg bw/day in pregnant SD rats.

Choi et al. (2022) studied the acute oral toxicity of D-allulose in ICR mice. Mice received a single oral dose of D-allulose (1,250, 2,500 or 5,000 mg/kg body weight). No mortality occurred and no changes were observed in clinical signs of toxicity, body weights, and blood serum chemistry. The LD50 was estimated to exceed 5,000 mg/kg.

**References:**

Choi, MN, Kim Y-S, Lee H, Shin K-C. 2022. A study on single-dose oral toxicity of D-allulose in ICR mice. Maejo International Journal of Science & Technology 16(3):170-178.

Sa S, Seol Y, Lee AW, Heo Y, Kim H-j, Park CJ. 2022. Teratogenicity of D-allulose. Toxicology Reports 9:821-824.

## Question #3 Attachments

Date: August 17, 2023

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## GRAS STATEMENT

RE: **GENSWEET® IGI-VHF** (A10022)[i]

To Whom It May Concern,

**GENSWEET® IGI-VHF** consists of consists of glucose isomerase (also known as xylose isomerase) produced using a *Streptomyces rubiginosus* production strain that has been genetically engineered. The glucose isomerase protein is not protein engineered. The glucose isomerase enzyme is not a genetically modified organism (GMO).

**GENSWEET® IGI-VHF** is Generally Recognized as Safe (GRAS) for use as processing aid in High Fructose Corn Syrup (HFCS) manufacture when the enzyme product is used within the product dose guidelines described in IFF's product literature. The glucose isomerase enzyme produced with *Streptomyces rubiginosus* is affirmed to be Generally Recognized as Safe ('GRAS'), under 21 CFR 184.1372.

**GENSWEET® IGI-VHF** also meets or exceeds the Joint FAO/WHO Expert Committee on Food Additives (JECFA)/Food Chemical Codex (FCC) specifications for microbial and metal contaminants in food enzymes.

IFF is committed to help our customers maximize the benefits of our technology, and we want to ensure successful use and safety of our products. Please contact your account manager if you should have further questions.

IFF Health & Biosciences

**Health & Biosciences**
200 Powder Mill Road
Wilmington, DE 19803
**T** +1.302.332.8420
**iff.com**

Liane Grieco
Global Regulatory Affairs
Global Regulatory Strategy Leader, Grain Processing
liane.m.grieco@iff.com

*This certificate is valid for one year from date of issue.*

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Date: August 17, 2023

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## CERTIFICATE OF SOURCE

RE: **GENSWEET® IGI-VHF** (A10022)[i]

To Whom It May Concern,

**GENSWEET® IGI-VHF** consists of consists of glucose isomerase (also known as xylose isomerase) produced by controlled fermentation in closed fermentation tanks, using a *Streptomyces rubiginosus* production strain that has been genetically engineered. The glucose isomerase protein is not protein engineered. The glucose isomerase enzyme is not a genetically modified organism (GMO).

After fermentation, the enzyme undergoes fixation and is immobilized onto an inert carrier matrix. IFF's immobilization process permanently cross-links the enzyme with matrix chemicals.

The final glucose isomerase product is available as an immobilized enzyme preparation approved for use as a processing aid in the production of high fructose corn syrup, a food ingredient.

All our enzyme products, whether obtained by genetic engineering or not, are only introduced into the market when their safety has been fully established according to internationally accepted assessments and regulatory procedures

IFF is committed to help our customers maximize the benefits of our technology, and we want to ensure successful use and safety of our products. Please contact your account manager if you should have further questions.

**Health & Biosciences**
200 Powder Mill Road
Wilmington, DE 19803
**T** +1.302.332.8420
**iff.com**

IFF Health & Biosciences

Liane Grieco
Global Regulatory Affairs
Global Regulatory Strategy Leader, Grain Processing
liane.m.grieco@iff.com

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SCIENTIFIC OPINION

ADOPTED: 12 December 2019

doi: 10.2903/j.efsa.2020.5978

# Safety evaluation of the food enzyme xylose isomerase from the genetically modified *Streptomyces rubiginosus* strain DP-Pzn37

EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), Vittorio Silano, José Manuel Barat Baviera, Claudia Bolognesi, Pier Sandro Cocconcelli, Riccardo Crebelli, David Michael Gott, Konrad Grob, Evgenia Lampi, Alicja Mortensen, Gilles Rivière, Inger-Lise Steffensen, Christina Tlustos, Henk van Loveren, Laurence Vernis, Holger Zorn, Boet Glandorf, Lieve Herman, Karl-Heinz Engel*, Andrew Smith*, Davor Želježić*, Margarita Aguilera-Gómez, Ana Gomes, Natália Kovalkovičová, Yi Liu, Joaquim Maia, Sandra Rainieri and Andrew Chesson

## Abstract

The food enzyme is a D-xylose aldose-ketose-isomerase (EC 5.3.1.5) produced with the genetically modified *Streptomyces rubiginosus* strain DP-Pzn37 by Danisco US Inc. Although the production strain contains antibiotic resistance genes, the food enzyme was shown to be free from viable cells of the production organism and its DNA. The food enzyme is intended to be used in an immobilised form for the isomerisation of glucose for the production of high fructose syrups. Residual amounts of total organic solids (TOS) are eliminated by the use of an immobilised food enzyme and further removed by the purification steps applied during the production of high fructose syrups using the immobilised enzyme; consequently, dietary exposure was not calculated. Genotoxicity tests did not raise safety concerns. The systemic toxicity was assessed by a repeated dose 90-day oral toxicity study in rats. The Panel identified a no observed adverse effect level of 85.2 mg TOS/kg body weight (bw) per day, the highest dose tested. Similarity of the amino acid sequence to those of known allergens was searched and no match was found. The Panel considered that, under the intended conditions of use, the risk of allergic sensitisation and elicitation reactions by dietary exposure cannot be excluded, but the likelihood is considered to be low. Based on the data provided, the immobilisation process and the removal of total organic solids during the production of high fructose syrups, the Panel concluded that this food enzyme does not give rise to safety concerns under the intended conditions of use.



**Keywords:** food enzyme, xylose isomerase, glucose isomerase, D-xylose aldose-ketose-isomerase, EC 5.3.1.5, *Streptomyces rubiginosus*

**Requestor:** European Commission

**Question number:** EFSA-Q-2016-00203

**Correspondence:** fip@efsa.europa.eu

* Member of the Working Group on Enzymes of the EFSA Panel Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) until 3-7-2018.

**Panel members:** José Manuel Barat Baviera, Claudia Bolognesi, Andrew Chesson, Pier Sandro Cocconcelli, Riccardo Crebelli, David Michael Gott, Konrad Grob, Evgenia Lampi, Alicja Mortensen, Gilles Rivière, Vittorio Silano, Inger-Lise Steffensen, Christina Tlustos, Henk Van Loveren, Laurence Vernis and Holger Zorn.

**Note:** The full opinion will be published in accordance with Article 12 of Regulation (EC) No 1331/2008 once the decision on confidentiality will be received from the European Commission.

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# 1. Introduction

Article 3 of the Regulation (EC) No 1332/2008[1] provides definition for 'food enzyme' and 'food enzyme preparation'.

> 'Food enzyme' means a product obtained from plants, animals or micro-organisms or products thereof including a product obtained by a fermentation process using micro-organisms: (i) containing one or more enzymes capable of catalysing a specific biochemical reaction; and (ii) added to food for a technological purpose at any stage of the manufacturing, processing, preparation, treatment, packaging, transport or storage of foods.
>
> 'Food enzyme preparation' means a formulation consisting of one or more food enzymes in which substances such as food additives and/or other food ingredients are incorporated to facilitate their storage, sale, standardisation, dilution or dissolution.

Before January 2009, food enzymes other than those used as food additives were not regulated or were regulated as processing aids under the legislation of the Member States. On 20 January 2009, Regulation (EC) No 1332/2008 on food enzymes came into force. This Regulation applies to enzymes that are added to food to perform a technological function in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food, including enzymes used as processing aids. Regulation (EC) No 1331/2008[2] established the European Union (EU) procedures for the safety assessment and the authorisation procedure of food additives, food enzymes and food flavourings. The use of a food enzyme shall be authorised only if it is demonstrated that:

i) it does not pose a safety concern to the health of the consumer at the level of use proposed;
ii) there is a reasonable technological need;
iii) its use does not mislead the consumer.

All food enzymes currently on the European Union market and intended to remain on that market, as well as all new food enzymes, shall be subjected to a safety evaluation by the European Food Safety Authority (EFSA) and approval via an EU Community list.

The 'Guidance on submission of a dossier on food enzymes for safety evaluation' (EFSA, 2009a) lays down the administrative, technical and toxicological data required.

## 1.1. Background and Terms of Reference as provided by the requestor

### 1.1.1. Background as provided by the European Commission

Only food enzymes included in the European Union (EU) Community list may be placed on the market as such and used in foods, in accordance with the specifications and conditions of use provided for in Article 7 (2) of Regulation (EC) No 1332/2008 on food enzymes.

Five applications have been introduced by the companies "BASF Enzymes LLC1" for the authorisation of the food enzyme Alpha-amylase from a genetically modified strain of *Pseudomonas fluorescens* (BD15754), "DSM Food Specialties B.V." for the authorisation of the food enzyme Phospholipase C from a genetically modified strain of *Pichia pastoris* (PRF), and "Danisco US Inc." for the authorisation of the food enzymes Alpha-amylase from a genetically modified strain of *Bacillus licheniformis* (DP-Dzb25), Xylose isomerase from a genetically modified strain of *Streptomyces rubiginosus* (DP-Pzn37), and Alpha-amylase from a genetically modified strain of *Bacillus amyloliquefaciens* (DP-Czb53).

Following the requirements of Article 12.1 of Commission Regulation (EU) No 234/2011[3] implementing Regulation (EC) No 1331/2008[2], the Commission has verified that the five applications fall within the scope of the food enzyme Regulation and contain all the elements required under Chapter II of that Regulation.

[1] Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on Food Enzymes and Amending Council Directive 83/417/EEC, Council Regulation (EC) No 1493/1999, Directive 2000/13/EC, Council Directive 2001/112/EC and Regulation (EC) No 258/97. OJ L 354, 31.12.2008, pp. 7–15.

[2] Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 354, 31.12.2008, pp. 1–6.

[3] Commission Regulation (EU) No 234/2011 of 10 March 2011 implementing Regulation (EC) No 1331/2008 of the European Parliament and of the Council establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 64, 11.3.2011, p. 15–24.

### 1.1.2. Terms of Reference

The European Commission requests the European Food Safety Authority to carry out the safety assessments on the food enzymes Alpha-amylase from a genetically modified strain of *Pseudomonas fluorescens* (strain BD15754), Phospholipase C from a genetically modified strain of *Pichia pastoris* (strain PRF), Alpha-amylase from a genetically modified strain of *Bacillus licheniformis* (strain DP-Dzb25), Xylose isomerase from a genetically modified strain of *Streptomyces rubiginosus* (strain DP-Pzn37), and Alpha-amylase from a genetically modified strain of *Bacillus amyloliquefaciens* (strain DP-Czb53) in accordance with Article 17.3 of Regulation (EC) No 1332/2008 on food enzymes.

## 1.2. Interpretation of the Terms of Reference

The present scientific opinion addresses the European Commission's request to carry out the safety assessment of food enzyme xylose isomerase from a genetically modified *S. rubiginosus* (strain DP-Pzn37).

# 2. Data and methodologies

## 2.1. Data

The applicant has submitted a dossier in support of the application for authorisation of the food enzyme xylose isomerase produced with a genetically modified *S. rubiginosus* strain DP-Pzn37. The dossier was updated on 28 July 2016.

Additional information was requested from the applicant during the assessment process on 29 May 2017, 28 November 2018 and 25 June 2019, and was consequently provided (see 'Documentation provided to EFSA').

Following the reception of additional data by EFSA on 26 April 2018, EFSA requested a clarification teleconference, which was held on 16 May 2018; after which the applicant provided additional data on 1 June 2018.

Following the requests for additional data sent by EFSA on 29 May 2017, 28 November 2018 and 25 June 2019, the applicant requested clarification teleconferences, which were held on 20 June 2017, 20 May 2019 and 5 July 2019.

