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June 5, 2018

Dr. Dennis Keefe
Director, Division of Biotechnology and GRAS Notice Review
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Subject: GRAS Notification – Erythritol

Dear Dr. Keefe:

On behalf of Cargill, Incorporated, 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, erythritol, 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.

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,

(b) (6)

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

GRAS Determination of Erythritol for Use in Human Food

JUNE 5, 2018

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GRAS Determination of Erythritol for Use in Human Food

SUBMITTED BY:

Cargill, Incorporated
15407 McGinty Road West
Wayzata, MN 55391

SUBMITTED TO:

U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
HFS-200
5100 Paint Branch Parkway
College Park MD 20740-3835

CONTACT FOR TECHNICAL OR OTHER INFORMATION

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JUNE 5, 2018

2

Table of Contents

Appendix D. Human Intake Assessment

Exhibit I. Report of the Expert Panel

4

List of Acronyms

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, and excretion
ANVISA	National Agency of Sanitary Surveillance
CAS	Chemical Abstract Service
CDC	Center for Disease Control
CFR	Code of Federal Regulations
cGMP	current Good Manufacturing Practices
CHL/IU	Chinese hamster fibroblast cells
CSF	Continuing Survey of Food Intakes by Individuals
EFSA	European Food Safety Authority
FAO	Food and Agriculture Organization
FCC	Food Chemicals Codex
FDA	U.S. Food and Drug Administration
FD&C	Federal Food Drug and Cosmetic Act
FSIS	Food Safety and Inspection Service
GI	gastrointestinal
GMP	Good Manufacturing Practices
GRAS	Generally Recognized as Safe
GRN	GRAS notification
JECFA	Joint FAO/WHO Expert Committee on Food Additives
NHANES	National Health and Nutrition Examination Survey
NLT	not less than
NMT	not more than
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
PZ	Pal Sweet Calorie Zero
SCF	European Commission Scientific Committee for Food
SCOGS	Select Committee on GRAS Substances
STZ	streptozotocin
USDA	United States Department of Agriculture
U.S.C.	United States Code
WHO	World Health Organization

5

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

(1) GRAS Notice Submission

Cargill, Incorporated (Cargill), 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 erythritol in human food.

(2) Name and Address

Cargill, Incorporated
15407 McGinty Road
Wayzata, MN 55391

(3) Name of Notified Substance

Erythritol

(4) Intended Use in Food

Erythritol is intended to be used as a flavor enhancer, formulation aid, humectant, nutritive sweetener, stabilizer and thickener, sequestrant, or texturizer in foods.

(5) Statutory Basis for GRAS Determination

Cargill, through its agent ToxStrategies, Inc., confirms that erythritol, 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

Cargill further asserts that the use of erythritol in foods, as described below, is exempt from the pre-market approval requirements of the Federal Food, Drug, and Cosmetic Act, based on a conclusion that the notified substance is GRAS under the conditions of its intended use.

(7) Availability of Information

The data and informational items 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 review and copying during customary business hours from ToxStrategies, Inc., Naperville, IL.

(8) Data and Information Confidentiality Statement

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

(9) GRAS Notice Certification

To the best of our knowledge, the GRAS determination is a complete, representative, and balanced document. Cargill is not aware of any information that would be inconsistent with a finding that the proposed uses for erythritol in food, which meets appropriate specifications and is used according to current Good Manufacturing Practices (cGMP), is GRAS. Recent reviews of the scientific literature revealed no potential adverse health concerns.

(10) Name/Position of Notifier

(b) (6)

06/05/2018

Donald F. Schmitt, M.P.H.
Senior Managing Scientist
ToxStrategies, Inc.
Agent for Cargill

Date

(11) FSIS Statement

Not applicable.

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

Identity

Erythritol is produced as odorless, white crystals from the fermentation broth of the yeast, *Moniliella pollinis.* The end product typically consists of more than 99.5% erythritol and is heat stable as well as nonhygroscopic. Erythritol is soluble in water, slightly soluble in alcohol, and practically insoluble in fats and ether. It has a melting point between 119°C and 123°C. Due to its negative heat of solution, erythritol provides a strong cooling effect. Erythritol has a sweetness of about 60%–70% that of sucrose, in a 10% solution (Goossens and Röper, 1994), and has a caloric value of 0.0 kcal/gram (21 CFR § 101.9).

Erythritol is a naturally occurring four-carbon sugar alcohol. It is commonly found in fruits such as watermelons, pears, and grapes. Additionally, it is found in wine, sake, beer, mushrooms, and soy sauce (Shindou et al., 1989; Dubernet et al., 1974). It has also been detected in the tissues and body fluids of humans and animals (Goossens and Röper, 1994).

Chemical Structure and Empirical Formula

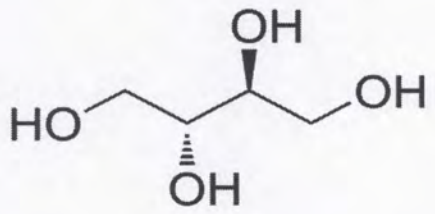

Figure 1. Chemical structure of erythritol ($C_4H_{10}O_4$)

Common or Chemical Names

Erythritol, *meso*-erythritol, tetrahydroxybutane, erythrol, erythrite, erythroglucin, antierythrite, phycite or 1,2,3,4-butanetetrol.

Chemical Abstracts Service (CAS) Registry Number

Erythritol has a CAS number of 149-32-6 and is recognized as E968.

Manufacturing Process

Erythritol is manufactured through a multi-step process that starts with the fermentation of a pure culture of a non-toxigenic, non-pathogenic microorganism—*Moniliella pollinis*—that feeds on a carbohydrate-based medium and ends with the purification of

erythritol from the fermentation broth. The erythritol in the fermentation broth is isolated from the organism and is then exposed to a purification treatment similar to that for other carbohydrate sweeteners and sugar alcohols (e.g., ion-exchange resin, activated charcoal, ultrafiltration, and crystallization). The final purified product contains at least 99.5% erythritol.

Fermentation Process

The manufacturing process for erythritol requires the fermentation of the microorganism, *Moniliella pollinis* (previously named *Tomentosa var. pollinis*), to consume fermentable sugars such as glucose or sucrose, which are then converted into erythritol. Glucose and sucrose, as fermentable sugars, may also contain small amounts of longer chain carbohydrates. Enzymes can be used in the fermentation process to allow these higher chain carbohydrates to become fermentable by *Moniliella pollinis* into erythritol. The erythritol is then separated from the fermented broth and purified.

The fermentation process begins when the strain inoculum preparation is transferred under aseptic conditions into a flask containing sterile medium. The sterile medium for the production culture contains glucose or sucrose in a liquid form, common fermentation nutrients or corn steep liquor, and antifoaming agents. All raw materials, reagents, and processing aids used are of food-grade quality or are suitable for use in foods. The fermentation apparatus is operated under aeration and maintained at a specified temperature range.

Purification Process

Prior to purification, the fermented broth is heated to kill the microorganisms. All of the *Moniella pollinis* production microorganisms are killed by this heat treatment; if enzymes are used in fermentation they will also be denatured by heat treatment or removed in subsequent processing steps. Purification can be carried out by one of the two processes described below, both of which produce a high purity erythritol (>99.5% pure). The single crystallization/ion exchange process is the primary process employed, while the double crystallization process produces the same high purity erythritol without using ion exchange. The batch data presented in Table 2 is from a single crystallization process but is equally representative of the double crystallization process.

Single crystallization/ion exchange purification process:

After separation from the fermentation broth, the hot, concentrated erythritol solution passes through softening resin. This softening resin is specifically designed for food applications to remove trace elements from the liquid erythritol. Next, the erythritol solution is pumped into a chromatography column and passed over its resin to further purify the erythritol. The chromatography resin is specifically designed for food applications, and its function is to separate the erythritol solution from other components such as non-fermentable carbohydrates. Once treated using the chromatography resin, the resulting solution is passed through an ion exchange resin station. The ion exchange

station consists of an anionic and cationic resin, specifically designed for food applications. Next, the solution may be decolorized using activated charcoal. Purification of the erythritol solution continues using ultrafiltration (cut-off 5 kD) and crystallized by cooling. The erythritol crystals are then centrifuged, washed with purified water, dried in a hot air stream, sifted, and packed in bags. The resulting erythritol is at least 99.5% pure.

Double crystallization purification process:

After separation from fermentation broth, the hot, concentrated erythritol solution passes through softening resin. This resin is specifically designed for food applications to remove trace elements from the liquid erythritol. Next, the erythritol solution is pumped into a crystallizer and cooled to stimulate crystallization of the product. The crystals are separated from the broth by centrifugation and washed with potable water. Once separated, the erythritol crystals are then dissolved in potable water, and the resulting solution may be decolorized using activated charcoal. Purification of the erythritol solution continues using ultrafiltration (cut-off 5 kD) and re-crystallization by cooling or evaporation. The erythritol crystals are then centrifuged, washed with purified water, dried in a hot air stream, sifted, and packed in bags. The resulting erythritol is at least 99.5% pure.

Product Specifications

The erythritol product that is the subject of this GRAS determination is produced to meet the specifications outlined in the Food Chemicals Codex (FCC) 2017 monograph for erythritol (Appendix A). Table 1 illustrates the correlation between Cargill's specification (Appendix B) and FCC. Table 2 demonstrates that erythritol is consistently made to meet the established specification and does not contain unacceptable levels of contaminants. Analytical results for three non-consecutive batches of erythritol can be found in Appendix C. The analytical (physical, chemical, and microbiological) results for erythritol summarized in the following tables and included in Appendix C confirm that the ingredient meets the proposed analytical specifications and demonstrates the consistency of production. The analytical results also confirm the lack of impurities/contaminants (e.g., heavy metals-lead, arsenic; microbiological contaminants-yeast, mold, coliforms).

Table 1. Proposed specifications for erythritol

Parameter	FCC Specification	Cargill Specification
Chemical and Physical Data		
Erythritol, %	99.5–100.5	(b) (4)
Ribitol & Glycerol, %	NMT 0.10	
Reducing Sugars. %	NMT 0.30	
Moisture, %	NA	
Loss on Drying*, %	NMT 0.2	
Loss on Ignition (Sulfated Ash)*, %	NMT 0.1	
Granulation, % NMT 250 μm	NA	
Impurities		
Lead, mg/kg	NMT 1.0	

FCC = Food Chemicals Codex; NLT = not less than; NMT = not more than; NA= Not Applicable

*Testing for loss on drying and loss on ignition is performed periodically and not on every batch. When conducted, the batches included in Appendix C meet FCC specifications.

Table 2. Analytical data for non-consecutive lots of erythritol (Appendix C)

Parameter	Supplier Specification	Batch Number		
		(b) (4)		
Erythritol, %	NLT 99.5	99.99	99.99	99.99
Ribitol & Glycerol, %	NMT 0.10	0.01	0.01	0.01
Reducing Sugars, %	NMT 0.30	0.01	0.02	0.01
Moisture, %	NMT 0.15	0.04	0.01	0.06
Loss on Drying, %	NMT 0.2	NR*	NR*	NR*
Loss on Ignition (Sulfated Ash), %	NMT 0.1	NR*	NR*	NR*
Granulation, % NMT 250 μm	NMT 20.0	7.3	8.9	7.6
Lead, mg/kg	NMT 0.5	<0.5	<0.5	<0.5

NLT = not less than; NMT = not more than; NR = Not Reported for these batches.

*Results from other batches tested over the last three years were reviewed and both parameters were within FCC specifications (NMT 0.2 and 0.1, respectively). Results are included in Appendix C.

12

Stability Data

Product should be stored in a clean, dry, and odor-free area at ambient temperature and humidity. The recommended best when used by date for erythritol standard granular under these conditions and in original unopened packaging is 3 years from the date of manufacture. For product in super sacks, the recommended best when used by date is 2 years from the date of manufacture.

13

§ 170.235 Part 3, Dietary Exposure

Erythritol is proposed for use in the United States (U.S.) in a number of additional foods and beverages. Table 3 summarizes proposed uses and use levels, some of which are new uses not covered in GRN 76 submitted by Cerestar in 2001. The estimated daily intake (EDI) per user of all intended uses of erythritol at that time was previously calculated by FDA to be 13 g/day at the mean and 30 g/day at the 90th percentile (US FDA 2001). The estimates in this dossier for the intake of erythritol were determined based on all existing and proposed additional food-uses and use-levels for erythritol in conjunction with food consumption data included in the U.S. National Center for Health Statistics' (NCHS) National Health and Nutrition Examination Surveys (NHANES) 2013-2014 (USDA, 2014, 2016; CDC, 2015a,b, 2016). Calculations for the mean and 90th percentile all-person and all-user intakes were performed for each of the individual proposed food-uses of erythritol and the percentage of consumers were determined. Similar calculations were used to estimate the total intake of erythritol resulting from all proposed food-uses of erythritol combined. In both cases, the per person and per kilogram body weight intakes were reported for the following population groups:

Infants and young children, up to and including 3 years;
Children, ages 4 to 11;
Female teenagers, ages 12 to 19;
Male teenagers, ages 12 to 19;
Female adults, ages 20 and up;
Male adults, ages 20 and up; and
Total population (all age and gender groups combined).

The individual proposed food-uses and use-levels for erythritol employed in the current intake analysis are summarized in Table 3. It should be noted that sauces and toppings include use on meat products, but not within or as part of the actual meat product. Food codes representative of each proposed food-use were chosen from the NHANES 2013-2014 (USDA, 2014, 2016; CDC, 2015a,b, 2016). Food codes were grouped in food-use categories according to Title 21, Section §170.3 of the Code of Federal Regulations (CFR, 2017). Product-specific adjustment factors were developed based on data provided in the food and nutrient database for dietary studies (FNDDS) (USDA ARS, 2016) or the Food Commodity Intake Database (FCID) (U.S. EPA, 2018). All food codes included in the current intake assessment (Intertek, 2018) are listed in the Intake Assessment report in Appendix D.

14

Table 3. Summary of the Individual Proposed Food-Uses and Use-Levels for Erythritol in the U.S. (2013-2014 NHANES Data)

Food Category (21 CFR 170.3) (CFR, 2017)	Food-Uses	Erythritol Use-Levels (%)
Baked Goods and Baking Mixes	Baked Goods and Baking Mixes (excluding regular bread)*	15
	Bars (Granola, High Protein)*	15
	Cakes	25
	Cookies	15
Beverages, Alcoholic	Alcoholic Beverages (Lite Beer, Coolers)*	3.5
Beverages and Beverage Bases	Flavored Quenchers*	3.5
	Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages (Excluding Soy-Based Drinks)	3.5
Breakfast Cereals	Hot Cereal – Oatmeal (Instant or Cooked)	3
	Ready-to-Eat Cereals**	30
Chewing Gum	Chewing Gum	75
Condiments and Relishes	BBQ Sauce*	15
	Tomato Sauce*	15
Dairy Product Analogs	Imitation Dairy Drinks (Soy, Almond, Cashew, Coconut, and Other Plant-Based Drinks)	6
	Non-Dairy Toppings*	10
Fats and Oils	Low Calorie Salad Dressings*	15
Frozen Dairy Desserts and Mixes	Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	10
Fruit and Water Ices	Fruit-Based Slushies	3.5
Gelatins, Puddings, and Filings	Fillings (Fruit, Custard, Cream, Pudding)	15
	Puddings (Instant, Phosphate Set)	10
Hard Candy	Hard Candy (Mints, Pressed, Candies, Cough Drops)	99
Jams and Jellies	Jams and Jellies*	15
Milk Products	Dairy drinks (Chocolate and Flavored Milks)	3.5
	Fat-Based Cream Used in Modified-Fat or Low-Calorie Cookies, Cakes and Pastries	60
	Yogurt	5
Processed Fruits and Fruit Juices	Fruit-Based Smoothies*	3.5
Snack Foods	Salty Snacks*	10
Soft Candy	Fruit Novelty Snacks (*e.g.*, Fruit Peel, Fruit Candy Bar, Fruit Leathers, Fruit Creams, Fruit Snack Candy, Gummy Fruits)	45
	Non-Chocolate Candies	45
	Soft Chocolate Candies	45
Sugar Substitutes	Sugar Substitutes	100
Sweet Sauces, Toppings, and Syrups	Canned Fruit (Syrup)*	15
	Regular or Low-Calorie Syrups or Toppings*	15

CFR = Code of Federal Regulations; U.S. = United States.

*New use not covered in 2001 GRN No. 76 (Cerestar)

**The attached intake assessment was conducted with all cereal food codes at a 30% use level and results in a significant overestimate of erythritol intake from cereals. A use level at or approaching 30% (by weight) would only be incorporated in light weight puffed cereals as a replacement for sugar. Heavy weight (i.e., denser) cereals would likely employ a much lower use level (usually 10% or less, if used at all). It should be noted that many cereals would not incorporate erythritol for sweetening purposes at all, but rather use ingredients such as fruit and nuts for sweetness/flavor purposes. Furthermore, Tables B-1 and B-2 of the Intertek (2018) intake assessment report (Exhibit 1) show mean and 90th percentile intakes for consumption of all cereals at a 30% use level, not just puffed cereals, that are near or below the NOEL (0.71 mg/kg bw) associated with GI intolerance (Jacqz-Aigrain et al., 2015).

Estimates for the total daily intakes of erythritol from proposed food-uses are provided in Tables 4 and 5. Table 4 summarizes the estimated total intake of erythritol on an absolute basis (g/person/day) from all proposed food-uses in the U.S. population group. Table 5 presents this data on a per kilogram body weight basis (mg/kg body weight/day). The percentage of users was high among all age groups evaluated in the current intake assessment; greater than 79.8% of the population groups consisted of users of those food products in which erythritol is currently proposed for use (Table 4). Children had the greatest percentage of users at 99.9%. Large user percentages within a population group typically lead to similar results for the all-person and all-user consumption estimates. Among the total population, the mean and 90th percentile all-user intakes of erythritol were determined to be 32.1 and 63.0 g/person/day, respectively. Of the individual population groups, male adults were determined to have the greatest mean and 90th percentile all-user intakes of erythritol on an absolute basis, at 35.6 and 69.6 g/person/day, respectively, while infants and young children had the lowest mean and 90th percentile all-user intakes of 20.6 and 41.3 g/ person/day, respectively (Table 4).

Table 4. Summary of the Estimated Daily Intake of Erythritol from Proposed Food-Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants and Young Children	0 to <4	16.5	36.5	79.8	568	20.6	41.3
Children	4 to 11	34.2	58.1	99.9	1,155	34.2	58.1
Female Teenagers	12 to 19	28.1	52.3	99.0	571	28.3	53.3
Male Teenagers	12 to 19	33.7	62.1	97.1	552	34.7	62.9
Female Adults	20 and up	29.2	59.1	98.3	2,337	29.7	59.8
Male Adults	20 and up	34.6	69.1	97.2	2,035	35.6	69.6
Total Population	All ages	31.1	62.1	97.0	7,218	32.1	63.0

n = sample size; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

On a body weight basis, the total population (all ages) mean and 90th percentile consumer-only intakes of erythritol were determined to be 551 and 1,179 mg/kg body weight/day, respectively. Among the individual population groups, infants and young children were identified as having the highest mean and 90th percentile all-user intakes of any population group, of 1,512 and 2,816 mg/kg body weight/day, respectively. Female adults had the lowest mean and 90th percentile all-user intakes of 405 mg/kg body weight/day, whereas male adults had the lowest 90th percentile consumer-only intakes of 815 mg/kg body weight/day (Table 5).