## 2.2. Methodologies

The assessment was conducted in line with the principles described in the EFSA 'Guidance on transparency in the scientific aspects of risk assessment' (EFSA, 2009b) as well as in the EFSA 'Statement on the characterisation of microorganisms used for the production of food enzymes' (EFSA CEP Panel, 2019) and following the relevant existing guidance's of EFSA Scientific Committees.

The current 'Guidance on the submission of a dossier on food enzymes for safety evaluation' (EFSA, 2009a) has been followed for the evaluation of the application with the exception of the exposure assessment, which was carried out in accordance to the methodology described in the CEF Panel statement on the exposure assessment of food enzymes (EFSA CEF Panel, 2016).

# 3. Assessment

| | |
|---|---|
| IUBMB nomenclature: | Xylose isomerase |
| Systematic name: | D-xylose aldose-ketose-isomerase |
| Synonyms: | Glucose isomerase; D-xylose isomerase; D-xylose ketol-isomerase |
| IUBMB No: | EC 5.3.1.5 |
| CAS No: | 9023-82-9 |
| EINECS No: | 232-944-6. |

The xylose isomerase catalyses the conversion of D-xylose to D-xylulose and of D-glucose to D-fructose. It is intended to be used for the isomerisation of glucose for the production of high fructose syrups. The food enzyme is intended to be used only in an immobilised form.[4] Based on its technical application, the term glucose isomerase is used throughout this dossier.

[4] Technical dossier/Additional data April 2018.

## 3.1. Source of the food enzyme

The glucose isomerase is produced with a genetically modified bacterium *S. rubiginosus* strain DP-Pzn37, which is deposited at the Westerdijk Fungal Biodiversity Institute (The Netherlands) with the deposit number [redacted][4]. The taxonomic identification of the production strain was performed on the basis of [redacted].

The whole genome sequence of the production strain was analysed for the presence of antimicrobial resistance genes. [redacted][5]

### 3.1.1. Characteristics of the parental and recipient microorganisms

The parental microorganism is the Actinobacterium *S. rubiginosus* strain [redacted].

The recipient strain *S. rubiginosus* [redacted] was derived [redacted][6]

### 3.1.2. Characteristics of the introduced sequences

The donor for the glucose isomerase encoding gene is [redacted][7]

[redacted][8]

### 3.1.3. Description of the genetic modification process

The production strain *S. rubiginosus* DP-Pzn37 was developed from the recipient strain [redacted].[8]

[redacted]

### 3.1.4. Safety aspects of the genetic modification

The technical dossier contains all necessary information on the recipient microorganism, the donor organism and the genetic modification process.

The production strain DP-Pzn37 differs from the recipient strain [redacted][7]

Genetic stability was demonstrated [redacted][9]

[redacted][5]

## 3.2. Production of the food enzyme

The food enzyme is manufactured according to the Food Hygiene Regulation (EC) No 852/2004[10], with food safety procedures based on hazard analysis and critical control points, and in accordance with current Good Manufacturing Practice.[11]

[5] Technical dossier/Additional data May 2019/Annex AH.
[6] Technical dossier/1st submission/Annex S and T.
[7] Technical dossier/1st submission/Annex S and Technical dossier/2nd submission/Annex U.
[8] Technical dossier/1st submission/Annex S.
[9] Technical dossier/2nd submission/Annex Z.
[10] Regulation (EC) No. 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of food additives. OJ L 226, 25.6.2004, pp. 3–21.
[11] Technical dossier/2nd submission/p. 40.

The production strain is grown as a pure culture using a typical industrial medium in a submerged, batch or fed-batch fermentation system with conventional process controls in place. After completion of the fermentation, the cells are lysed and the enzyme is immobilised [redacted] The immobilised food enzyme preparation is then separated from the liquid fraction by filtration. Afterwards, the preparation is extruded, dried and sieved.[12] The applicant provided information on the identity of the substances used to control the fermentation and in the subsequent downstream processing of the food enzyme.[4]

The Panel considered that sufficient information has been provided on the manufacturing process and the quality assurance system implemented by the applicant to exclude issues of concern.

## 3.3. Characteristics of the food enzyme

### 3.3.1. Properties of the food enzyme

The glucose isomerase is a single polypeptide of [redacted] amino acids.[13] The molecular mass, derived from the amino acid sequence, was calculated to be [redacted] kDa.[14] The food enzyme was analysed by sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS–PAGE). A consistent protein pattern was observed across all batches. The gels showed a single major protein band corresponding to an apparent molecular mass of about [redacted] kDa, consistent with the expected mass of the enzyme.[15] No other enzymatic side activities were reported.

The in-house determination of free glucose isomerase activity is based on the conversion of glucose to fructose (reaction conditions: pH 6.85, 30°C, 30 min). The enzymatic activity is determined by measuring the fructose formed by high-performance liquid chromatography (HPLC). The glucose isomerase activity is quantified relative to an internal enzyme standard and expressed in glucose isomerase units (GIU)/g.[16]

The free food enzyme has a temperature optimum around 80–85°C (pH 7.5) and a pH optimum around pH 8.0–8.5 (60°C). Thermostability was tested after a pre-incubation of the food enzyme for 32 min at different temperatures (pH 7.5). The glucose isomerase activity decreased rapidly above 85°C, showing no residual activity above 95°C.[17]

### 3.3.2. Chemical parameters

Data on the chemical parameters of the food enzyme were provided for five food enzyme batches, three batches used for commercialisation and two batches produced for the toxicological tests (Table 1).[18] The average total organic solids (TOS) of the three food enzyme batches for commercialisation was 14.4%. The average enzyme activity/TOS ratio of the three food enzyme batches for commercialisation is 21.2 GIU/mg TOS.

[12] Technical dossier//1st submission/Annex K and S and Additional data May 2019/Annex AA.
[13] Technical dossier/1st submission/Annex G.
[14] Technical dossier/Additional data May 2019.
[15] Technical dossier/2nd submission/p. 30.
[16] Technical dossier/1st submission/Annex C.
[17] Technical dossier/2nd submission/p. 34–36.
[18] Technical dossier/Additional data June 2018/Annexes F, G, H, L and M.

**Table 1:** Compositional data of the food enzyme prior to immobilisation and batches used for toxicological studies

| Parameter | Unit | Batches | | | | |
|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4[(a)] | 5[(b)] |
| Glucose isomerase activity | GIU/g batch[(c)] | 2,831 | 3,238 | 2,980 | 434.32 | 3,530 |
| Protein | % | 12.30 | 14.47 | 11.37 | 4.79 | 20.19 |
| Ash | % | 0.17 | 0.73 | 0.37 | 2.30 | 9.61 |
| Water | % | 85.77 | 82.26 | 87.48 | 89.18 | 44.00 |
| Total organic solids (TOS)[(d)] | % | 14.06 | 17.01 | 12.15 | 8.52 | 46.39 |
| Glucose isomerase activity/mg TOS | GIU/mg TOS | 20.14 | 19.04 | 24.53 | 5.10 | 7.61 |

(a): Batch used for the Bacterial reverse mutation test and Repeated dose 90-day oral toxicity study in rodents.
(b): Batch used for the *in vitro* chromosomal aberrations test.
(c): GIU/g: glucose isomerase units/g (see Section 3.3.1).
(d): TOS calculated as 100% − % water − % ash.

### 3.3.3. Purity

The lead content in the three commercial batches and in the two batches used for toxicological studies was below 0.05 mg/kg which complies with the specification for lead (< 5 mg/kg) as laid down in the general specifications and considerations for enzymes used in food processing (FAO/WHO, 2006).[18,19]

The food enzyme complies with the microbiological criteria as laid down in the general specifications and considerations for enzymes used in food processing (FAO/WHO, 2006), which stipulate that *Escherichia coli* and *Salmonella* species are absent in 25 g of sample and total coliforms should not exceed 30 colony forming units (CFU) per gram.[18] No antimicrobial activity was detected in any of these batches (FAO/WHO, 2006).[20]

The Panel considered that the information provided on the purity of the food enzyme is sufficient.

### 3.3.4. Viable Cells and DNA of the production strain

The absence of the production strain has been demonstrated [redacted] The production strain was not detected [redacted][21]

No recombinant DNA was detected [redacted][22]

## 3.4. Toxicological assessment

A battery of toxicological tests including a bacterial gene mutation assay (Ames test), an *in vitro* mammalian chromosomal aberration test, and a repeated dose 90-day oral toxicity study in rats has been provided. The batches 4 and 5 (Table 1) used in these studies have lower specific activity compared to the batches used for commercialisation, and thus are considered suitable for toxicological testing.

### 3.4.1. Genotoxicity

#### 3.4.1.1. Bacterial reverse mutation test

A bacterial reverse mutation assay (Ames test) was performed according to Organisation for Economic Co-operation and Development (OECD) Test Guideline 471 (OECD, 1997a) and following Good Laboratory Practice (GLP).[23] Five strains of *Salmonella* Typhimurium (TA 98, TA 100, TA 102, TA

[19] LoD: Pb = 0.05 mg/kg.
[20] Technical dossier/Additional data June 2018/Annex I.
[21] Technical dossier/2nd submission/Annex E and Technical dossier/Additional data April 2018.
[22] Technical dossier/Additional data September 2019.
[23] Technical dossier/1st submission/Annex M.

1535, TA 1537) were tested in the presence or absence of metabolic activation applying the 'treat and plate' assay. Two experiments were carried out using five different concentrations of the food enzyme for strains TA 98, TA 100, TA 102, TA 1535 (50, 166, 500, 1,660 and 5,000 μg total protein/plate, corresponding to 88.9, 295, 889, 2,953 and 8,894 μg TOS/plate), and three experiments using ten different concentrations for strain TA 1537 (0.166, 0.5, 1.66, 5, 16.6, 50, 166, 500, 1,660 and 5,000 μg total protein/plate, corresponding to 0.30, 0.89, 2.95, 8.89, 29.5, 88.9, 295, 889, 2,953 and 8,894 μg TOS/plate). Growth reductions of the background lawn were observed, in some cases severe, due to toxicity. Upon treatment with the food enzyme, there was no significant increase in revertant colony numbers above the control values in any strain with or without S9-mix.

The Panel concluded that the food enzyme glucose isomerase did not induce gene mutations under the test conditions employed in this study.

#### 3.4.1.2. *In vitro* mammalian chromosomal aberrations test

The *in vitro* chromosomal aberrations test was carried out according to the OECD Test Guideline 473 (OECD, 1997b) and following GLP.[24] The food enzyme was tested for its ability to induce chromosomal aberrations in human peripheral blood lymphocytes with and without metabolic activation (S9-mix). Based on the results obtained in a dose-range finding test, the cells were treated with 1,250, 2,500 and 5,000 total protein μg/mL (corresponding to 2,872, 5,744 and 11,488 μg TOS/mL) applying a 4 + 20 h short-term treatment and recovery in the presence and absence of S9-mix, and a continuous treatment (20 + 0 h) in the absence of S9-mix. In all the tested conditions, the frequency of cells with structural and numerical chromosomal aberrations in treated cultures was comparable to the values detected in negative controls and within the range of the laboratory historical negative control data.

The Panel concluded that the food enzyme glucose isomerase did not induce chromosomal aberrations under the test conditions employed for this study.

### 3.4.2. Repeated dose 90-day oral toxicity study in rodents

The repeated dose 90-day oral toxicity study in rodents was performed in accordance with OECD Test Guideline 408 (OECD, 1998), and following GLP.[25] Groups of 10 male and 10 female Ntac:SD Sprague–Dawley rats received the food enzyme by gavage in doses corresponding to 21.3, 42.6 and 85.2 mg TOS/kg body weight (bw) per day. Controls received the vehicle (saline solution 2% NaCl).

There were three unscheduled deaths. Two deaths (one control female and one high-dose male) were related to misdosing. The third animal (low-dose male) was found dead and the cause of death could not be established at necropsy due to autolysis.

A statistically significant increase in monocytes in mid-dose females in comparison to the control group was observed. However, in the absence of a dose response and similar finding in males, this finding was considered to be incidental.

Among clinical chemistry parameters statistically significant differences to controls included increased serum sodium concentration in high-dose males and increased cholesterol and albumin concentrations in high-dose females. As these findings lacked consistency between sexes, and the values were within the historical control range (sodium and cholesterol) for the laboratory or slightly higher (albumin: 49.5 ± 2.1 g/L compared to 95% interval of historical control data of 37.89–48.7 g/L) they were considered of no toxicological significance.