Table 5. Summary of the Estimated Daily Per Kilogram Body Weight Intake of Erythritol from Proposed Food-Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants and Young Children	0 to <4	1,206	2,681	79.7	563	1,512	2,816
Children	4 to 11	1,209	2,256	99.9	1,149	1,210	2,256
Female Teenagers	12 to 19	457	971	99.3	564	460	971
Male Teenagers	12 to 19	514	1,013	97.1	550	529	1,013
Female Adults	20 and up	398	815	98.3	2,323	405	817
Male Adults	20 and up	403	805	97.2	2,026	415	815
Total Population	All ages	535	1,159	97.0	7,175	551	1,179

bw = body weight; n = sample size; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

In summary, consumption data and information pertaining to the individual proposed food-uses of erythritol were used to estimate the all-person and all-user intakes of erythritol for specific demographic groups and for the total U.S. population. This type of intake methodology is generally considered to be 'worst case' as a result of several conservative assumptions made in the consumption estimates. For example, it is often assumed that all food products within a food category contain the ingredient at the maximum specified level of use. Furthermore, it is often assumed that all food products within a food category contain the ingredient at the maximum specified level of use; however, a significant number of other polyols are available on the market to manufacturers to formulate food products, so it is unlikely that erythritol would be used at the maximum use-level in every food use category.

In addition, it is well established that the length of a dietary survey affects the estimated consumption of individual users. Short-term surveys, such as the typical 2- or 3-day dietary surveys, may overestimate the consumption of food products that are consumed relatively infrequently (Anderson, 1988). Survey duration has been shown to affect the estimated percent of consumers, as well as the classification of individuals as high or low consumers of a given food (Lambe and Kearney, 1999; Lambe et al., 2000). As reviewed by Lambe and colleagues (1999, 2000), shorter surveys are associated with misclassification of individuals, inaccurate correlation coefficients, reduced power, and overestimation of percentage of high and low intakes. These effects of survey duration are thought to be due to the within-person and day-to-day variation for a given self-selected diet. The percentage of respondents who consume a food increases as the survey duration increases; the longer duration begins to incorporate days with no consumption, thus decreasing the mean intakes among consumers over time. The impact of the length of dietary surveys on the user consumption of different types of food products has been investigated in a multi-country study conducted by the Institute of European Food Studies (1998). In general, user mean consumption was found to decrease over the length of the study,

depending on the food type, and overall the average decrease in the mean or 90th percentile consumption was found to be 1.9- to 2-fold.

In summary, on an all-user basis, the mean and 90th percentile intakes of erythritol by the total population from all proposed food-uses in the U.S. were estimated to be 32.1 g/person/day (551 mg/kg body weight/day) and 63.0 g/person/day (1,179 mg/kg body weight/day), respectively. Of the individual population groups, the highest mean and 90th percentile intakes of erythritol, as observed in male adults, were estimated to be 35.6 g/person/day (415 mg/kg body weight/day) and 69.6 g/person/day (815 mg/kg body weight/day), respectively. Applying the above model, the calculated intake estimates for erythritol should be adjusted downwards by a factor of approximately 2. Taking this into account, actual intakes for the user population mean and 90th percentile levels are likely in the range of 16.1 g/day (275.5 mg/kg body weight/day) and 31.5 g/day (589.5 mg/kg body weight/day), respectively. Similarly, actual intake in the highest exposure group, infants and young children, would not likely exceed 1,408 mg/kg body weight/day. These estimates are similar to the EDI per user of all intended uses of erythritol previously calculated by FDA to be 13 g/day at the mean and 30 g/day at the 90th percentile (US FDA 2001).

170.240 Part 4, Self-Limiting Levels of Use

The use of erythritol in foods is considered to be self-limiting for technological reasons, such as product texture and/or flavor profile, either of which could affect consumer acceptability.

19

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

While erythritol has been commonly used in food, the statutory basis for our conclusion of GRAS status in the notice is based on scientific procedures and not common use in food.

20

§ 170.250 Part 6, GRAS Narrative

History of Use and Regulatory Approval of Erythritol

Erythritol has had widespread use in beverages and foods in the U.S. for more than a decade without any reported adverse health effects in children and adults, at the dietary exposure levels that have been in practice over that time. Numerous erythritol ingredients are recognized as GRAS for their intended uses in foods, and the erythritol ingredients listed in Table 6 have received "no questions" letters from the Food and Drug Administration (FDA).

Table 6. Erythritol GRAS Notifications

GRN No.	Erythritol Product	Date of Closure
401	Erythritol	03/22/12
382	Erythritol	11/21/11
297	Erythritol fatty acid esters	12/15/09
208	Erythritol	01/25/07
76	Erythritol	09/11/01

Erythritol is considered GRAS for use as a flavor enhancer, formulation aid, humectant, non-nutritive sweetener, stabilizer and thickener, sequestrant and texturizer in a variety of foods. It has been used in the following human foods: bakery fillings, cakes and cookies, chewing gum, dairy drinks, fat-based cream used in modified fat/calorie cookies, pastries, hard candies, frozen dairy desserts, puddings, reduced and low-calorie beverages, soft candies, sugar substitutes, yogurt, and others.

In addition, erythritol is listed in 21 CFR § 101.80 as a noncariogenic carbohydrate sweetener with permitted health claims related to dietary carbohydrates and the occurrence of dental caries.

Globally, erythritol has achieved regulatory acceptance in multiple countries, including the European Union, Canada, Mexico, and Brazil. It is approved for use in Europe under E968, and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) reviewed it in 1999 and assigned an acceptable daily intake (ADI) of "not specified" (JECFA, 2000). In Canada, it was approved for use as a food additive in November 2004. In Mexico, it is authorized for use at GMP levels. Brazil received approval effective in March 2008; it is included in the National Agency of Sanitary Surveillance (ANVISA) Sweeteners list. Erythritol is listed in Table 3 of the CODEX General Standard for Food Additives (CODEX, 2001), as a flavor enhancer, humectant and sweetener, and can be used in all categories of foods at GMP levels.

21

Safety Introduction

Erythritol is a naturally-occurring compound found in a variety of foods and beverages including melons, pears, grapes, soy sauce, wine, miso paste, and sake. It also exists endogenously in tissues and body fluids of human and animals (Niwa et al., 1993; Goosens and Roper, 1994). Erythritol is currently marketed for use in reduced sugar/calorie foods such as confectionary, bakery products, and beverages.

Regulatory authorities have conducted comprehensive reviews of the safety of erythritol and found it to be safe for use in human food (JECFA, 2000; SCF, 2003; FDA, 2001, 2007, 2011, 2012, EFSA, 2015). Numerous studies and publications have been reviewed and support the safety of erythritol, including *in vitro* studies, *in vivo* animal studies, and clinical studies in humans. A summary of the most relevant studies of erythritol as found in previous GRNs and reviews by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and SCF include acute and subchronic toxicity, reproductive and developmental toxicity, mutagenicity and genotoxicity, chronic toxicity, carcinogenicity in animals along with clinical studies (see Table 7).

Safety Data

Literature searches were performed to identify available safety data on erythritol. This included searching sources of information such as publicly available assessments, databases, or reviews from organizations including EFSA, JECFA, U.S. FDA, and the World Health Organization (WHO), general Internet searching, as well as searching databases such as EMBASE and PubMed through October, 2017.

The published study data, additional unpublished supporting data, and reviews by U.S. and international regulatory authorities were included in previous GRAS notifications (e.g., GRN Nos. 76, 208, 382, 401), and support the conclusion that Cargill's erythritol ingredient is safe and GRAS for use as a flavor enhancer, formulation aid, humectant, nutritive sweetener, stabilizer and thickener, sequestrant, or texturizer in human food.

Toxicological Studies

Studies of Erythritol in Animals

Absorption, Distribution, Metabolism, and Excretion (ADME)

Numerous reviews of erythritol ADME data for both animals and humans have been published (Munro et al., 1998; JECFA, 2000; SCF, 2003). Following oral ingestion, erythritol is rapidly absorbed from the small intestine (60-90%) and primarily excreted unchanged in the urine. Absorbed erythritol is rapidly distributed in both animals and humans (i.e., within 1 hour of ingestion). The unabsorbed fraction of erythritol undergoes microbial fermentation in the large intestine. Fermentation of erythritol in the large intestine produces volatile short-chain fatty acids and gas (Oku and Noda, 1990; Noda and Oku, 1992).

Acute Toxicity

The acute oral LD50 value in male and female rats administered erythritol by oral gavage is 13.1 and 13.5 g/kg bw (Yamamoto et al., 1987, as cited in Munro et al., 1998) and >5 g/kg in dogs (Eapen et al., 2017; Ozeki et al., 1988, as cited in Munro et al., 1998). The results demonstrate that erythritol is of very low acute toxicity.

Short-term Toxicity

Several 28-day studies have been conducted in Wistar rats (Till and Modderman, 1996; Kanai et al., 1992, as cited in Munro et al., 1998; Oku and Noda, 1990; Shibata, 1991, as cited in Munro et al., 1998). Erythritol was administered either by oral gavage or incorporated in the diet. In all the studies, the NOAEL was considered the highest dose administered, up to as high as 10% in the diet, or approximately 10 g/kg/bw/day.

Subchronic Toxicity

Three subchronic studies of 13-weeks duration were conducted in Wistar rats or CD-1 mice (Yamamoto, 1989, as cited in Munro et al., 1998; Til et al., 1996). Erythritol was administered either by oral gavage or incorporated in the diet at concentrations as high as 20%. Common findings included increased water intake and urine volume, laxation effects, cecal enlargement, and increased kidney weights. There were no significant findings in histopathological examinations of select tissues and organs. In a previously unpublished study in dogs (Eapen et al., 2017), 36 young adult beagle dogs were randomly assigned to 4 treatment groups that received 0, 1.25, 2.5 or 5 g erythritol/kg body weight/day. Three animals/sex/group were assigned to the primary necropsy following completion of the dosing period, while two animals/sex/group were assigned to the recovery necropsy following the 4-week non-dosing period in the control and 2.5 and 5 g/kg dose groups. The dogs assigned to the study were administered water (control) or high purity erythritol in water via oral intubation daily for 13-weeks. The erythritol test article was well-tolerated. Clinical signs included increased water intake and urine output. Clinical pathology endpoints suggested changes in hydration status. Microscopic changes observed in the kidney (i.e., slight dilatation, eosinophilic degeneration, pyknosis, epithelial desquamation, hydropic degeneration and slight necrosis of the kidney tubules) were consistent with increased water consumption and urinary output, but were not considered adverse. Therefore, the NOAEL was considered to be 5 g/kg bw/day, the highest dose level administered.

Chronic Toxicity/Carcinogenicity

Three chronic toxicity studies of 6 months to two years were conducted in Wistar rats (Kamata, 1990a, as cite in Munro et al., 1998; Til and van Nesselrooij, 1994, as cited in Munro et al., 1998; Lina et al., 1996). Erythritol was administered intravenously for 6 months or incorporated in the diet at concentrations as high as 10%. Changes like those noted in the subchronic studies above were observed (i.e., increased water intake and urine volume, laxation, cecal enlargement, increased kidney weights). Histopathological examinations did not reveal abnormalities, including non-neoplastic, pre-neoplastic, or neoplastic changes attributable to treatment with erythritol. In addition, two studies were conducted in dogs, a six-month intravenous study and a

one-year dietary study Dean et al., 1996; Kamata, 1990b, as cite in Munro et al., 1998. In the dietary study, erythritol was administered at concentrations of 0, 2, 5 and 10% in the diet for 52 weeks. Daily administration of erythritol in the diet was well tolerated. Urine chemistry changes associated with mild diuresis were noted in erythritol-treated dogs. The NOAEL was considered 10% in the diet, the highest concentration administered; equivalent to 3.5 g/kg bw/day. In the intravenous study, erythritol was administered intravenously to beagle dogs at doses of 0, 1, 2.2, and 5 g/kg bw/day for 26 weeks. Increased urinary output was observed, consistent with diuretic effects seen in previous oral studies. No significant microscopic changes were observed in the kidney. The NOAEL was considered the highest dose level administered, 5 g/kg bw/day.

Genotoxicity

Numerous *in vitro* and *in vivo* mutagenicity/genotoxicity studies were conducted (Chung and Lee, 2013; Kawamura et al., 1996; Blijtleven, 1990, as cited in Munro et al., 1998). *In vitro* studies included the Ames assay, a chromosome aberration study in Chinese hamster lung fibroblast cells, a micronucleus assay in mouse lymphoma cells, and the comet assay using L5178Y tk+/− cells; the *in vivo* study was a micronucleus assay that assessed the incidence of micronuclei formation in bone-marrow cells of mice. The results of all studies indicated that erythritol was not mutagenic or genotoxic.

Reproductive/Developmental Toxicity

Numerous reproductive/developmental toxicity studies have been conducted in mice, rats and rabbits, including teratology studies and one- and two-generation reproduction studies (Tateishi, 1989, 1992, both as cited in Munro et al., 1998; Smits-van Prooije et al., 1996; Waalkens-Berendsen et al., 1996; Ota, 1990, as cited in Munro et al., 1998; Shimizu et al., 1996). In all of the studies, erythritol was not embryotoxic or teratogenic, and no adverse effects were noted in maternal toxicity or reproductive performance.

Other studies

Several studies were conducted in other rat models to evaluate the effects of erythritol in obese rats or its potential effect on bone resorption (Chung et al., 2012; Matilla et al., 1996). No effect on bone resorption was noted. However, as observed in other preclinical studies, laxation was noted followed by adaptation.

Table 7. Summary of Preclinical Toxicological Study Data of Erythritol in Animals

Findings/Observations	**Reference**
Acute Toxicity	
Results: Oral LD50s in rats of >18 g/kg and 13.1 (male) and 13.5 (female) g/kg.	Beck et al., 1936 and Yamamoto et al., as cited in JECFA 2000 and Munro et al., 1998

Results: No mortality observed. Transient clinical signs included emesis, mucosal redness, and cold skin sensation. No effect on food consumption, body weight gain, organ weights, or gross pathology. Oral LD_{50} in male dogs, >5 g/kg.	Eapen et al., 2017[1]
Short-Term Toxicity	
Study Design: Erythritol was administered to groups of Wistar rats at 0, 5, and 10% in the diet (equivalent to approximately 0, 5, and 10 g/kg bw/day) for 28 days. **Results:** Soft stools/diarrhea in high-dose males and females and mid-dose females early in study; disappeared over course of study. Slight decrease in body weight of high-dose males; no differences in females. Increased water consumption, cecal and kidney weights were noted. No biologically significant changes in clinical pathology parameters. NOAEL, 10% in the diet (approx. 10 g/kg bw/day).	Till and Modderman, 1996
Study Design: Erythritol was administered to groups of nephrectomized Wistar rats at 0, 2, and 5% in the diet (equivalent to approximately 0, 2, and 5 g/kg bw/day) for 28 days. **Results:** No significant effects on mortality, clinical signs of toxicity (including laxation), body weight gain, or food consumption. Increase in water consumption noted. NOAEL, 5% in the diet (approx. 5 g/kg bw/day).	Kanai et al., 1992, as cited in Munro et al., 1998
Study Design: Erythritol was administered to groups of Wistar rats at 0, 5, and 10% in the diet (equivalent to approximately 0, 5, and 10 g/kg bw/day) for 28 days. **Results:** Diarrhea in high-dose males and females early in study; disappeared over course of study. Increased water consumption, urine volume, and relative cecal weights. No biologically significant changes in clinical pathology parameters. NOAEL, 10% in the diet (approx. 10 g/kg bw/day).	Oku and Noda, 1990
Study Design: Erythritol was administered to groups of Wistar rats by oral gavage at 0 or 8 g/kg bw/day for 28 days; or at 8 g/kg bw/day with either a high or low electrolyte solution for 28 days. **Results:** Study observations in erythritol-treated rats included soft stools and increases in water intake, urine volume and minor changes in urinalysis parameters, and kidney weights.	Shibata, 1991, as cited in Munro et al., 1998
Subchronic Toxicity	
Study Design: Erythritol was administered to groups of twelve male and female Slc:Wistar rats per by oral gavage at 0, 1, 2, 4, or 8 g/kg bw/day for 13 weeks. A satellite group of six male and female rats received a similar treatment followed by a 4-week recovery period. **Results:** No mortality or effects on sensory response, ophthalmological findings, or hematology parameters. Transient laxative effects were noted in rats that received 4 or 8 g/kg bw/day and were likely due to the osmotically active nature of erythritol. Decreased body weight gain in high-dose males from week 7 on. Increased water intake, urine volume (high-dose male and females), and minor changes in urinalysis parameters (sodium and chloride excretion, specific gravity and osmotic	Yamamoto, 1989, as cited in Munro et al., 1998

[1] the study was previously conducted and utilized in the original safety review for erythritol but was recently published in order to meet the general recognition standard.

pressure) for all groups. Increased serum BUN in high-dose males and females and 4 g/kg bw/day females. As in other erythritol studies, cecal enlargement (due to fermentation of erythritol by enterobacteria in the caecum and the osmotic water loading of the large intestine) and increased kidney weight (related to diuresis) was observed in the high-dose group. No histopathological abnormalities noted; only minor changes related to the diuretic nature of erythritol.	
Study Design: Erythritol was administered to groups of Wistar rats at 0, 5, 10, and 20% (approximately 0, 5, 10, or 20 g/kg bw/day) in the diet for 13 weeks. **Results:** No treatment-related mortalities. Laxative effects in high-dose rats; also, slightly, yet significantly, reduced body weights in 20% group. Increased food and water intake at high-dose as well as increased urine volume with increasing dose and minor changes in urine electrolytes. Increased serum alkaline phosphatase and decreased GGT in high-dose rats. Increased cecal and relative kidney weights in in 10 and 20% groups. No histopathological abnormalities noted.	Til et al., 1996
Study Design: Erythritol was administered to groups of CD-1 mice at 0, 5, 10, and 20% (approximately 0, 6, 11, or 23 g/kg bw/day) in the diet for 13 weeks. **Results:** No treatment-related mortalities. In comparison to rats, laxative effects were not observed at any dose level. Slightly reduced body weights male mice of 20% group. Increased food and water intake and urine volume with increasing erythritol dose, as well as changes in urine electrolytes in 10 and 20% groups. Cecal enlargement noted in 20% dose group and increased relative and absolute kidney weights in both sexes of the 20% group and in male mice of the 5 and 10% groups. No histopathological abnormalities noted in kidney despite osmotic diuresis related to the high dose levels of erythritol.	Til et al., 1996
Study Design: Erythritol was administered by oral intubation to beagle dogs at doses of 0, 1.25, 2.5, and 5 g/kg bw/day for 13 weeks. **Results:** Test article well-tolerated. Clinical signs included increased water intake and urine output. Clinical pathology endpoints suggested changes in hydration status. Microscopic changes observed in the kidney (i.e., slight dilatation, eosinophilic degeneration, pyknosis, epithelial desquamation, hydropic degeneration and slight necrosis of the kidney tubules) were consistent with increased water consumption and urinary output, but were not considered adverse. NOAEL considered to be 5 g/kg bw/day, the highest dose level administered.	Eapen et al., 2017[2]
Chronic Toxicity	
Study Design: Erythritol was administered to groups of 28 male and female Slc:Wistar rats by intravenous injection at 0, 1, 1.73, or 3 g/kg bw/day for 6 months. Six rats/sex/group in the control, mid-, and high-dose groups included a one month recovery period. **Results:** No mortality or clinical signs noted, No effects on the results of ophthalmological, gross pathological, or histopathological examinations.	Kamata, 1990a, as cited in Munro et al., 1998

[2] the study was previously conducted and utilized in the original safety review for erythritol but was recently published in order to meet the general recognition standard.