Ophthalmological examination was not performed. However, no changes in the eyes were recorded during weekly clinical examinations, at necropsy and by microscopy of the eyes of control and treated groups.

No other significant effects were observed.

Overall, the Panel identified a no observed adverse effect level (NOAEL) of 85.2 mg TOS/kg bw per day, the highest dose tested.

### 3.4.3. Allergenicity

The allergenicity assessment considers only the food enzyme and not any carrier or other excipient, which may be used in the final formulation.

[24] Technical dossier/1st submission/Annex N.
[25] Technical dossier/1st submission/Annex O.

The potential allergenicity of the glucose isomerase produced with the genetically modified *S. rubiginosus* strain DP-Pzn37 was assessed by comparing its amino acid sequence with those of known allergens according to the scientific opinion on the assessment of allergenicity of genetically modified plants and microorganisms and derived food and feed of the Scientific Panel on Genetically Modified Organisms (EFSA GMO Panel, 2010). Using higher than 35% identity in a sliding window of 80 amino acids as the criterion, no match was found.[26]

No information is available on oral sensitisation or elicitation reactions of this glucose isomerase. In addition, no allergic reactions upon dietary exposure to any glucose isomerase have been reported in the literature. Therefore, it can be concluded that allergic reactions upon oral ingestion of this glucose isomerase, produced with the genetically modified *S. rubiginosus* strain DP-Pzn37 cannot be excluded, but the likelihood of such a reaction to occur is considered to be low.

Quantifying the risk for allergenicity is not possible in view of the individual susceptibility to food allergens. Allergenicity can be ruled out only if the proteins are fully removed. Considering that the food enzyme is only used in immobilised form and in the glucose isomerisation for the production of high fructose syrups, experimental data showed a significant removal (below LoDs) of protein. However, traces of protein could be present in high fructose syrups.

The Panel considered that, under the intended conditions of use, the risk of allergic sensitisation and elicitation reactions upon dietary exposure to this food enzyme cannot be excluded but the likelihood of such reactions occurring is considered to be low.

## 3.5. Dietary exposure

### 3.5.1. Intended use of the food enzyme

The food enzyme is intended to be used to isomerise glucose for the production of high fructose syrup at the maximum use level proposed by the applicant of 1 mg TOS/kg glucose syrup derived from cereals,[27] for the immobilised food enzyme only.

As the food enzyme is intended to be used only in its immobilised form, the transfer of TOS into the final product, i.e. high fructose syrups, is expected to be negligible. Additionally, experimental data have been provided showing low ash contents (less than 0.01 g/100 g dry matter syrup), and protein, fat and fibres contents in the final high fructose syrup, after purification steps are applied (i.e. ion exchange chromatography, treatment with active carbon), are not detectable (Annex B in EFSA CEF Panel, 2016a). Amounts of [redacted] in the final food samples have been experimentally shown to be not detectable.[28,29] The Panel considers that the residual amount of TOS (including substances other than proteins, such as DNA fragments) in the final high fructose syrups will be removed.

### 3.5.2. Dietary exposure estimation

Considering that the food enzyme is intended to be used only in its immobilised form (see Section 3.5.1), and as residual amounts of TOS are removed by the purification steps applied during the production of high fructose syrups, a dietary exposure was not calculated.

# 4. Conclusion

Based on the data provided, immobilisation of the food enzyme and the removal of TOS during purification steps applied during the production of high fructose syrups, the Panel concluded that the food enzyme glucose isomerase produced with the genetically modified *S. rubiginosus* strain DP-Dzn37 does not give rise to safety concerns under the intended conditions of use.

The production strain of the food enzyme contains a known antimicrobial resistance gene in a multicopy plasmid together with sequences showing homology with genes known to confer resistance to macrolides. However, based on the absence of viable cells and DNA from the production organism in the food enzyme, this is not considered to be a risk.

[26] Technical dossier/1st submission/Annex R.
[27] Technical dossier/2nd submission/p. 74 and Additional data May 2019.
[28] Technical dossier/1st submission/Annex W and Additional data May 2019/Annexes AB, AC and AD.
[29] LoDs: [redacted].

## Documentation provided to EFSA

1) Technical dossier 'Application for authorisation of xylose isomerase from a genetically modified strain of *Streptomyces rubiginosus* (DP-Pzn37)'. January 2016. Submitted by Danisco US Inc.
2) Additional information. April 2018. Submitted by Danisco US Inc.
3) Additional information. June 2018. Submitted by Danisco US Inc.
4) Additional information. May 2019. Submitted by Danisco US Inc.
5) Additional information. September 2019. Submitted by Danisco US Inc.

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[redacted]

## Abbreviations

| | |
|---|---|
| bw | body weight |
| CAS | Chemical Abstracts Service |
| CEF | EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids |
| CEP | EFSA Panel on Food Contact Materials, Enzymes and Processing Aids |
| CFU | colony forming units |
| EINECS | European Inventory of Existing Commercial Chemical Substances |
| FAO | Food and Agricultural Organisation |
| GIU | glucose isomerase units |
| GLP | Good Laboratory Practice |
| GMO | EFSA Panel on Genetically Modified Organisms |
| HPLC | high-performance liquid chromatography |
| IUBMB | International Union of Biochemistry and Molecular Biology |

| | |
|---|---|
| LoD | limit of detection |
| NOAEL | no observed adverse effect level |
| OECD | Organisation for Economic Cooperation and Development |
| SDS–PAGE | sodium dodecyl sulfate–polyacrylamide gel electrophoresis |
| TOS | total organic solids |
| WHO | World Health Organisation |

## Question #11 Attachment

Exponent

EXTERNAL MEMORANDUM

| | |
|---|---|
| TO: | Lore Kolberg (Tate & Lyle) |
| FROM: | Exponent |
| DATE: | September 8, 2023 |
| PROJECT: | 2103250.000 |
| SUBJECT: | Revised Cumulative Estimated Daily Intake of Allulose |

At the request of Tate and Lyle, Exponent prepared this memorandum to provide the updated cumulative estimated daily intake (CEDI) for allulose. The update was made in response to the following FDA's review comments on the dietary exposure estimate summarized in GRN 001057:

> "Considering that GRNs 001024 and 001029 submitted for the use of D-psicose recently received "no questions" letters from FDA, we request that the notifier update the dietary exposure estimates provided in Tables 10 and 12 to account for the recently notified additional uses of D-psicose…
>
> Specifically, GRN 001024 includes the use of D-psicose in 'Alcoholic beverages (pre-mixed cocktails, wine coolers, and malt beverages, low/reduced calorie)' that the notifier should consider including in the updated background and cumulative dietary exposure estimates.
>
> We note that we consider the cumulative dietary exposure to D-psicose that was estimated in GRN 001024 to be 22.9 g/person (p)/d at the 90$^{th}$ percentile for the US population aged 2 years and older as the current dietary exposure to D-psicose. When revising the notifier's dietary exposures, the dietary exposure presented in GRN 001024 could be used to represent the background dietary exposure to D-psicose."

## Revised Proposed Uses

As per FDA's comment, the use of allulose in alcoholic beverages (pre-mixed cocktails, wine coolers, and malt beverages, low/reduced calorie) were included in GRN 001024 and should be considered part of the background exposure and CEDI. As such, Tate and Lyle excluded alcoholic beverages from its proposed uses. Tate and Lyle also reduced the proposed use level in nutrition bars to 15% (previously 25%). Tate and Lyle's revised proposed uses of allulose is provided in **Table 1**. The list of food codes included in this assessment is provided in **Appendix A**.

Revised estimated daily intake (EDI) for allulose from the proposed uses in Table 1 were based on food consumption records collected in the WWEIA component of NHANES conducted in 2017-2018 (NHANES 2017-2018). In the previous intake assessment report, Exponent used two NHANES survey cycles (NHANES 2015-2018). However, NHANES 2017-2018 was used in this update in order to be consistent with GRN 001024. The updated results from Tate and Lyle's proposed new uses of allulose are provided in **Table 2**.

## Table 1. Tate and Lyle's revised proposed uses

| No.* | **Food category** | **Description of Foods Selected for Analysis** | **Tate and lye's proposed new uses (%)** |
|---|---|---|---|
| 2b | Nutritional beverages | All nutritional drinks such as Carnation Instant Breakfast, Muscle Milk, Slim Fast, and all other nutritional drinks or shakes | 2.5 |
| 2c | PediaSure | PediaSure | 3.5 |
| 5a | RTE and cooked, regular | RTE and cooked cereals identified as containing added sugar | 12** |
| 5b | RTE and cooked, low calorie, reduced calorie, sugar-free | RTE and cooked cereals identified as low calorie, reduced sugar, or sugar-free | 12** |
| 5d | Grain-free, no sugar, high protein RTE cereal | No grain-free, no sugar, high protein RTE cereals were reported consumed, hence, zero-sugar added RTE cereals were selected as surrogates. | 20 |
| 9 | Frozen dairy (ice cream, soft serve, sorbet), low calorie, reduced calorie, sugar-free | Desserts including ice cream, soft serve, sorbet - all identified as low calorie, reduced calorie, sugar-free, or NFS‡ | 8** |
| 11 | Nutrition bars | Meal replacement bars, protein bars, energy bars, etc. | 15 |
| 16 | Ketchup and barbecue sauces | Ketchup and barbecue sauces | 10 |
| 19 | Cranberries, dried | Dried cranberries (i.e., Craisins) | 25 |
| 20 | Jerky (meat or poultry based) | Jerky (meat or poultry based) | 15 |

* Numbering in **Table 1. Maximum allulose use levels by types of foods and beverages**, in Exponent's March 28, 2022 report.
** Existing Use levels from previous GRNs are below Tate & Lyle's proposed levels

## Table 2. Two-day average EDI of allulose from Tate and Lyle's revised proposed uses by the U.S. 2+ y and subpopulations (g/day); NHANES 2017-2018

| **Sub-population** | **Unweighted N** | **% Users** | **EDI of allulose (g/day)** | | | |
|---|---|---|---|---|---|---|
| | | | **Per Capita** | | **Per User** | |
| | | | **Mean** | **90th Percentile** | **Mean** | **90th Percentile** |
| US 2+ y | 6184 | 62.3 | 3.4 | 9.6 | 5.4 | 11.9 |
| 2-12 y | 1262 | 77.1 | 3.3 | 8.0 | 4.3 | 8.6 |
| 13-18 y | 682 | 64.3 | 3.3 | 8.9 | 5.1 | 10.7 |
| 19+ y | 4240 | 59.4 | 3.4 | 10.0 | 5.7 | 12.8 |

## Revised Cumulative Estimated Daily Intake

FDA commented that the CEDI of 22.9 g/person (p)/d at the 90th percentile for the US population aged 2 years and older in GRN 001024 is the current dietary exposure to allulose. As recommended by the FDA, Exponent relied on the dietary exposure presented in GRN 001024 to represent the background dietary exposure to allulose. Specifically, Exponent relied on the data provided in **Table 1. Updated Cumulative Allulose Intake (g/day)** on page 232 of GRN 001024.[1]

The revised CEDI for allulose from both Tate and Lyle's proposed uses and background uses for the US 2+ y and sub-populations are summarized in **Table 3**.

**Table 3. CEDI of allulose from background uses and Tate and Lyle's proposed uses by the U.S. 2+ y and subpopulations (g/day); NHANES 2017-2018**

| Sub-population | Background EDI (g/day) (GRN 001024) | | EDI (g/day) from Proposed Uses | Cumulative Estimated Daily Intake (g/day) | | |
|---|---|---|---|---|---|---|
| | % Users | Mean per capita | Mean per capita | Mean per capita | Mean per user* | Pseudo 90th** Per user |
| US 2+ y | 77.0 | 7.8 | 3.4 | 11.2 | 14.5 | 29.0 |
| 2-12 y | 70.5 | 4.2 | 3.3 | 7.5 | 10.6 | 21.2 |
| 13-18 y | 62.9 | 3.6 | 3.3 | 6.9 | 10.9 | 21.8 |
| 19+ y | 81.2 | 8.9 | 3.4 | 12.3 | 15.1 | 30.2 |

* Mean per capita divided by % users to derive mean per user
* Pseudo 90th is derived based on 2 x mean (FDA 2006 guidance)[2]

[1] Jan 19, 2023 letter from Katrina Emmel of GRAS Associations, LLC. to the US FDA, attention Stephanie Hice; Re: GRN 1024-Allulose response to questions posted in an email dated 1/4/2023.