Decreased body weight gain noted in both sexes of high-dose group at various time points, but were comparable to the control group by the end of the treatment period. Increased water intake, urine volume and frequency were noted in all animals, but particularly high-dose animals. Minor changes observed in urinalysis parameters (i.e., electrolytes). Minor changes in hematological parameters (i.e., decreased RBC, hematocrit, hemoglobin) in males of all groups and females of the top two dose groups. Changes considered related to injection of distilled water vehicle and/or the highly osmotic dosing solution. Increased serum BUN was noted in high-dose females and was considered related to diuretic action of erythritol and of no clinical significance given a lack of renal pathology. Similarly, increased kidney weights were observed in high-dose rats without related changes in kidney pathology. No histopathological abnormalities were noted.	
Study Design: Erythritol was administered to groups of Wistar rats at 0, 1, 3, and 10% (approximately 0, 6, 11, or 23 g/kg bw/day) in the diet for 78 weeks. **Results:** No treatment-related mortality occurred. Soft feces observed only in first weeks of the study. Decreased body weight gain in high-dose males. Food intake increased at several time points in the mid-dose group. Increased water intake across groups, but significant change noted in high-dose group. Increased alkaline phosphatase in high-dose animals. No other toxicologically significant changes in hematology or blood chemistry parameters. Increased urinary output along with calcium excretion. Increased absolute and relative cecal weights in mid- and high-dose groups. No histopathological abnormalities were noted.	Til and van Nesselrooij, 1994, as cited in Munro et al., 1998
Study Design: Erythritol was administered to groups of Wistar rats at 0, 2, 5, and 10% (approximately 0, 0.86, 2.2, or 4.6 and 0, 1.0, 2.6, and 5.4 g/kg bw/day for male and female rats, respectively) in the diet for 105 to 107 weeks. **Results:** No treatment-related mortality or clinical signs such as laxation were noted. Decreased body weight gain noted during most of the study in mid-dose males and high-dose males and females. No treatment-related changes in hematology or blood chemistry parameters. Increased urinary volume noted with increasing dose and accompanied by increased excretion of urinary calcium and citrate. Minor increases observed in urinalysis parameters (i.e., electrolytes, protein, GGT) in primarily the high-dose group. Increased relative cecal weights were noted in mid-and high-dose groups along with increased relative kidney weights in the high-dose group. Histopathological examinations did not reveal nonneoplastic, preneoplastic, or neoplastic changes attributable to treatment with erythritol.	Lina et al., 1996
Study Design: Erythritol was administered to beagle dogs at concentrations of 0, 2, 5 and 10% in the diet for 53 weeks. **Results:** Daily administration of erythritol in the diet was well tolerated, with no diarrhea. Urine chemistry changes associated with mild diuresis were noted in erythritol-treated dogs. NOAEL was considered 10% in the diet, the highest concentration administered; equivalent to 3.5 g/kg bw/day.	Dean et al., 1996

27

Study Design: Erythritol was administered intravenously to beagle dogs at doses of 0, 1, 2.2, and 5 g/kg bw/day for 26 weeks. **Results:** Increased urinary output observed, consistent with diuretic effects seen in previous oral studies. No significant microscopic changes observed in the kidney. NOAEL considered the highest dose level administered, 5 g/kg bw/day.	Kamata, 1990b, as cited in Munro et al., 1998
Reproductive/Developmental Toxicity	
Study Design: In a single-generation reproduction toxicity study, erythritol was administered by oral gavage to CD-1 mice at doses of 0, 1, 2, 4, or 8 g/kg bw/day. Males were dosed for 9 weeks and then mated with females and continued to be treated until vaginal plugs were noted. Females were dosed daily for 15 days prior to mating and until day 6 of gestation. **Results:** No treatment-related adverse effects were noted on reproduction or fetal development and the NOAEL was considered 8 g/kg bw/day, the highest dose tested. As in other safety studies, loose stools were observed early in the study in the 4 and 8 g/kg bw day groups.	Tateishi, 1989, as cited in Munro et al., 1998
Study Design: In a single-generation reproduction toxicity study, erythritol was administered intravenously to CD-1 mice at doses of 0, 1.0, 1.73, or 3 g/kg bw/day. Males were dosed for 9 weeks and then mated with females and continued to be treated until vaginal plugs were noted. Females were dosed daily for 15 days prior to mating and until day 6 of gestation. **Results:** No treatment-related adverse effects were noted on reproductive performance, fetotoxicity, or fetal development and the NOAEL was considered 3 g/kg bw/day, the highest dose tested. Only minor effects related to administration of the highly osmotic solution were noted.	Tateishi, 1992, as cited in Munro et al., 1998
Study Design: In a embryotoxicity and teratogenicity study, erythritol was administered in the diet to female Wistar rats at concentrations of 0, 2.5, 5, or 10% from day 0 to 21 of gestation. **Results:** No deaths occurred over the course of the study and signs of GI intolerance such as diarrhea were observed. Body weight gain was reduced in week 2 of gestation for the high-dose 10% erythritol group only. No adverse effects were noted on reproduction performance or fetal development. Erythritol was not fetotoxic, embryotoxic, or teratogenic. The NOAEL was identified as 10% in the diet (equivalent to approximately 6.6 g/kg bw/day), the highest dose tested.	Smits-van Prooije et al., 1996
Study Design: In a two-generation reproduction study, erythritol was administered in the diet to Wistar rats of both sexes at concentrations of 0, 2.5, 5, or 10% for two successive generations. **Results:** Initial reductions in body weight gain were observed in both generations and were the results of reduced food consumption and occurrence of transient diarrhea until the rats adapted to the consumption of erythritol. The authors concluded that administration of erythritol in the diet at concentrations up to 10% in the diet had no effect on fertility or reproductive performance in on parenteral Wistar rats or their progeny. In addition, no treatment-related macro- or microscopic changes were noted in reproductive organs of parental animals. The	Waalkens-Berendsen et al., 1996

NOAEL was identified as 10% in the diet (equivalent to approximately 7.6 g/kg bw/day), the highest dose tested.	
Study Design: In a teratology study, erythritol was administered intravenously to female pregnant CD-1 mice at doses of 0, 1, 2, or 4 g/kg bw/day on days 6-15 of gestation. **Results:** Transient clinical signs were noted and included hypoactivity and staggering gait, immediately following the completion of dosing. Two deaths in the high-dose groups were considered related to an osmotic balance created the large dose volume administered intravenously. A slight increase in external abnormalities of the high-dose group was observed. The changes were considered non-specific in nature and due to the hypertonicity of the test article solution. Therefore, it was concluded that erythritol was not embryotoxic or teratogenic in mice administered erythritol by the intravenous route.	Ota, 1990, as cited in Munro et al., 1998
Study Design: In a teratology study in KBL:JW rabbits, erythritol was administered intravenously to female rabbits at doses of 0, 1.0, 2.24, or 5 g/kg bw/day on days 6-18 of gestation followed by sacrifice on day 28. **Results:** Water intake was increased in all groups at various timepoints during the study and was attributed to the diuretic action of erythritol. No other effects were noted in low-or mid-dose group animals. Occasional auricular edema and bradypragia were noted in high-dose group animals following intravenous administration. However, the intravenous administration of erythritol to pregnant rabbits had no effect on reproductive performance or fetal development and any dose level.	Shimizu et al., 1996
Genotoxicity/Mutagenicity	
Study Designs: Erythritol was evaluated in several *in vitro* and *in vivo* genetic toxicity assays. The potential mutagenicity erythritol was investigated in the Ames assay using *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 at concentrations of 156.3 – 5,000 µg erythritol/plate, in the presence and absence of S9 fraction from the livers of Aroclor-induced rats. The ability of erythritol (0 – 5000 µg/ml) to induce chromosomal aberrations was evaluated using Chinese hamster lung fibroblast cells, with and without metabolic activation. Erythritol (0 – 5,000 µg/ml) was tested in an *in vitro* micronucleus study in L5178Y $^{+/-}$ mouse lymphoma cells. Erythritol (0 – 5,000 µg/ml) was tested in a comet assay using L5178Y tk$^{+/-}$ cells. Lastly, erythritol (0 – 5,000 µg/ml) was tested in an *in vivo* micronucleus study in male ICR mice and the incidence of micronucleated polychromatic erythrocytes evaluated. **Results:** Erythritol was not mutagenic to bacterial cells and there was no evidence of chromosomal damage in mammalian cells in *in vitro* and *in vivo* assays.	Chung and Lee, 2013
Study Designs: Erythritol was tested in the Ames reverse mutation assay and in an *in vitro* mammalian chromosome aberration test in Chinese hamster fibroblast cells (CHL/IU). **Results:** Erythritol was not mutagenic in the Ames reverse mutation assay employing four different *Salmonella* strains and the WP2 *uvr*A strain of *Escherichia coli*. Similarly, erythritol did not affect the incidence of polyploid cells or gap-, break-, or exchange-type	Kawamura et al., 1996

29

aberrations in the chromosome aberration test at concentrations of 1.25 – 10.0 mM.	
Study Design: Erythritol was tested for mutagenic activity in the Ames reverse mutation assay, with and without metabolic activation at concentrations ranging from 0.37 – 30 mg/plate. *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA 1538 were used. **Results:** Erythritol was not mutagenic in the Ames reverse mutation assay using five different *Salmonella* tester strains at concentrations up to a maximum of 30 mg/plate.	Blijtleven, 1990, as cited in Munro et al., 1998
Additional Safety-Related Studies	
Study Design: Erythritol administered to groups of obese Sprague-Dawley rats at concentration of 5% in a normal or high-fat diet for 8 weeks. **Results:** No decrease in body weight gain, food intake, or visceral fat with erythritol administration. No changes in serum biochemical parameters; cholesterol, triglycerides, LDL-C, and HDL-C compared to controls.	Chung et al., 2012
Study Design: Xylitol, sorbitol, mannitol, or erythritol was administered to groups of Sprague-Dawley rats (3-4 g polyol/day) for one month. The rats were pretreated with radiolabeled tetracycline as a marker of bone resorption. **Results:** Diarrhea was observed in the 1st week of treatment with erythritol, followed by adapatation. Erythritol had no effect on bone resorption, whereas the other polyols had a positive effect.	Matilla et al., 1996

Human Studies

Numerous reviews of erythritol safety in humans have been published (Munro et al., 1998; JECFA, 2000; SCF, 2003) and include summaries of dozens of clinical studies that examined gastrointestinal tolerance, carbohydrate metabolism, and the energy value of erythritol in humans.

Erythritol Tolerability

Transient minor gastrointestinal (GI) effects, consisting of loose stools, nausea, gurgling, and flatulence have been reported following large acute bolus (liquid) doses of erythritol, particularly when administered on an empty stomach (Munro et al., 1998; Makinen, 2016; Wolnerhanssen et al., 2016). These GI effects were considered to be physiological responses to osmotic loading of no toxicological significance, were generally self-limiting, and not severe or indicative of toxicity per se but rather of tolerability.

Toxicokinetic studies have shown that erythritol is rapidly absorbed, with plasma erythritol levels peaking within 1 to 2 hours, and the majority of an oral dose (80 to 90%) eliminated in the urine within 24 hours (Ishikawa et al., 1996). The fact that the majority of an orally administered dose of erythritol is rapidly absorbed indicates 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 erythritol is highly dependent on mode and timeline of ingestion. For

example, Tetzloff et al. (1996) demonstrated that repeated ingestion of erythritol, as divided doses with food over the course of a day, was well-tolerated for 7 days at daily doses of 1.0 g/kg body weight.

A number of more recent publications investigating the tolerability of erythritol in clinical studies were identified. In the first study, the GI tolerance of erythritol consumed as a beverage was investigated in a randomized, double-blind, placebo-controlled study in healthy male (n = 34) and female (n = 36) young adults, 18 to 24 years of age (Storey et al., 2007). Test drinks were non-carbonated 400 mL beverages containing 20, 35, or 50 g of erythritol or 45 g of sucrose (placebo). Subjects consumed each test drink, including the placebo, separated by 7-day washout periods. Drinks were consumed in a single 15-minute sitting as a mid-morning or mid-afternoon drink, following consumption of a normal breakfast or lunch. The incidence and the magnitude of GI responses were ranked on a hedonic scale for 24 hours post-consumption. The 2 lower intakes of erythritol did not increase total bowel movement frequency or alter feces consistency compared to the control group and were well tolerated by all subjects. Only consumption of the highest amount of erythritol (50 g or 0.78 g/kg body weight) led to a significant increase in the number of subjects experiencing mild nausea (20 of 64 subjects, $P<0.01$) and borborygmi (24 of 64 subjects, $P<0.05$). Overall, the data from the study demonstrated that when consumed as a liquid in a beverage up to 50 g erythritol (0.78 g/kg body weight, based on mean body weight of male and female subjects combined) was associated with mild GI distress and a dose of 35g of erythritol was tolerated well by healthy volunteers.

In another study of erythritol tolerance, the threshold for transitory diarrhea induced by erythritol was investigated in male (n = 24) and female (n = 26) young adults (mean age of males, 19.9 ± 1.2 years; females, 21.2 ± 2.2 years) (Oku and Nakamura, 2007). Erythritol (20, 30, 40, or 50 g) was dissolved in 150 mL of distilled water and ingested 2 to 3 hours following a meal (usually breakfast). Subjects consumed each test drink with a 1-week washout period in between, starting with the lowest concentration, and stopped at the dose that induced diarrhea. As such, only 42 out of 50 total subjects, 24 females and 18 males, consumed the 50 g dose. Subjects recorded abdominal symptoms, frequency of defecation, and stool shape following erythritol intake. Ingestion of 50 g of erythritol was associated with GI distress resulting in diarrhea in 27.8% of the male subjects and in 25.0% of the female subjects; however, the authors reported the occurrence of diarrhea in 45.8% of males and 30.8% of females, by assuming that the subjects who were excluded due to diarrhea at a lower dose would in fact experience diarrhea at 50 g. No statistical analyses were performed on any of this data. An intake of 50 g of erythritol was calculated to be equivalent to 0.79 g/kg body weight in males and 1.00 g/kg body weight in females, based on the average body weights of the 2 independent populations. Ingestion of 40 g resulted in diarrhea in 25.0% of males (0.63 g/kg body weight) and 7.7% of females (0.80 g/kg body weight). Ingestion of 30 g of erythritol did not induce any diarrhea in both males and females. Although this study reported a lower threshold for diarrhea induction by erythritol than the study conducted by Storey et al. (2007), these results should be interpreted with caution due to issues relating to study design. In addition to a lower number of subjects enrolled in this study compared to the previous study, no information was provided on randomization or blinding, and not all subjects were tested at all doses; very soft or muddy feces was defined as diarrhea at which point erythritol intake ceased, and as a result only 18 males were administered 50 g of

erythritol, for example. As such, the lack of statistical evaluation of the data combined with the absence of a placebo/control group prevents the quantitative determination of a threshold dose for diarrhea from this study data.

Kim et al. (2011) studied the effect of erythritol on fructose absorption in the small intestine in a randomized, double-masked, controlled, crossover study and found that simultaneous ingestion of the 2 sweeteners appeared to increase GI symptoms in healthy adults (13 male, 24 female; aged 18 to 75 years (mean age 23.0 ± 0.5 years). Study subjects were instructed to consume a standard low-residue, low-fiber dinner and then the following day consume a 500 mL test beverage containing fructose (50 g) and erythritol (33.3 g), a control beverage containing only fructose (50 g), or a positive control beverage containing fructose (50 g) and glucose (50 g). The washout period between consumption of test beverages was 3 to 14 days (no further details provided). Breath samples were collected for hydrogen, methane, and carbon dioxide measurement, and subjects recorded GI intolerance symptoms for 24 hours post-ingestion. Combination of fructose and erythritol led to significant increases in breath hydrogen levels ($P<0.001$) and GI intolerance symptoms, such as increased flatulence, cramping, number of loose stools ($P<0.05$) and bowel movements ($P<0.05$) compared to fructose alone. No cases of diarrhea were reported. Although the authors speculate that erythritol impaired fructose absorption leading to fructose malabsorption and increased GI intolerance symptoms, this could not be confirmed due to the lack of an erythritol alone reference group. Kim et al. concluded that inclusion of an erythritol-only beverage would have helped to identify which carbohydrate, fructose or erythritol, was malabsorbed in the fructose/erythritol beverage.

The tolerability of erythritol as a result of bolus administration was also recently established in young children aged 4 to 6 years of age following a single drinking occasion (Jacqz-Aigrain et al., 2015; Makinen, 2016). A total of 185 children completed the study (99 males, 86 females) divided into 4 test groups. In a rising dose study design, investigators began the study by administering a noncarbonated fruit-flavored beverage containing 5 g of erythritol to the first test group ($n = 14$) 2 hours after breakfast was consumed, and so long as significant GI effects were not observed compared to placebo (sucrose beverage of equivalent sweetness), the next group received 10 g more. The crossover period between test substance and placebo was at least 5 days. The second group received 15 g ($n = 57$), the third group received 25 g ($n = 56$), and the fourth group was reduced to 20 g ($n = 58$) due to occurrence of severe GI symptoms at the highest dose. The authors established that a 15 g dose of erythritol, when administrated within a 15-minute time frame was the NOEL for laxation, which equates to a bolus concentration of 0.71 g/kg body weight. A higher dose of 25 g (1.23 g/kg body weight) resulted in a small but statistically significant effect on laxation, including an increase in daily stool frequency compared to control (2.32 vs. 1.86 stools over 48 hours, $P=0.0244$). Likewise, mean stool consistency also increased significantly compared to control over 48 hours (4.43 vs. 3.32, $P<0.0001$) measured by the Bristol Stool Score. The incidences of nausea, vomiting, borborygmi, excess flatus, and abdominal pain were not different between erythritol and control groups; however, abdominal bloating was higher in the 25 g dose group compared to control (7% vs. 0%; $P=0.046$).

In response to this study, the European Food Safety Authority (EFSA) recently released a scientific opinion on extending the use of erythritol as a flavor enhancer to beverages (EFSA, 2015). Previously, the EU approval of erythritol did not include use in beverages due to concerns

of its laxative effects, particularly in children. The results of the study by Jacqz-Aigrain et al. (2015) revealed that the age of the consumer has no impact upon the sensitivity to the laxative effects of erythritol; based on this data, the NOEL for laxation is similar between adults and children consuming bolus doses of erythritol, estimated at 780 and 710 mg/kg body weight, respectively (EFSA, 2015). The EFSA panel concluded that the consumption of erythritol at a maximum use-level of 1.6% would not raise concerns for laxation in children or adults, as the resulting acute bolus intake calculated in children (600 mg/kg body weight) was lower than the NOEL for laxation (710 mg/kg body weight) determined by Jacqz-Aigrain et al. (2015).

Although under the proposed uses of erythritol, male and female adults are estimated to consume up to 815 and 817 mg/kg body weight/day, respectively (90th percentile), and infants and young children are estimated to consume 2,816 mg/kg body weight/day (90th percentile), consideration must be given to the fact that these values were calculated based on daily consumption over multiple eating occasions, not single bolus doses. It is highly unlikely that the NOEL for laxation would be reached in a single eating occasion. For example, a 16 oz. (473mL) beverage in the U.S. containing erythritol at the maximum use-level of 3.5% for "Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages" would provide 16.5 g of erythritol per serving. In children, bolus doses containing a minimum of 20 g of erythritol have been shown to cause laxation (Jacqz-Aigrain et al., 2015) and EFSA recognized 0.71 g/kg bw (710 mg/kg bw) as a NOEL in children consuming a bolus dose; therefore, a child would need to consume 720 mL of a 3.5% erythritol sweetened beverage in a single serving to reach levels of intake that would induce laxation. This level of beverage consumption is an extremely unlikely scenario, as the volume of liquid that would be consumed in one sitting would equate to approximately 75% of the mean daily fluid intake for a child.

This is further supported by the intake assessment conducted based on the U.S. NHANES (2013-2014) dataset. Children up to 3 years of age had estimated intake mean and 90th percentile intakes of 4.1 and 8.4 g/day, respectively, from Reduced and Low-Calorie Carbonated and Non-Carbonated Beverages or 292 mg/kg bw/day and 669 mg/kg bw/day for the mean and 90th percentile users. In children 4-11 years of age, the mean and 90th percentile intake was 5.4 g/day and 8.7 g/day, respectively, or 171 mg/kg bw/day and 310 mg/kg bw/day. These are intakes below those that would be expected to cause GI Effects (Intertek, 2018). Furthermore, use of the U.S. NHANES (2013-2014) dataset resulted in estimates of current uses and use-levels for infants and young children up to 2816 mg/kg body weight/day of erythritol (90th percentile). Since 2011, to date there have been no reported instances of GI intolerance (laxation) within infants and children in the U.S. Therefore, on the basis that erythritol has had widespread use in beverages and foods in the U.S. for over a decade without any reported laxative effects in both children and adults, it is considered unlikely that such effects would manifest themselves at the similar intake levels that were estimated for the proposed uses of Cargill (Tetzloff et al., 1996).