[2] U.S. Food and Drug Administration (FDA), Center for Food Safety and Nutrition, Office of Food Additive Safety. 2006. Guidance for Industry: Estimating Dietary Intake of Substances in Food. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-estimating-dietary-intake-substances-food

# Appendix A. Food Codes Included In Analysis of Proposed Uses

| Food Category | | |
|---|---|---|
| 2b | Nutritional beverages | |
| | Food code | Food description |
| | 11553120 | Fruit smoothie, with whole fruit and dairy, added protein*,** |
| | 64134020 | Fruit smoothie, with whole fruit, no dairy, added protein*,** |
| | 78101110 | Fruit and vegetable smoothie, added protein*,** |
| | 78101118 | Fruit and vegetable smoothie, non-dairy, added protein*,** |
| | 95102000 | Nutritional drink or shake, ready-to-drink (Carnation Instant Breakfast) |
| | 95105000 | Nutritional drink or shake, ready-to-drink (Kellogg's Special K Protein) |
| | 95106000 | Nutritional drink or shake, ready-to-drink (Muscle Milk) |
| | 95106010 | Nutritional drink or shake, ready-to-drink, light (Muscle Milk) |
| | 95110000 | Nutritional drink or shake, ready-to-drink (Slim Fast) |
| | 95110010 | Nutritional drink or shake, ready-to-drink, sugar free (Slim Fast) |
| | 95110020 | Nutritional drink or shake, high protein, ready-to-drink (Slim Fast) |
| | 95120000 | Nutritional drink or shake, ready-to-drink, NFS |
| | 95120010 | Nutritional drink or shake, high protein, ready-to-drink, NFS |
| | 95120020 | Nutritional drink or shake, high protein, light, ready-to-drink, NFS |
| | 95201000 | Nutritional powder mix (Carnation Instant Breakfast)** |
| | 95201010 | Nutritional powder mix, sugar free (Carnation Instant Breakfast)** |
| | 95201200 | Nutritional powder mix (EAS Whey Protein Powder)** |
| | 95201300 | Nutritional powder mix (EAS Soy Protein Powder)** |
| | 95201500 | Nutritional powder mix, high protein (Herbalife)** |
| | 95201600 | Nutritional powder mix (Isopure)** |
| | 95201700 | Nutritional powder mix (Kellogg's Special K20 Protein Water)** |
| | 95202000 | Nutritional powder mix (Muscle Milk)** |
| | 95210000 | Nutritional powder mix (Slim Fast)** |
| | 95210020 | Nutritional powder mix, high protein (Slim Fast)** |
| | 95220000 | Nutritional powder mix, NFS** |
| | 95220010 | Nutritional powder mix, high protein, NFS** |
| | 95230000 | Nutritional powder mix, whey based, NFS** |
| | 95230010 | Nutritional powder mix, protein, soy based, NFS** |
| | 95230020 | Nutritional powder mix, protein, light, NFS** |
| | 95230030 | Nutritional powder mix, protein, NFS** |
| 2c | PediaSure | |
| | Food code | Food description |
| | 11710800 | Infant formula, NS as to form (PediaSure) |
| | 11710801 | Infant formula, ready-to-feed (PediaSure) |
| | 11710806 | Infant formula, with fiber, ready-to-feed (PediaSure Fiber) |
| 5a | RTE and cooked, regular | |
| | Food code | Food description |
| | 56201360 | Grits, instant, made with non-dairy milk, fat added |
| | 56201540 | Cornmeal, Puerto Rican Style |
| | 56202905 | Oatmeal, from fast food, maple flavored |
| | 56202910 | Oatmeal, from fast food, fruit flavored |
| | 56202920 | Oatmeal, from fast food, other flavors |
| | 56203075 | Oatmeal, regular or quick, made with non-dairy milk, NS as to fat |

| | | |
|---|---|---|
| | 56203076 | Oatmeal, regular or quick, made with non-dairy milk, no added fat |
| | 56203077 | Oatmeal, regular or quick, made with non-dairy milk, fat added |
| | 56203106 | Oatmeal, instant, plain, made with non-dairy milk, no added fat |
| | 56203125 | Oatmeal, instant, maple flavored, NS as to fat |
| | 56203130 | Oatmeal, instant, maple flavored, no added fat |
| | 56203135 | Oatmeal, instant, maple flavored, fat added |
| | 56203150 | Oatmeal, instant, fruit flavored, NS as to fat |
| | 56203155 | Oatmeal, instant, fruit flavored, no added fat |
| | 56203160 | Oatmeal, instant, fruit flavored, fat added |
| | 56203175 | Oatmeal, instant, other flavors, no added fat |
| | 56203180 | Oatmeal, instant, other flavors, fat added |
| | 56205080 | Rice, creamed, made with milk and sugar, Puerto Rican style |
| | 56207027 | Cream of wheat, regular or quick, made with non-dairy milk, fat added |
| | 56207030 | Cream of wheat, instant, made with water, no added fat |
| | 56207060 | Cream of wheat, instant, made with water, fat added |
| | 56207094 | Cream of wheat, instant, made with milk, fat added |
| | 56207095 | Cream of wheat, instant, made with milk, no added fat |
| | 56207102 | Cream of wheat, instant, made with non-dairy milk, no added fat |
| | 57100100 | Cereal, ready-to-eat, NFS |
| | 57101000 | Cereal (Kellogg's All-Bran) |
| | 57103000 | Cereal (Post Alpha-Bits) |
| | 57103100 | Cereal (General Mills Cheerios Apple Cinnamon) |
| | 57104000 | Cereal (Kellogg's Apple Jacks) |
| | 57106050 | Cereal (Post Great Grains Banana Nut Crunch) |
| | 57106060 | Cereal (General Mills Cheerios Banana Nut) |
| | 57106100 | Cereal (General Mills Basic 4) |
| | 57106250 | Cereal (General Mills Kix Berry Berry) |
| | 57106260 | Cereal (General Mills Cheerios Berry Burst) |
| | 57107000 | Cereal (General Mills Boo Berry) |
| | 57110000 | Cereal (Kellogg's All-Bran Bran Buds) |
| | 57117000 | Cereal (Quaker Cap'n Crunch) |
| | 57117500 | Cereal (Quaker Christmas Crunch) |
| | 57119000 | Cereal (Quaker Cap'n Crunch's Crunchberries) |
| | 57120000 | Cereal (Quaker Cap'n Crunch's Peanut Butter Crunch) |
| | 57124030 | Cereal (General Mills Chex Chocolate) |
| | 57124050 | Cereal (General Mills Chex Cinnamon) |
| | 57124100 | Cereal (General Mills Cheerios Chocolate) |
| | 57124200 | Cereal, chocolate flavored, frosted, puffed corn |
| | 57124300 | Cereal (General Mills Lucky Charms Chocolate) |
| | 57125000 | Cereal (General Mills Cinnamon Toast Crunch) |
| | 57125900 | Cereal (General Mills Honey Nut Clusters) |
| | 57126000 | Cereal (Kellogg's Cocoa Krispies) |
| | 57127000 | Cereal (Post Cocoa Pebbles) |
| | 57128000 | Cereal (General Mills Cocoa Puffs) |
| | 57130000 | Cereal (General Mills Cookie Crisp) |
| | 57132000 | Cereal (General Mills Chex Corn) |
| | 57134000 | Cereal, corn flakes |
| | 57135000 | Cereal (Kellogg's Corn Flakes) |

| | | |
|---|---|---|
| | 57137000 | Cereal, corn puffs |
| | 57139000 | Cereal (General Mills Count Chocula) |
| | 57143000 | Cereal (Kellogg's Cracklin' Oat Bran) |
| | 57143500 | Cereal (Post Great Grains, Cranberry Almond Crunch) |
| | 57148000 | Cereal (Kellogg's Crispix) |
| | 57148500 | Cereal, crispy brown rice |
| | 57151000 | Cereal, crispy rice |
| | 57201900 | Cereal (General Mills Dora The Explorer) |
| | 57206710 | Cereal (General Mills Fiber One Honey Clusters) |
| | 57206715 | Cereal (General Mills Fiber One Raisin Bran Clusters) |
| | 57207000 | Cereal, bran flakes |
| | 57208000 | Cereal (Kellogg's All-Bran Complete Wheat Flakes) |
| | 57209000 | Cereal (Post Bran Flakes) |
| | 57211000 | Cereal (General Mills Frankenberry) |
| | 57213000 | Cereal (Kellogg's Froot Loops) |
| | 57213010 | Cereal (Kellogg's Froot Loops Marshmallow) |
| | 57213850 | Cereal (General Mills Cheerios Frosted) |
| | 57214000 | Cereal (Kellogg's Frosted Mini-Wheats) |
| | 57218000 | Cereal (Kellogg's Frosted Krispies) |
| | 57221700 | Cereal, fruit rings |
| | 57221810 | Cereal (General Mills Cheerios Fruity) |
| | 57223000 | Cereal (Post Fruity Pebbles) |
| | 57224000 | Cereal (General Mills Golden Grahams) |
| | 57227000 | Cereal, granola |
| | 57228000 | Granola, homemade |
| | 57229000 | Cereal (Kellogg's Low Fat Granola) |
| | 57229500 | Cereal (Kellogg's Low Fat Granola with Raisins) |
| | 57231000 | Cereal (Post Grape-Nuts Flakes) |
| | 57231200 | Cereal (Post Great Grains Raisins, Dates, and Pecans) |
| | 57231250 | Cereal (Post Great Grains Double Pecan Whole Grain Cereal) |
| | 57237100 | Cereal (Post Honey Bunches of Oats Honey Roasted) |
| | 57237200 | Cereal (Post Honey Bunches of Oats with Vanilla Bunches) |
| | 57237300 | Cereal (Post Honey Bunches of Oats with Almonds) |
| | 57237900 | Cereal (Post Honey Bunches of Oats Just Bunches) |
| | 57238000 | Cereal (Post Honeycomb) |
| | 57240100 | Cereal (General Mills Chex Honey Nut) |
| | 57241000 | Cereal (General Mills Cheerios Honey Nut) |
| | 57241200 | Cereal (Post Shredded Wheat Honey Nut) |
| | 57243000 | Cereal (Kellogg's Honey Smacks) |
| | 57301505 | Cereal (Kashi Autumn Wheat) |
| | 57301510 | Cereal (Kashi GOLEAN) |
| | 57301511 | Cereal (Kashi GOLEAN Crunch) |
| | 57301512 | Cereal (Kashi GOLEAN Crunch Honey Almond Flax) |
| | 57301530 | Cereal (Kashi Heart to Heart Honey Toasted Oat) |
| | 57303100 | Cereal (General Mills Kix) |
| | 57303105 | Cereal (General Mills Honey Kix) |
| | 57303200 | Cereal (Kellogg's Krave) |
| | 57304100 | Cereal (Quaker Life) |