Diabetes Studies

The potential for erythritol to act as an effective sugar substitute for patients with type 2 diabetes has been evaluated in a number of studies in recent years. A study in Japan set out to evaluate the effect of the erythritol containing sweetener Pal Sweet Calorie Zero® (PZ) on postprandial blood glucose levels in previously untreated mild diabetics or borderline diabetics

(Fukada et al., 2010). PZ sweetener is composed of 98.98% erythritol, 0.25% acesulfame K, and 0.58% aspartame and is commonly used in Japan. The study was a randomized, double-blind, crossover trial where meals were sweetened with glucose (control) or PZ at equivalent sweetness levels. Subjects (23 male, 10 females; aged 20 to 65 years), participated in 4 meal challenges, 2 controls and 2 PZ sweetened (meal 1, ~11 g erythritol, ~0.18 g/kg; meal 2, ~17 g erythritol, ~0.28 g/kg), with a washout period of 2 weeks between the consumption of each test meal. Blood was collected once before the meal challenge and 5 times postprandially (0.5, 1, 1.5, 2, and 3 hours). Sweetening meals with PZ was found to significantly suppress postprandial rises in blood glucose compared to control (meals 1 and 2, $P<0.001$) in addition to significantly lowering levels of insulin and C-peptide (meals 1 and 2, $P<0.001$), whereas free fatty acid concentrations were found to increase (meal 1, $P<0.1$; meal 2 $P<0.001$). The authors concluded that PZ sweetener shows promise as an effective sugar substitute for borderline diabetics and that the ability of PZ sweetener to prevent postprandial rises in blood glucose should be investigated in diabetic patients undergoing treatment.

Hyperglycemia in patients with type 2 diabetes is associated with a number of diabetic complications including cardiovascular disease. Endothelial dysfunction is thought to be involved in such vascular diabetic complications. Erythritol was found to prevent endothelial dysfunction in a study with diabetic rats (den Hartog et al., 2010). Following induction of diabetes mellitus in Wistar rats by streptozotocin (STZ) administration, rats (5/sex/group) were treated with 1,000 mg/kg body weight/day of erythritol in the drinking water for 3 weeks or consumed normal drinking water as the control group. Thoracic aortas were collected and aortic rings prepared to study endothelial contraction and relaxation. It was found that the endothelium of the diabetic rats in the control group was damaged, preventing proper relaxation, whereas erythritol-treated diabetic rats did not display endothelial damage and endothelial relaxation was restored to normal levels; however, these findings did not reach statistical significance.

The preclinical findings have been extended to an open-label pilot study in humans, where vascular function was assessed in patients with type 2 diabetes (11 males, 13 females, mean age 56 ± 5 years) after 4 weeks of erythritol intake (36 g/day, 12 g of powder dissolved in 8 oz water, 3 times per day) (Flint et al., 2014). An acute-on-chronic scenario was also generated for all patients, where 24 g of erythritol was given as the last dose and assessment was carried out 2 hours later. Vascular function was evaluated and biochemical measurements obtained at baseline and endpoint. Acute consumption of 24 g of erythritol led to improved fingertip endothelial function compared to baseline ($P=0.005$), whereas chronic erythritol intake led to a reduction in arterial stiffness ($P=0.02$). Furthermore, chronic erythritol exposure appeared to have an anti-hypertensive effect on those patients with higher blood pressure, as measured by central pulse pressure ($P=0.004$). The results from this pilot study suggest that erythritol did improve vascular function in patients with type 2 diabetes, but a randomized, placebo-controlled was recommended before definitive conclusions could be made.

Overall, based upon the safety evaluations conducted in the previous GRAS determinations and notifications on erythritol, and the recent survey of the scientific literature, there is no evidence to indicate or suggest that erythritol, under the current conditions of use, would be associated with any adverse health effects. Therefore, erythritol is considered safe for use in food for human

consumption, and its safe use has been confirmed by regulatory bodies and governmental agencies such as JECFA, EFSA, and FDA.

Safety Data Summary

Erythritol is a naturally-occurring compound found in a variety of foods and beverages including melons, pears, grapes, soy sauce, wine, miso paste, and sake. It also exists endogenously in tissues and body fluids of human and animals (Niwa et al., 1993; Goosens and Roper, 1994). Erythritol has had widespread use in beverages and foods in the U.S. for more than a decade without any reported adverse health effects in children and adults, at the dietary exposure levels that have been in practice over that time. Numerous erythritol ingredients are recognized as GRAS for their intended uses in foods, and several erythritol GRNs have received "no questions" letters from the Food and Drug Administration (FDA). Erythritol is considered GRAS for use as a flavor enhancer, formulation aid, humectant, nutritive sweetener, stabilizer and thickener, sequestrant and texturizer in a variety of foods. It has been used in the following human foods: bakery fillings, cakes and cookies, chewing gum, dairy drinks, fat-based cream used in modified fat/calorie cookies, pastries, hard candies, frozen dairy desserts, puddings, reduced and low-calorie beverages, soft candies, sugar substitutes, yogurt, and others.

A recent exposure assessment resulted in estimated mean and 90th percentile intakes of erythritol (on an all-user basis) for the total population from all proposed food-uses in the U.S. of 32.1 g/person/day (551 mg/kg body weight/day) and 63.0 g/person/day (1,179 mg/kg body weight/day), respectively. The intake methodology employed is generally considered to be 'worst case' as a result of several conservative assumptions made in the consumption estimates. For example, it is often assumed that all food products within a food category contain the ingredient at the maximum specified level of use. Furthermore, it is often assumed that all food products within a food category contain the ingredient at the maximum specified level of use; however, a significant number of other polyols are available on the market to manufacturers to formulate food products, so it is unlikely that erythritol would be used at the maximum use-level in every food use category. In addition, it is well established that the length of a dietary survey affects the estimated consumption of individual users. Short-term surveys, such as the typical 2- or 3-day dietary surveys, may overestimate the consumption of food products that are consumed relatively infrequently. Survey duration has been shown to affect the estimated percent of consumers, as well as the classification of individuals as high or low consumers of a given food. Shorter surveys are associated with misclassification of individuals, inaccurate correlation coefficients, reduced power, and overestimation of percentage of high and low intakes. The impact of the length of dietary surveys on the user consumption of different types of food products has been investigated and in general, user mean consumption was found to decrease over the length of the study, depending on the food type, and overall the average decrease in the mean or 90th percentile consumption was found to be 1.9- to 2-fold. Applying the above model, actual intakes for the user population mean and 90th percentile levels are likely in the range of 16.1 g/day (275.5 mg/kg body weight/day) and 31.5 g/day (589.5 mg/kg body weight/day), respectively. These estimates are similar to the EDI per user for all intended uses of erythritol previously calculated by FDA to be 13 g/day at the mean and 30 g/day at the 90th percentile (US FDA, 2001). For most food uses, intake of this much erythritol would be unlikely and studies

show that intakes at this level (i.e.., 30 g/day) spread over the entire day are unlikely to cause GI intolerance (Storey et al., 2007; Oku and Nakamura, 2007).

Regulatory authorities have reviewed the safety of erythritol and found it to be safe for use in human food. Numerous studies and publications support the safety of erythritol, including *in vitro* studies, *in vivo* animal studies, and clinical studies in humans. A summary of the most relevant studies on erythritol ADME, acute and subchronic toxicity, reproductive and developmental toxicity, mutagenicity and genotoxicity, chronic toxicity, carcinogenicity in animals along with clinical studies have been summarized and reviewed. The available published scientific data on the safety of erythritol in animals and man are extensive. The compositional profile of erythritol presents no obvious safety concerns. As a result, erythritol has been reviewed and approved around the world for addition to food for human consumption. In summary, the published study data, additional unpublished supporting data, and previous reviews by regulatory authorities (e.g., GRN Nos. 76, 208, 382, 401), support the conclusion that Cargill's erythritol ingredient is safe for use as a sweetener, at the proposed use levels foods.

Basis for the GRAS Determination

Introduction

The regulatory framework for determining whether a substance can be considered generally recognized as safe (GRAS) in accordance with section 201(s) (21 U.S.C. § 321(s)) of the Federal Food, Drug, and Cosmetic (FD&C) 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 erythritol for use in human food is GRAS based upon 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 FD&C Act.

General Recognition of the Safety of Erythritol

The intended use of erythritol 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:

- The erythritol product that is the subject of this GRAS determination is a polyol or sugar alcohol and is found in foods and beverages such as melons, pears, grapes, soy sauce, wine, miso paste, and sake. It also exists endogenously in tissues and body fluids of human and animals.

- The erythritol manufacturing process includes fermentation and purification steps, and these steps in processing have been reviewed and employed for over a decade. Erythritol is manufactured consistent with cGMP for food (21 CFR Part 110). The raw materials and processing aids used in the manufacturing process are food grade and/or commonly used in food manufacturing processes.

- There is common knowledge of a long history of human consumption of erythritol. Erythritol is currently marketed for use in reduced sugar/calorie foods such as confectionary, bakery products, and beverages. Numerous erythritol ingredients are recognized as GRAS for their intended uses in foods (e.g., GRN Nos. 76, 208, 382, 401), and the erythritol ingredients have received "no questions" letters from the FDA.

- Accounting for the conservative assumptions in the current intake assessment (i.e., short survey duration, maximum use level applied to all foods, all identified foods contain only erythritol as sweetener, individuals consume all identified foods every day), actual intake estimates are similar to the EDI per user of all intended uses of erythritol previously calculated by FDA to be 13 g/day at the mean and 30 g/day at the 90th percentile (US FDA 2001).