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| | 57305100 | Cereal (General Mills Lucky Charms) |
| | 57305150 | Cereal, frosted oat cereal with marshmallows |
| | 57305160 | Cereal (Malt-O-Meal Blueberry Muffin Tops) |
| | 57305165 | Cereal (Malt-O-Meal Cinnamon Toasters) |
| | 57305170 | Cereal (Malt-O-Meal Coco-Roos) |
| | 57305174 | Cereal (Malt-O-Meal Colossal Crunch) |
| | 57305175 | Cereal (Malt-O-Meal Cocoa Dyno-Bites) |
| | 57305180 | Cereal (Malt-O-Meal Corn Bursts) |
| | 57305200 | Cereal (Malt-O-Meal Crispy Rice) |
| | 57305210 | Cereal (Malt-O-Meal Frosted Flakes) |
| | 57305215 | Cereal (Malt-O-Meal Frosted Mini Spooners) |
| | 57305300 | Cereal (Malt-O-Meal Fruity Dyno-Bites) |
| | 57305400 | Cereal (Malt-O-Meal Honey Graham Squares) |
| | 57305500 | Cereal (Malt-O-Meal Honey Nut Toasty O's) |
| | 57305600 | Cereal (Malt-O-Meal Marshmallow Mateys) |
| | 57306130 | Cereal (Malt-O-Meal Raisin Bran) |
| | 57306500 | Cereal (Malt-O-Meal Golden Puffs) |
| | 57306800 | Cereal (Malt-O-Meal Tootie Fruities) |
| | 57308190 | Cereal, muesli |
| | 57308400 | Cereal (General Mills Cheerios Multigrain) |
| | 57309100 | Cereal (Nature Valley Granola) |
| | 57316300 | Cereal (Health Valley Oat Bran Flakes) |
| | 57316380 | Cereal (General Mills Cheerios Oat Cluster Crunch) |
| | 57316385 | Cereal (General Mills Cheerios Protein) |
| | 57316450 | Cereal (General Mills Oatmeal Crisp with Almonds) |
| | 57316710 | Cereal (Quaker Honey Graham Oh's) |
| | 57320500 | Cereal (Quaker Granola with Oats, Honey, and Raisins) |
| | 57321900 | Cereal (Nature's Path Organic Flax Plus) |
| | 57326000 | Cereal (Barbara's Puffins) |
| | 57327450 | Cereal (Quaker Toasted Oat Bran) |
| | 57327500 | Cereal (Quaker Oatmeal Squares) |
| | 57329000 | Cereal, raisin bran |
| | 57330000 | Cereal (Kellogg's Raisin Bran) |
| | 57330010 | Cereal (Kellogg's Raisin Bran Crunch) |
| | 57331000 | Cereal (Post Raisin Bran) |
| | 57332050 | Cereal (General Mills Total Raisin Bran) |
| | 57332100 | Cereal (General Mills Raisin Nut Bran) |
| | 57335550 | Cereal (General Mills Reese's Puffs) |
| | 57336000 | Cereal (General Mills Chex Rice) |
| | 57337000 | Cereal, rice flakes |
| | 57339000 | Cereal (Kellogg's Rice Krispies) |
| | 57339500 | Cereal (Kellogg's Rice Krispies Treats Cereal) |
| | 57341200 | Cereal (Kellogg's Smart Start Strong) |
| | 57341300 | Cereal (Kellogg's Smorz) |
| | 57344000 | Cereal (Kellogg's Special K) |
| | 57344001 | Cereal (Kellogg's Special K Blueberry) |
| | 57344005 | Cereal (Kellogg's Special K Chocolatey Delight) |
| | 57344007 | Cereal (Kellogg's Special K Low Fat Granola) |

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| | 57344010 | Cereal (Kellogg's Special K Red Berries) |
| | 57344015 | Cereal (Kellogg's Special K Fruit & Yogurt) |
| | 57344020 | Cereal (Kellogg's Special K Vanilla Almond) |
| | 57344025 | Cereal (Kellogg's Special K Cinnamon Pecan) |
| | 57347000 | Cereal (Kellogg's Corn Pops) |
| | 57348000 | Cereal, frosted corn flakes |
| | 57349000 | Cereal (Kellogg's Frosted Flakes) |
| | 57355000 | Cereal (Post Golden Crisp) |
| | 57406100 | Cereal (General Mills Total) |
| | 57407100 | Cereal (General Mills Trix) |
| | 57411000 | Cereal (General Mills Chex Wheat) |
| | 57416010 | Cereal, puffed wheat, sweetened |
| | 57418000 | Cereal (General Mills Wheaties) |
| 5b | RTE and cooked, low calorie, reduced calorie, sugar-free | |
| | Food code | Food description |
| | 56203510 | Oatmeal, reduced sugar, plain, no added fat |
| | 56203550 | Oatmeal, reduced sugar, flavored, NS as to fat |
| | 56203555 | Oatmeal, reduced sugar, flavored, no added fat |
| | 56203560 | Oatmeal, reduced sugar, flavored, fat added |
| | 57125010 | Cereal (General Mills 25% Less Sugar Cinnamon Toast Crunch) |
| | 57128005 | Cereal (General Mills 25% Less Sugar Cocoa Puffs) |
| | 57407110 | Cereal (General Mills 25% Less Sugar Trix) |
| 5d | Grain-free, no sugar, high protein RTE cereal | |
| | Food code | Food description |
| | 57206700 | Cereal (General Mills Fiber One) |
| | 57230000 | Cereal (Post Grape-Nuts) |
| | 57301500 | Cereal (Kashi 7 Whole Grain Puffs) |
| | 57307500 | Cereal, millet, puffed |
| | 57340000 | Cereal, puffed rice |
| | 57341000 | Cereal (Post Shredded Wheat'n Bran) |
| | 57408100 | Cereal (Uncle Sam) |
| | 57416000 | Cereal, puffed wheat, plain |
| | 57417000 | Cereal (Post Shredded Wheat) |
| 9 | Frozen dairy (ice cream, soft serve, and sorbet), low calorie, reduced calorie, sugar-free | |
| | Food code | Food description |
| | 13110000 | Ice cream, NFS |
| | 13110320 | Ice cream, no sugar added, flavors other than chocolate |
| | 13110330 | Ice cream, no sugar added, chocolate |
| | 13120740 | Ice cream cone, NFS |
| | 13121000 | Ice cream sundae, NFS |
| | 13130300 | Light ice cream, vanilla |
| | 13130310 | Light ice cream, chocolate |
| | 13130320 | Light ice cream, no sugar added, NS as to flavor |
| | 13130330 | Light ice cream, no sugar added, flavors other than chocolate |
| | 13130340 | Light ice cream, no sugar added, chocolate |
| | 13135000 | Light ice cream sandwich, vanilla |
| | 13135010 | Light ice cream sandwich, chocolate |
| | 13136000 | Ice cream sandwich, made with light, no sugar added ice cream |

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| | 13140000 | Light ice cream bar, vanilla |
| | 13140100 | Light ice cream bar, vanilla, chocolate coated |
| | 13140115 | Light ice cream bar, chocolate |
| | 13140575 | Light ice cream, no sugar added, cone, flavors other than chocolate |
| | 13140580 | Light ice cream, no sugar added, cone, chocolate |
| | 13142100 | Light ice cream cone, vanilla, prepackaged |
| | 13142110 | Light ice cream cone, chocolate, prepackaged |
| | 13160160 | Fat free ice cream, no sugar added, flavors other than chocolate |
| | 13161600 | Fudgesicle, light |
| | 13161630 | Light ice cream, bar or stick, with low-calorie sweetener, chocolate coated |
| 11 | Nutrition bars | |
| | Food code | Food description |
| | 53710800 | Cereal or granola bar (Kashi Chewy) |
| | 53710802 | Cereal or granola bar (Kashi Crunchy) |
| | 53720100 | Nutrition bar (Balance Original Bar) |
| | 53720200 | Nutrition bar (Clif Bar) |
| | 53720210 | Nutrition bar (Clif Kids Organic Zbar) |
| | 53720300 | Nutrition bar (PowerBar) |
| | 53720400 | Nutrition bar (Slim Fast Original Meal Bar) |
| | 53720500 | Nutrition bar (Snickers Marathon Protein Bar) |
| | 53720600 | Nutrition bar (South Beach Living Meal Bar) |
| | 53720610 | Nutrition bar (South Beach Living High Protein Bar) |
| | 53720700 | Nutrition bar (Tiger's Milk) |
| | 53720800 | Nutrition bar (Zone Perfect Classic Crunch) |
| | 53729000 | Nutrition bar or meal replacement bar, NFS |
| 16 | Ketchup and barbecue sauces | |
| | Food code | Food description |
| | 21304210 | Beef, shortribs, barbecued, with sauce, lean and fat eaten* |
| | 21304220 | Beef, shortribs, barbecued, with sauce, lean only eaten* |
| | 22701030 | Pork, spareribs, barbecued, with sauce, NS as to fat eaten* |
| | 22701040 | Pork, spareribs, barbecued, with sauce, lean and fat eaten* |
| | 22701050 | Pork, spareribs, barbecued, with sauce, lean only eaten* |
| | 24103070 | Chicken, NS as to part, grilled with sauce, NS as to skin eaten* |
| | 24103075 | Chicken, NS as to part, grilled with sauce, skin eaten* |
| | 24103080 | Chicken, NS as to part, grilled with sauce, skin not eaten* |
| | 24123310 | Chicken breast, grilled with sauce, skin eaten* |
| | 24123311 | Chicken breast, grilled with sauce, skin not eaten* |
| | 24134150 | Chicken leg, drumstick and thigh, grilled with sauce, skin eaten* |
| | 24134151 | Chicken leg, drumstick and thigh, grilled with sauce, skin not eaten* |
| | 24142510 | Chicken drumstick, grilled with sauce, skin eaten* |
| | 24142511 | Chicken drumstick, grilled with sauce, skin not eaten* |
| | 24154020 | Chicken thigh, grilled with sauce, skin eaten* |
| | 24154021 | Chicken thigh, grilled with sauce, skin not eaten* |
| | 24164010 | Chicken wing, grilled with sauce* |
| | 24168001 | Chicken "wings" with other sauces or seasoning, from fast food / restaurant* |
| | 24168011 | Chicken "wings" with other sauces or seasoning, from precooked* |
| | 24168021 | Chicken "wings" with other sauces or seasoning, from other sources* |
| | 24168030 | Chicken "wings", boneless, with hot sauce, from fast food / restaurant* |

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| | 24168031 | Chicken "wings", boneless, with hot sauce, from other sources* |
| | 24209000 | Turkey with barbecue sauce, skin eaten* |
| | 24209001 | Turkey with barbecue sauce, skin not eaten* |
| | 27111500 | Beef sloppy joe, no bun* |
| | 27116200 | Beef with barbecue sauce* |
| | 27116300 | Beef with sweet and sour sauce* |
| | 27120030 | Ham or pork with barbecue sauce* |
| | 27120060 | Sweet and sour pork* |
| | 27146011 | Chicken, shredded or pulled, with barbecue sauce* |
| | 27150170 | Sweet and sour shrimp* |
| | 27160010 | Meat with barbecue sauce, NS as to type of meat* |
| | 27315250 | Stuffed cabbage rolls with beef and rice* |
| | 27510145 | Cheeseburger, 1 miniature patty, with condiments, on miniature bun, from fast food / restaurant* |
| | 27510165 | Cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| | 27510170 | Cheeseburger (Burger King)* |
| | 27510171 | Whopper Jr with cheese (Burger King)* |
| | 27510175 | Cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant (Wendy's Jr. Cheeseburger Deluxe)* |
| | 27510205 | Cheeseburger, 1 small patty, with condiments, on white bun* |
| | 27510206 | Cheeseburger, 1 small patty, with condiments, on wheat bun* |
| | 27510207 | Cheeseburger, 1 small patty, with condiments, on whole wheat bun* |
| | 27510225 | Cheeseburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| | 27510251 | Cheeseburger, 1 medium patty, with condiments, on white bun* |
| | 27510252 | Cheeseburger, 1 medium patty, with condiments, on wheat bun* |
| | 27510253 | Cheeseburger, 1 medium patty, with condiments, on whole wheat bun* |
| | 27510266 | Cheeseburger, 1 large patty, with condiments, on bun, from fast food / restaurant* |
| | 27510276 | Bacon cheeseburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| | 27510312 | Bacon cheeseburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| | 27510341 | Bacon cheeseburger, 1 medium patty, with condiments, on white bun* |
| | 27510342 | Bacon cheeseburger, 1 medium patty, with condiments, on wheat bun* |
| | 27510343 | Bacon cheeseburger, 1 medium patty, with condiments, on whole wheat bun* |
| | 27510346 | Bacon cheeseburger, 1 large patty, with condiments, on bun, from fast food / restaurant* |
| | 27510376 | Double cheeseburger, 2 small patties, with condiments, on bun, from fast food / restaurant* |
| | 27510386 | Double cheeseburger (Burger King)* |
| | 27510406 | Double cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| | 27510431 | Double bacon cheeseburger, 2 small patties, with condiments, on bun, from fast food / restaurant (Burger King Bacon Double Cheeseburger)* |
| | 27510451 | Double bacon cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| | 27510465 | Double bacon cheeseburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Wendy's Baconator)* |
| | 27510475 | Double bacon cheeseburger, 2 large patties, with condiments, on bun, from fast food / restaurant* |

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| | 27510486 | Triple cheeseburger, 3 medium patties, with condiments, on bun, from fast food / restaurant* |
| | 27510506 | Hamburger, 1 miniature patty, with condiments, on miniature bun, from fast food / restaurant* |
| | 27510511 | Hamburger, 1 miniature patty, on miniature bun, from school* |
| | 27510536 | Hamburger, 1 small patty, with condiments, on bun, from fast food / restaurant* |
| | 27510551 | Hamburger (Burger King)* |
| | 27510552 | Whopper Jr (Burger King)* |
| | 27510555 | Hamburger, 1 small patty, with condiments, on bun, from fast food / restaurant (Wendy's Jr. Hamburger)* |
| | 27510565 | Hamburger, from school cafeteria* |
| | 27510585 | Hamburger, 1 small patty, with condiments, on white bun* |
| | 27510587 | Hamburger, 1 small patty, with condiments, on whole wheat bun* |
| | 27510606 | Hamburger, 1 medium patty, with condiments, on bun, from fast food / restaurant* |
| | 27510641 | Hamburger, 1 medium patty, with condiments, on white bun* |
| | 27510642 | Hamburger, 1 medium patty, with condiments, on wheat bun* |
| | 27510643 | Hamburger, 1 medium patty, with condiments, on whole wheat bun* |
| | 27510667 | Double hamburger, 2 small patties, with condiments, on bun, from fast food / restaurant* |
| | 27510676 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant* |
| | 27510681 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Burger King Double WHOPPER)* |
| | 27510682 | Double hamburger, 2 medium patties, with condiments, on bun, from fast food / restaurant (Wendy's 1/2 lb Double)* |
| | 27520500 | Pork sandwich, on white roll, with onions, dill pickles and barbecue sauce* |
| | 27520510 | Pork barbecue sandwich or Sloppy Joe, on bun* |
| | 27545010 | Turkey or chicken burger, with condiments, on bun, from fast food / restaurant* |
| | 27545200 | Turkey or chicken burger, with condiments, on white bun* |
| | 27545210 | Turkey or chicken burger, with condiments, on wheat bun* |
| | 27545220 | Turkey or chicken burger, with condiments, on whole wheat bun* |
| | 28110620 | Beef short ribs, boneless, with barbecue sauce, potatoes, vegetable, frozen meal* |
| | 28160650 | Stuffed green pepper, frozen meal* |
| | 74401010 | Ketchup |
| | 74406010 | Barbecue sauce |
| | 81308100 | Fry sauce* |
| 19 | Cranberries, dried | |
| | Food code | Food description |
| | 42500000 | Trail mix, NFS* |
| | 42501000 | Trail mix with nuts and fruit* |
| | 42501500 | Trail mix with chocolate* |
| | 42502100 | Trail mix with pretzels, cereal, or granola* |
| | 53710810 | Cereal or granola bar (KIND Fruit and Nut Bar)* |
| | 53713010 | Cereal or granola bar, fruit and nut* |
| | 62101000 | Fruit, dried, NFS, uncooked |
| | 62101050 | Fruit mixture, dried* |
| | 62109100 | Cranberries, dried |
| 20 | Jerky (meat or poultry based) | |
| | Food code | Food description |

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|---|---|---|
| | 21602100 | Beef jerky |
| | 22002800 | Pork jerky |
| | 23321900 | Venison/deer jerky |

* Only the component of the food (by weight) with existing or proposed use of allulose was included in the analysis
** Non-reconstituted dry powder was adjusted to the reconstituted/prepared amount

## Question #12 Attachment

Literature search documentation
Allulose GRAS
Last search conducted 9/1/23
Dates limited from 1/1/20 to current (9/1/23)
150 total results after deduplication (combination of PubMed and Embase searches below)

**PubMed:**

(Allulose OR “DL-Psicose” OR Psicose OR 23140-52-5[rn])
AND
(safe OR safety OR toxic OR toxicity OR NOAEL OR LD50 OR "consumer product safety"[MeSH Terms] OR “Toxicity Tests”[MeSH Terms] OR “body weight” OR “weight gain” OR “mortality rate” OR microbiota OR microbial OR microflora OR intestinal OR digest* OR liver OR absorption OR distribution OR metabolism OR excretion OR ADME[tiab] OR allergy OR allergen OR allergenicity OR allergic OR allergens[MeSH Terms] OR sensitiz* OR "hypersensitivity"[MeSH Terms] OR "hypersensitivity"[All Fields] OR "allergy and immunology"[MeSH Terms] OR atopic[All Fields] OR LLNA OR “Local Lymph Node Assay”[MeSH Terms] OR “Local Lymph Node Assay” OR (toxicity AND (development OR developmental OR reproductive)) OR “Teratogenesis”[MeSH Terms] OR teratogen OR teratogenic OR “Reproductive and Urinary Physiological Phenomena”[MeSH Terms] OR neoplastic OR cancer OR carcinogen* OR carcinoma OR tumor OR tumors OR “animal bioassay” OR oncogenic* OR malignant OR malignancy OR malignancies OR genotoxic OR genotoxicity OR clastogen* OR mutagen OR mutagenic OR mutation* OR “cytogenetic aberration” OR "chromosome aberrations"[MeSH Terms] OR micronucle* OR “DNA damage” OR “DNA fragmentation”[Mesh] OR “Mutagenicity Tests”[MeSH Terms] OR “comet assay”)

Results = 354
Results (limited from 2020 – current) = 116

**Embase:**

(allulose OR 'psicose'/exp OR psicose OR 23140-52-5:rn)
AND
('risk assessment'/exp OR 'safety'/exp OR 'toxic substance'/exp OR 'toxicity'/exp OR 'ld50'/exp OR 'lc50'/exp OR 'product safety'/exp OR 'toxicity testing'/exp OR 'drug toxicity'/exp OR 'toxicity assay'/exp OR 'adverse drug reaction'/exp OR 'pharmacokinetics'/exp OR 'metabolism'/exp OR 'excretion'/exp OR 'hypersensitivity'/exp OR 'allergen'/exp OR 'sensitization'/exp OR 'local lymph node assay'/exp OR 'developmental toxicity'/exp OR 'reproductive toxicity'/exp OR 'teratogenicity'/exp OR 'teratogenic agent'/exp OR 'teratogenesis'/exp OR 'malignant neoplasm'/exp OR 'carcinogen'/exp OR 'oncogenesis and malignant transformation'/exp OR 'carcinoma'/exp OR 'genotoxicity'/exp OR 'genotoxicity assay'/exp OR 'mutagenesis'/exp OR 'chromosome aberration'/exp OR 'genetic damage'/exp OR 'mutagenic agent'/exp)

Results = 351
Results (limited from 2020 – current) = 107

| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2023 | S. Wulansari, S. Heng, P. Ketbot, S. Baramee, R. Waeonukul, P. Pason, K. Ratanakhanokchai, A. Uke, A. Kosugi and C. Tachaapaikoon | A Novel D-Psicose 3-Epimerase from Halophilic, Anaerobic Iocasia fonsfrigidae and Its Application in Coconut Water | Int J Mol Sci | 10.3390/ijms24076394 |
| 2023 | K. Fukunaga, T. Yoshimura, H. Imachi, T. Kobayashi, T. Saheki, S. Sato, N. Saheki, W. Jiang and K. Murao | A Pilot Study on the Efficacy of a Diabetic Diet Containing the Rare Sugar D-Allulose in Patients with Type 2 Diabetes Mellitus: A Prospective, Randomized, Single-Blind, Crossover Study | Nutrients | 10.3390/nu15122802 |
| 2023 | S. Duan, Y. Chen, G. Wang, Z. Li, S. Dong, Y. Wu, Y. Wang, C. Ma and R. Wang | A study of targeted mutation of l-rhamnose isomerase to improve the conversion efficiency of D-allose | Enzyme Microb Technol | 10.1016/j.enzmictec.2023.110259 |
| 2023 | T. Yuma, M. Tokuda, N. Nishimoto, H. Yokoi and K. Izumori | Allulose for the attenuation of postprandial blood glucose levels in healthy humans: A systematic review and meta-analysis | PLoS ONE | 10.1371/journal.pone.0281150 |
| 2023 | Y. Gao, F. Li, Y. Wang, Z. Chen and Z. Li | An artificial multienzyme cascade for the whole-cell synthesis of rare ketoses from glycerol | Biotechnol Lett | 10.1007/s10529-023-03415-6 |
| 2023 | H. Samreen and S. Dhaneshwar | Artificial Sweeteners: Perceptions and Realities | Current Diabetes Reviews | 10.2174/1573399818666220429083052 |
| 2023 | M. Akiyama, T. Akiyama, D. Saigusa, E. Hishinuma, N. Matsukawa, T. Shibata, H. Tsuchiya, A. Mori, Y. Fujii, Y. Mogami, C. Tokorodani, K. Kuwahara, Y. Numata-Uematsu, K. Inoue and K. Kobayashi | Comprehensive study of metabolic changes induced by a ketogenic diet therapy using GC/MS- and LC/MS-based metabolomics | Seizure | 10.1016/j.seizure.2023.03.014 |
| 2023 | A. Sclafani, A. Castillo, I. Carata, R. Pines, E. Berglas, S. Joseph, J. Sarker, M. Nashed, M. Roland, S. Arzayus, N. Williams, J. I. Glendinning and R. J. Bodnar | Conditioned preference and avoidance induced in mice by the rare sugars isomaltulose and allulose | Physiol Behav | 10.1016/j.physbeh.2023.114221 |

| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2023 | M. Yamazaki, M. Okito, A. Harada, K. Miyake, T. Tamiya and T. Nakamura | d-Allulose Supplementation Prevents Diet-Induced Hepatic Lipid Accumulation via miR-130-Mediated Regulation in C57BL/6 Mice | Molecular nutrition & food research | 10.1002/mnfr.202200748 |
| 2023 | L. Stefanie, M. Sophie, W. Judith, L. Ilona and P. Püschel Gerhard | Different impact of the ketoses fructose and allulose on hepatocyte glucose metabolism | Zeitschrift fur Gastroenterologie | 10.1055/s-0042-1759987 |
| 2023 | H. Pullmann-Lindsley, A. Bartlett-Miller and R. J. Pitts | Diols and sugar substitutes in attractive toxic sugar baits targeting Aedes aegypti and Aedes albopictus (Diptera: Culicidae) mosquitoes | | 10.1101/2023.02.09.527878 |
| 2023 | Y. Kohara, S. Ikai, A. Yoshihara, K. Murao and Y. Sugiyama | Effect of chronic exposure to ketohexoses on pancreatic β-cell function in INS-1 rat insulinoma cells | Bioscience, biotechnology, and biochemistry | 10.1093/bbb/zbac190 |
| 2023 | J. Tak, M. Bok, H. Rho, J. H. Park, Y. Lim, S. Chon and H. Lim | Effect of diabetes-specific oral nutritional supplements with allulose on weight and glycemic profiles in overweight or obese type 2 diabetic patients | Nutr Res Pract | 10.4162/nrp.2023.17.2.241 |
| 2023 | F. Teysseire, V. Bordier, A. Budzinska, N. Weltens, C. Beglinger, L. Van Oudenhove, B. K. Wölnerhanssen and A. Meyer Gerspach | Efficacy and safety of acute administration of D-allulose and erythritol in healthy participants | Obesity Facts | 10.1159/000530456 |
| 2023 | H. Zhang, A. Zhao, L. Qu, W. Xiong, M. A. Alam, J. Miao, W. Wang, J. Xu and Y. Lv | Engineering an efficient whole-cell catalyst for d-allulose production from glycerol | Biotechnology Journal | 10.1002/biot.202200600 |

| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2023 | L. Wang, K. Chen, P. Zheng, X. Huo, F. Liao, L. Zhu, M. Hu and Y. Tao | Enhanced production of D-psicose from D-fructose by a redox-driven multi-enzyme cascade system | Enzyme and Microbial Technology | 10.1016/j.enzmictec.2022.110172 |
| 2023 | K. D. Medak, A. J. Weber, H. Shamshoum, G. L. McKie, M. K. Hahn and D. C. Wright | Enhancing endogenous levels of GLP1 dampens acute olanzapine induced perturbations in lipid and glucose metabolism | Frontiers in Pharmacology | 10.3389/fphar.2023.1127634 |
| 2023 | Y. Chen, Y. Chen, D. Ming, L. Zhu and L. Jiang | Highly efficiency production of D-allulose from inulin using curli fiber multi-enzyme cascade catalysis | International Journal of Biological Macromolecules | 10.1016/j.ijbiomac.2023.124468 |
| 2023 | Y. Gao, Z. Chen, H. Nakanishi and Z. Li | Highly Efficient Synthesis of Rare Sugars from Glycerol in Endotoxin-Free ClearColi by Fermentation | Foods | 10.3390/foods12163078 |
| 2023 | K. Kishida, T. Iida, T. Yamada and Y. Toyoda | Intestinal absorption of D-fructose isomers, D-allulose, D-sorbose, and D-tagatose, via glucose transporter type 5 (GLUT5) but not sodium-dependent glucose cotransporter 1 (SGLT1) in rats | British Journal of Nutrition | 10.1017/S0007114523001113 |
| 2023 | Y. Guo, Z. Zhu, J. Lv, Y. Li, J. Chen, X. Cheng, N. Li and J. Liu | Irreversible biosynthesis of D-allulose from D-glucose in Escherichia coli through fine-tuning of carbon flux and cofactor regeneration engineering | Journal of the science of food and agriculture | 10.1002/jsfa.12623 |
| 2023 | J. Li, Q. Dai, Y. Zhu, W. Xu, W. Zhang, Y. Chen and W. Mu | Low-calorie bulk sweeteners: Recent advances in physical benefits, applications, and bioproduction | Critical reviews in food science and nutrition | 10.1080/10408398.2023.2171362 |

| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2023 | F. Teysseire, V. Bordier, A. Budzinska, L. Van Oudenhove, N. Weltens, C. Beglinger, B. K. Wölnerhanssen and A. C. Meyer-Gerspach | Metabolic Effects and Safety Aspects of Acute D-allulose and Erythritol Administration in Healthy Subjects | Nutrients | 10.3390/nu15020458 |
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| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2021 | C. Li, L. Li, Z. Feng, L. Guan, F. Lu and H. M. Qin | Two-step biosynthesis of D-allulose via a multienzyme cascade for the bioconversion of fruit juices | Food Chemistry | 10.1016/j.foodchem.2021.129746 |
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| 2020 | Y. Han, E. Y. Kwon and M. S. Choi | Anti-Diabetic Effects of Allulose in Diet-Induced Obese Mice via Regulation of mRNA Expression and Alteration of the Microbiome Composition | Nutrients | 10.3390/nu12072113 |
| 2020 | A. Trincone | Application-Oriented Marine Isomerases in Biocatalysis | Mar Drugs | 10.3390/md18110580 |
| 2020 | Y. Wang, Y. Ravikumar, G. Zhang, J. Yun, Y. Zhang, A. Parvez, X. Qi and W. Sun | Biocatalytic Synthesis of D-Allulose Using Novel D-Tagatose 3-Epimerase From Christensenella minuta | Front Chem | 10.3389/fchem.2020.622325 |
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| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2020 | A. Kanasaki, T. Iida, K. Murao, B. Shirouchi and M. Sato | d-Allulose enhances uptake of HDL-cholesterol into rat's primary hepatocyte via SR-B1 | Cytotechnology | 10.1007/s10616-020-00378-8 |
| 2020 | C. R. Braunstein, J. C. Noronha, T. A. Khan, S. B. Mejia, T. M. Wolever, R. G. Josse, C. W. Kendall and J. L. Sievenpiper | Effect of fructose and its epimers on postprandial carbohydrate metabolism: A systematic review and meta-analysis | Clinical Nutrition | 10.1016/j.clnu.2020.03.002 |
| 2020 | I. S. Surono, A. A. Wardana, P. Waspodo, B. Saksono, J. Verhoeven and K. Venema | Effect of functional food ingredients on gut microbiota in a rodent diabetes model | Nutr Metab (Lond) | 10.1186/s12986-020-00496-2 |
| 2020 | J. E. Nijesh, R. Srudhy and P. E. Chaly | Effect of various sweeteners on cariogenicity features ostreptococcus mutans: In-vitro study | Medico-Legal Update | 10.37506/mlu.v20i4.2189 |
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| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2020 | S. R. Dedania, V. K. Patel, S. S. Soni and D. H. Patel | Immobilization of Agrobacterium tumefaciens D-psicose 3-epimerase onto titanium dioxide for bioconversion of rare sugar | Enzyme and Microbial Technology | 10.1016/j.enzmictec.2020.109605 |
| 2020 | S. J. Lee, W. K. Yu, H. R. Park, H. Kim, J. H. Kim, J. Park and K. S. Shin | Improved effect of palatinose syrup bioconverted from sucrose on hyperglycemia and regulation of hepatic lipogenesis in male C57BL/6J mice | Journal of food biochemistry | 10.1111/jfbc.13201 |
| 2020 | S. Moon, Y. H. Kim and K. Choi | Inhibition of 3T3-L1 Adipocyte Differentiation by D-allulose | Biotechnology and Bioprocess Engineering | 10.1007/s12257-019-0352-7 |
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| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2020 | C. Li, L. Gao, K. Du, H. Lin, Y. Ren, J. Lin and J. Lin | Production of D-allose from D-fructose using immobilized L-rhamnose isomerase and D-psicose 3-epimerase | Bioprocess Biosyst Eng | 10.1007/s00449-019-02262-y |
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| 2020 | S. Jiang, W. Xiao, X. Zhu, P. Yang, Z. Zheng, S. Lu, S. Jiang, G. Zhang and J. Liu | Review on D-Allulose: In vivo Metabolism, Catalytic Mechanism, Engineering Strain Construction, Bio-Production Technology | Front Bioeng Biotechnol | 10.3389/fbioe.2020.00026 |
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| 2020 | J. Franceus and T. Desmet | Sucrose phosphorylase and related enzymes in glycoside hydrolase family 13: Discovery, application and engineering | International Journal of Molecular Sciences | 10.3390/ijms21072526 |
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| Year | Author | Title | Journal | DOI |
|---|---|---|---|---|
| 2020 | Y. Liu, J. Liu, A. Abozeid, K. X. Wu, X. R. Guo, L. Q. Mu and Z. H. Tang | UV-B radiation largely promoted the transformation of primary metabolites to phenols in Astragalus mongholicus seedlings | Biomolecules | 10.3390/biom10040504 |

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|---|---|
| **From:** | Kolberg, Lore |
| **To:** | Hice, Stephanie |
| **Subject:** | [EXTERNAL] Re: GRN 001057 - Questions for Notifier_Addendum to Notifier response |
| **Date:** | Thursday, September 28, 2023 12:29:49 PM |
| **Attachments:** | image009.png<br>image011.png<br>image012.png<br>image013.png<br>image014.png<br>image015.png<br>image016.png<br>image017.png<br>image018.png<br>image019.png<br>image020.png<br>image021.png<br>image022.png<br>image023.png<br>image002.png<br>2023 Tate & Lyle_GRAS statement_GENSWEET IGI-VHF 27SEP2023.pdf |

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Dear Dr. Hice,

The attached document is intended as an addendum to Tate & Lyle's response to question #3 regarding GRN 1057. We received this document yesterday from the supplier of the glucoisomerase.
The document includes an expert opinion statement regarding the GRAS status of the enzyme and thus provides additional rationale for the supplier's GRAS statement, which we shared with you previously.
The supplier has given us permission to share the attached document.

Best regards,
Lore

**Lore Kolberg**
**Director, Regulatory & Scientific Affairs**
Innovation and Commercial Development
Tate & Lyle
Mob. +1 224 355 9013

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**From:** Don Schmitt <dschmitt@toxstrategies.com>
**Sent:** Friday, September 15, 2023 4:53 PM
**To:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Cc:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Subject:** Re: [EXTERNAL] Re: GRN 001057 - Questions for Notifier

Hi Stephanie,

Attached are Tate & Lyle's responses to FDA's questions regarding GRN 1057.

Sincerely,

Don

Donald F. Schmitt, M.P.H.
Senior Managing Scientist


ToxStrategies

739 Thornapple Drive
Naperville, IL 60540
phone: 630.352.0303
email: dschmitt@toxstrategies.com



---

**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Date:** Wednesday, August 23, 2023 at 1:07 PM
**To:** Don Schmitt <dschmitt@toxstrategies.com>

**Cc:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Subject:** RE: [EXTERNAL] Re: GRN 001057 - Questions for Notifier



Dear Mr. Schmitt,

Thank you for the update. Yes, an extension until September 15, 2023, is fine.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)

---

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We are working on responses to the list of questions you provided on August 14. One of the questions requires that the intake assessment be revised and this will take Exponent a few weeks to complete, given their previous commitments. Therefore, Tate & Lyle is requesting a 3-week extension of the time to reply to all 12 questions. That would be Friday, September 15.

Thank you for considering this extension request.

Best regards,

Don

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Senior Managing Scientist

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**Date:** Monday, August 14, 2023 at 8:07 AM
**To:** Don Schmitt <dschmitt@toxstrategies.com>
**Subject:** GRN 001057 - Questions for Notifier



Dear Mr. Schmitt,

During our evaluation of GRAS Notice No. 001057, we noted questions that need to be addressed and are attached to this email.

We respectfully request a response within **10 business days**. If you are unable to complete the response within that time frame, please contact me to discuss further options. Please do not include any confidential information in your response.

If you have questions or need further clarification, please feel free to contact me. Thank you in advance for your attention to our comments.

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|---|---|
| **From:** | Kolberg, Lore |
| **To:** | Hice, Stephanie |
| **Subject:** | [EXTERNAL] GRN 1057 glucoisomerase |
| **Date:** | Tuesday, October 3, 2023 3:56:44 PM |
| **Attachments:** | image001.png<br>image004.png<br>image005.png<br>image006.png<br>image007.png<br>image008.png<br>image003.png<br>2023_GRAS Statement_GENSWEET IGI-VHF_A10022.pdf |

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Dear Stiffy,

IFF responded regarding my request for the GRAS Expert Opinion document, in a version not marked Confidential. They will not/cannot share the GRAS Expert Opinion with us except the version I shared with you that's marked Confidential. The only related document they could share as non-Confidential is the attached GRAS statement.

I hope you can use the attached document. Please let me know if there are other issues.
Best regards,
Lore

**Lore Kolberg**
**Director, Regulatory & Scientific Affairs**
Innovation and Commercial Development
Tate & Lyle
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stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)


Date: August 17, 2023

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& creativity meet

## GRAS STATEMENT

RE: **GENSWEET® IGI-VHF** (A10022)[i]

To Whom It May Concern,

**GENSWEET® IGI-VHF** consists of consists of glucose isomerase (also known as xylose isomerase) produced using a *Streptomyces rubiginosus* production strain that has been genetically engineered. The glucose isomerase protein is not protein engineered. The glucose isomerase enzyme is not a genetically modified organism (GMO).

**GENSWEET® IGI-VHF** is Generally Recognized as Safe (GRAS) for use as processing aid in High Fructose Corn Syrup (HFCS) manufacture when the enzyme product is used within the product dose guidelines described in IFF's product literature. The glucose isomerase enzyme produced with *Streptomyces rubiginosus* is affirmed to be Generally Recognized as Safe ('GRAS'), under 21 CFR 184.1372.

**GENSWEET® IGI-VHF** also meets or exceeds the Joint FAO/WHO Expert Committee on Food Additives (JECFA)/Food Chemical Codex (FCC) specifications for microbial and metal contaminants in food enzymes.

IFF is committed to help our customers maximize the benefits of our technology, and we want to ensure successful use and safety of our products. Please contact your account manager if you should have further questions.

IFF Health & Biosciences

**Health & Biosciences**
200 Powder Mill Road
Wilmington, DE 19803
**T** +1.302.332.8420
**iff.com**

Liane Grieco
Global Regulatory Affairs
Global Regulatory Strategy Leader, Grain Processing
liane.m.grieco@iff.com

*This certificate is valid for one year from date of issue.*

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| | |
|---|---|
| **From:** | Kolberg, Lore |
| **To:** | Hice, Stephanie |
| **Cc:** | Santa Maria, Juan Cristian |
| **Subject:** | [EXTERNAL] GRN 001057 - Questions for Notifier |
| **Date:** | Friday, October 13, 2023 1:53:52 PM |
| **Attachments:** | image007.png<br>image009.png<br>image010.png<br>image011.png<br>image012.png<br>image013.png<br>image014.png<br>image015.png<br>image016.png<br>image017.png<br>image018.png<br>image019.png<br>image002.png<br>GRN 001057 - questions for notifier and responses to FDA 101323.pdf |



Dear Stephanie,

Attached are Tate & Lyle's responses to FDA's additional questions regarding GRN 1057.

Sincerely,
Lore

**Lore Kolberg**
**Director, Regulatory & Scientific Affairs**
Innovation and Commercial Development
Tate & Lyle
Mob. +1 224 355 9013

TATE & LYLE
Science \ Solutions \ Society

**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Sent:** Wednesday, October 4, 2023 2:51 PM
**To:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Subject:** [EXTERNAL] GRN 001057 - Questions for Notifier

Dear Lore,

During our evaluation of GRAS Notice No. 001057, we noted additional questions that need to be addressed and are below.

1. In the September 15, 2023, amendment (response to question 9), the notifier provides a revised copy of Table 6, with the specifications for mold listed as "≤10 CFU/g" and states that the revised specifications align with the COAs presented in Appendix B of the notice. On pages 58-59, the units for mold for "Dolcia Prima DS" is listed as "CFU/10 g", while on page 60 it is listed as "CFU/g". For the administrative record, please confirm the units and specification for mold for crystalline allulose.

2. In the September 15, 2023, amendment (response to question 11), the notifier provides a revised cumulative eaters-only dietary exposure to D-psicose of 14.5 g/person (p)/d at the mean and 29 g/p/d at the pseudo 90$^{th}$ percentile (Table 3), based on the summation of the following:

   The *per capita* mean estimate from background sources (reported as the cumulative *per capita* mean estimate in Table 1 of the January 19, 2023, amendment to GRN 001024), and the *per capita* mean estimate from the proposed uses in GRN 001057 (reported in Table 2 of the September 15, 2023, amendment).

   The notifier further notes that the resulting cumulative *per capita* mean estimate is divided by the percent eaters (77%) to derive the revised cumulative eaters-only mean estimate of 14.5 g/p/d and that the revised cumulative eaters-only pseudo 90$^{th}$ percentile estimate of 29 g/p/d is derived by multiplying the eaters-only mean estimate by 2.

   Please provide revised cumulative estimates derived using a fraction of eaters of any or all the foods in which D-psicose is used calculated based on the percent eaters reported in both GRN 001024 (77% eaters) and GRN 001057 (62.3% eaters). Information on how to calculate the fraction of eaters is available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-estimating-dietary-intake-substances-food.

We respectfully request a response within **10 business days**. If you are unable to complete the response within that time frame, please contact me to discuss further options. Please do not include any confidential information in your response.

If you have questions or need further clarification, please feel free to contact me. Thank you in advance for your attention to our comments.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
*Regulatory Review Scientist & Microbiology Reviewer*

**Division of Food Ingredients**
**Office of Food Additive Safety**
**Center for Food Safety and Applied Nutrition**
**U.S. Food and Drug Administration**
stephanie.hice@fda.hhs.gov

Pronouns: They-Them-Their (what is this?)


October 13, 2023

**GRN 1057 Questions for Notifier and Notifier Responses**

1. In the September 15, 2023, amendment (response to question 9), the notifier provides a revised copy of Table 6, with the specifications for mold listed as "≤10 CFU/g" and states that the revised specifications align with the COAs presented in Appendix B of the notice. On pages 58-59, the units for mold for "Dolcia Prima DS" is listed as "CFU/10 g", while on page 60 it is listed as "CFU/g". For the administrative record, please confirm the units and specification for mold for crystalline allulose.

**Response**:

The correct unit of measure in the specification and analyses for mold for DS (crystalline) allulose is CFU/g.

There was a typo in two of the original COAs that were submitted for crystalline allulose, for sample numbers LO19F90351 and LO18J90596, in which the unit of measure for mold was erroneously reported as CFU/10g. The results for mold in all three sample lots of crystalline allulose should have been reported as CFU/g, as shown in revised Table 6.

Revised Table 6 (below, which we submitted in our September 15 response to questions) contains the correct units of measure and specification for mold for crystalline allulose.

***Table 6. Analytical results for three non-consecutive lots of crystalline allulose***

| Specification | | Lot No. LO18J90596 | Lot No. LO19F90351 | Lot No. LO18J90294 |
|---|---|---|---|---|
| Allulose (%, dry basis) | >99.1 | 99.4 | 99.8 | 99.2 |
| Total non-allulose saccharides (%) | <0.9 | 0.27 | 0.06 | 0.29 |
| Moisture (%) | <0.5 | 0.14 | 0.12 | 0.10 |
| Ash (%) | <0.5 | <0.1 | <0.1 | <0.1 |
| Sulfur dioxide (ppm) | <10 | <10 | <10 | <10 |
| Total plate count | ≤200 cfu/g | <10 | 10 | 10 |
| Yeast | ≤10 cfu/g | <10 | 10 | <10 |
| Mold | ≤10 cfu/g | <10 | 10 | <10 |
| Arsenic (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Cadmium (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Lead (ppm) | <0.1 | <0.005 | <0.005 | <0.005 |
| Mercury (ppm) | <0.01 | <0.005 | <0.005 | <0.005 |

Likewise, in Table 4 of our original submission there was a typo in the unit of measure for mold in the specifications for crystalline allulose (Crystalline Granules). Table 4 should read as corrected below.

**Table 4. Specifications for allulose**

| Parameter | Liquid Syrup | Crystalline Granules |
|---|---|---|
| Mold | ≤ 10 CFU/10g | ≤ 10 CFU/g |

2. In the September 15, 2023, amendment (response to question 11), the notifier provides a revised cumulative eaters-only dietary exposure to D-psicose of 14.5 g/person (p)/d at the mean and 29 g/p/d at the pseudo 90$^{th}$ percentile (Table 3), based on the summation of the following:

   The *per capita* mean estimate from background sources (reported as the cumulative *per capita* mean estimate in Table 1 of the January 19, 2023, amendment to GRN 001024), and the *per capita* mean estimate from the proposed uses in GRN 001057 (reported in Table 2 of the September 15, 2023, amendment).

   The notifier further notes that the resulting cumulative *per capita* mean estimate is divided by the percent eaters (77%) to derive the revised cumulative eaters-only mean estimate of 14.5 g/p/d and that the revised cumulative eaters-only pseudo 90$^{th}$ percentile estimate of 29 g/p/d is derived by multiplying the eaters-only mean estimate by 2.

   Please provide revised cumulative estimates derived using a fraction of eaters of any or all the foods in which D-psicose is used calculated based on the percent eaters reported in both GRN 001024 (77% eaters) and GRN 001057 (62.3% eaters). Information on how to calculate the fraction of eaters is available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-estimating-dietary-intake-substances-food.

**Response**:

Revised Table 3 is below.

**Revised Table 3. CEDI of allulose from background uses and Tate and Lyle's proposed uses by the U.S. 2+ y and subpopulations (g/day); NHANES 2017-2018**

| Sub-population | Background EDI (g/day) (GRN 001024) | | EDI (g/day) from Proposed Uses GRN 001057 | | Cumulative Estimated Daily Intake (g/day) | | | |
|---|---|---|---|---|---|---|---|---|
| | % Users | Mean per capita | %Users | Mean per capita | % Users*** | Mean per capita | Mean per user* | Pseudo 90$^{th}$** Per user |
| US 2+ y | 77.0 | 7.8 | 62.3 | 3.4 | 91.33 | 11.2 | 12.3 | 24.5 |
| 2-12 y | 70.5 | 4.2 | 77.1 | 3.3 | 93.24 | 7.5 | 8.0 | 16.1 |
| 13-18 y | 62.9 | 3.6 | 64.3 | 3.3 | 86.76 | 6.9 | 8.0 | 15.9 |
| 19+ y | 81.2 | 8.9 | 59.4 | 3.4 | 92.37 | 12.3 | 13.3 | 26.6 |

* Mean per capita divided by % users to derive mean per user
** Pseudo 90$^{th}$ is derived based on 2 x mean (FDA 2006 guidance)[1]
***calculated per FDA 2006 Guidance

| | |
|---|---|
| **From:** | Santa Maria, Juan Cristian |
| **To:** | Hice, Stephanie |
| **Subject:** | [EXTERNAL] RE: GRN 001057 - Questions for Notifier |
| **Date:** | Thursday, December 7, 2023 2:15:21 PM |
| **Attachments:** | image007.png<br>image009.png<br>image010.png<br>image011.png<br>image012.png<br>image013.png<br>image014.png<br>image015.png<br>image016.png<br>image017.png<br>image018.png<br>image019.png<br>image001.png |

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Dear Mrs. Hice,

I hope this message finds you well. Please be aware that Lore Kolberg retired on November 1st. I am therefore responding on behalf of Tate & Lyle to your message below. You can direct any subsequent communication related to GRN 1057 directly to me.

In response to your questions:

1. I hereby confirm the intended use of D-psicose does not include use in infant formula.
2. I hereby confirm Tate & Lyle concurs with FDA's approach to estimating the dietary exposure to allulose and the resulting estimate of 24.0 g/p/d.

Please do not hesitate to contact me should you need any additional information.

Kind regards,

Juan Cristián

**Juan Cristián Santa María**
**Senior Director, Global Regulatory & Scientific Affairs**
Innovation and Commercial Development
Tate & Lyle
Mob. +1 (470) 373-7122


External use permitted

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**From:** Hice, Stephanie <Stephanie.Hice@fda.hhs.gov>
**Sent:** Thursday, December 7, 2023 9:59 AM
**To:** Kolberg, Lore <lore.kolberg@tateandlyle.com>
**Cc:** Santa Maria, Juan Cristian <JuanCristian.SantaMaria@tateandlyle.com>
**Subject:** [EXTERNAL] GRN 001057 - Questions for Notifier

Dear Lore,

During our evaluation of GRAS Notice No. 001057, we noted additional questions that need to be addressed and are below. For your awareness, I received an automated undeliverable message when transmitting question one on Tuesday, December 5, 2023, and Wednesday, December 6, 2023. As such, I've CC'd your colleague, who you included on your last correspondence to us, dated October 13, 2023.

1. For the administrative record, please state whether the intended use of D-psicose includes use in infant formula.

2. In the amendment dated October 13, 2023, we note that the notifier's cumulative mean "per capita" dietary exposure to allulose was obtained by summing the mean per capita dietary exposures from GRN 001024 (background) and GRN 001057 (intended uses). This exposure was then converted to an "eaters-only" mean dietary exposure by dividing the calculated percent (%) eaters of at least one food containing allulose. The cumulative eaters-only dietary exposure of 24.5 g/person (p)/d at the pseudo-90$^{th}$ percentile was obtained by multiplying the cumulative eaters-only mean dietary exposure to allulose by two.

   We have independently confirmed the notifier's dietary exposure estimate using a method described in FDA's Guidance for Industry: Estimating Dietary Intake of Substances in Food (2006)**.** Unlike in the notifier's approach, we estimated the cumulative total sample mean (cumulative mean per capita) dietary exposure to allulose by multiplying the eaters-only mean dietary exposures from GRN 001024 (background) and GRN 001057 (intended uses) by the corresponding percent (%) eaters and summing the resulting total sample mean dietary exposures. The cumulative eaters-only mean dietary exposure to allulose was obtained by dividing the cumulative total sample mean dietary exposure by the calculated percent (%) eaters of at least one food containing allulose. The cumulative eaters-only dietary exposure of 24.0 g/p/d at the pseudo-90$^{th}$ percentile was obtained by multiplying the cumulative eaters-only mean dietary exposure by two. We note that our estimate is slightly lower than your estimate of 24.5 g/p/d.

   For the administrative record, we request that the notifier please confirm that they concur with our approach to estimating the dietary exposure to allulose and the resulting estimate of 24.0 g/p/d.

FDA's Guidance for Industry: Estimating Dietary Intake of Substances in Food, 2006. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-estimating-dietary-intake-substances-food

We respectfully request a response within **10 business days**. If you are unable to complete the response within that time frame, please contact me to discuss further options. Please do not include any confidential information in your response.

If you have questions or need further clarification, please feel free to contact me. Thank you in advance for your attention to our comments.

Sincerely,

Stiffy Hice

**Stephanie (Stiffy) Hice, Ph.D. (they/them/their)**
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