- Numerous studies and publications support the safety of erythritol, including *in vitro* studies, *in vivo* animal studies, and clinical studies in humans. The relevant studies covered all toxicological endpoints relevant to human oral consumption and included ADME, acute and subchronic toxicity, reproductive and developmental toxicity, mutagenicity and genotoxicity, chronic toxicity, and carcinogenicity in animals and/or humans.

- Erythritol 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 erythritol 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 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) or fructooligosaccharides such as inulin.

- Regulatory authorities (e.g., SCOGS, EFSA, FDA) have reviewed studies on the composition and safety of erythritol and found no issues of concern associated with their current use levels in a wide range of human foods.

- Therefore, the publicly available scientific literature on the safety of erythritol in animal and human studies, as well its history of consumption in human food, is extensive and sufficient to support the safety and GRAS status of the proposed uses in human food.

Since 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 erythritol that is the subject of this self-determination has been made through the deliberations of an Expert Panel convened by Cargill and comprised of Michael Carakostas, DVM, Ph.D., Stanley M. Tarka, Jr., Ph.D., F.A.T.S., and Thomas Vollmuth, Ph.D. These individuals are qualified by scientific training and experience to evaluate the safety of substances intended to be added to animal foods. They have critically reviewed and evaluated the publicly available information summarized in this document and have individually and collectively concluded that erythritol, produced consistent with cGMP and meeting the specifications described herein, is safe under its intended conditions of use. The Panel further unanimously concluded that the use of erythritol in human food is GRAS based on scientific procedures, and that other experts qualified to assess the safety of animal food and feed additives would concur with these conclusions. The Panel's GRAS opinion is included as Exhibit 1 to this document.

It is also Cargill's opinion that other qualified scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion. Cargill has concluded that erythritol 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.

Cargill is not aware of any information that would be inconsistent with a finding that the proposed use of erythritol 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.

§ 170.250 Part 7, Supporting Data and Information

The following references are all generally available, unless otherwise noted. Appendix B - D and Exhibit 1 (analytical information and data for erythritol, intake assessment report, signed Expert Panel report) are not generally available, but are attached for reference.

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44

APPENDIX A

Food Chemicals Codex Specifications

45

Three pages have been removed in accordance with copyright laws. The removed reference is:

Food Chemical Codex (10th edition) monograph for erythritol. Please see https://www.foodchemicalscodex.org/

APPENDIX B

Technical Product Sheet

Technical Data

Zerose™ Erythritol
STANDARD GRANULAR

Product Description
Zerose™ erythritol standard granular is a high purity, white crystalline powder of erythritol produced by fermentation of carbohydrates.

Application / Functionality
Zerose™ erythritol standard granular is recommended for use in sugar-free, calorie-reduced, sugar-reduced crystallized confectionery, fruit preparations, jams, baked goods, condiments, sauces, toppings, syrups, chocolate coatings, frozen dairy and non-dairy desserts, and beverages. It provides taste improvement and qualitative synergy to high potency sweeteners in soft drinks and helps to mask the bitter taste in beverages, providing greater shelf stability.

Chemical and Physical Data

Purity (%)	≥ 99.50
Ribitol & Glycerol (%)	≤ 0.10
Moisture (%)	≤ 0.15
pH	5.0 – 7.0
Reducing Sugars (%)	≤ 0.30
Granulation	
< 250µm (%)	≤ 20.0
Lead (ppm)	≤ 0.5

Microbiological Data

Total Plate Count (cfu/g)	≤ 300
Yeast (cfu/g)	≤ 50
Mold (cfu/g)	≤ 50

Nutritional Information

Calories	0	Cal/100g
Calories from Fat	0	Cal/100g
Total Fat	0	g/100g
Saturated Fat	0	g/100g
Trans Fat	0	g/100g
Cholesterol	0	mg/100g
Sodium	1.1	mg/100g
Potassium	0.3	mg/100g
Total Carbohydrates	99.9	g/100g
Sugar Alcohols	99.9	g/100g
Dietary Fiber	0	g/100g
Sugars	<0.3	g/100g
Protein	0	g/100g
Calcium	2.3	mg/100g
Iron	0.1	mg/100g
Phosphorus	0.2	mg/100g
Magnesium	0.4	mg/100g
Zinc	0.4	mg/100g
Ash	<0.1	g/100g

This product is not a significant source of Vitamin A, Vitamin C, Thiamine, Niacin, or Riboflavin.

Nutritional values are typical and not analyzed every lot. These values are from a combination of calculations and analytical data.

Allergen Status
In accordance with the 2004 USA Food Allergen Labeling and Consumer Protection Act (FALCPA), no allergen declarations are required for this product.

This information reflects US requirements for ingredients and allergens declaration. For countries other than US, please consult with local Cargill regulatory group.

Storage / Shelf-life

Product should be stored in a clean, dry, and odor-free area at ambient temperature and humidity.

The recommended best before date for Zerose™ erythritol standard granular under these conditions and in original unopened packaging is 3 years from the date of manufacture. For product in super sacks, the recommended best before date is 2 years from the date of manufacture. Product stored beyond the best before date should be evaluated periodically for fitness of use.

Packaging: 20 kg. paper bags with inside PE lining and super sacks

Applicable Certifications

Certified Kosher by the Orthodox Union (OU)

Certified Halal by the Islamic Food and Nutrition Council of America (IFANCA)

Additional Information

Material Numbers:

100010712	20 kg. bag
100010722	1000 kg. super sack

SAP Material Name:
ZEROSE™ ERYTHRITOL STD GRAN

Legacy #: 16952

Country of Origin: USA

Regulatory Status

Zerose™ erythritol standard granular is produced in accordance with current food Good Manufacturing Practices (GMPs) under a comprehensive Hazard Analysis and Critical Control Points (HACCP) program and in compliance with applicable parts of 21 CFR, part 110 of the Code of Federal Regulations.

Zerose™ erythritol standard granular complies with the Food Chemicals Codex 9th edition (FCC IX) monograph for Erythritol.

Foods that contain erythritol as the only sweetener or in combination with another sugar alcohol and that otherwise comply with 21 CFR paragraph 101.80 may bear the non-cariogenicity dental health claim in labeling.

Flavor / Flavor Modifier Use

Zerose™ erythritol standard granular has the status of Generally Recognized As Safe (GRAS), in accordance with the Flavor and Extract Manufacturers Association (FEMA) of the United States, when used as a flavor modifier in selected beverage categories, up to 1.25%. Please contact Customer Service for more details.

Ingredient Use

Ingredient: erythritol

Zerose™ erythritol standard granular has the status of Generally Recognized As Safe (GRAS), in accordance with United States Food and Drug Administration (US FDA) regulations for use as a direct food substance, when used in accordance with the table below:

Regulatory Status, cont.

Baked Goods and Baking Mixes	
• Baked Goods and Baking Mixes (excluding regular bread); Bars (Granola, High Protein); Cookies	15%
• Cakes	25%
Beverages, Alcoholic	
• Alcoholic Beverages (Lite Beer, Coolers)	3.5%
Beverages and Beverage Bases	
• Flavored Quenchers	6%
• Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages (excluding soy-based drinks and flavored quenchers)	3.5%
Breakfast Cereals	
• Hot Cereal – Oatmeal (Instant or Cooked)	3%
• Ready-to-Eat Cereals	10%
Chewing Gum	75%
Condiments and Relishes	
• BBQ Sauce; Tomato Sauces	15%
Dairy Product Analogs	
• Imitation Dairy Drinks (Soy-Based)	6%
• Non-Dairy Toppings	10%
Fats and Oils	
• Low Calorie Salad Dressings	15%
Frozen Dairy Desserts and Mixes	
• Frozen Desserts(Regular Ice Cream, Soft Serve, and Sorbet)	10%
Fruit and Water Ices	
• Fruit-Based Slushies	5%
Gelatins, Puddings, and Fillings	
• Fillings (Fruit, Custard, Cream, Pudding)	15%
• Puddings (Instant, Phosphate Set)	10%
Hard Candy (Mints, Pressed, Candies, Cough Drops)	99%
Jam and Jellies	15%
Milk Products	
• Dairy Drinks (Chocolate and Flavored Milks)	3.5%
• Fat-Based Cream Used in Modified-Fat or Low-Calorie Cookies, Cakes, and Pastries	60%
• Yogurt (Regular and Frozen Yogurt)	7.5%
Processed Fruits and Fruit Juices	
• Fruit-Based Smoothies	7%
Snack Foods	
• Salty Snacks	10%
Soft Candy	
• Fruit Novelty Snacks (e.g., fruit peel, fruit candy bar, fruit leathers, fruit creams, fruit snack candy, gummy fruits); Non-Chocolate Candies; Soft Chocolate Candies	45%
Sugar Substitutes	100%
Sweet Sauces, Toppings, and Syrups	
• Canned Fruit (Syrup); Regular or Low-Calorie Syrups or Toppings	15%

Claims: *The labeling, substantiation and decision making of all claims for your products is your responsibility. We recommend you consult regulatory and legal advisors familiar with all applicable laws, rules and regulations prior to making labeling and claims decisions.*

Contact

Cargill, Incorporated
Corn Milling North America
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Wayzata, MN 55391

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www.CargillFoods.com

APPENDIX C

Analytical Results

				Absorbance @ 420nm	Absorbance @ 720nm	Appearance	Ash	Color
			Min Spec			PASS TEST		
			Max Spec	0.03	0.03		0.01	0.03
			Unit				%	
	Material Code	Batch	Inspection Start Date					
Standard Granular Erythritol	100010712	(b) (4)	1/23/2017	0	0	PASS TEST	0	0
Standard Granular Erythritol	100010712		2/15/2017	0	0	PASS TEST	0	0
Standard Granular Erythritol	100010712		3/31/2017	0	0	PASS TEST	0	0

Infrequent Parameter verification				Residue On Ignition	Loss on Drying
Standard Granular Erythritol	100010712	(b) (4)	4/11/2014	<0.1%	0.01%
Standard Granular Erythritol	100010712		3/20/2015	<0.1%	0.15%
Standard Granular Erythritol	100010712		4/18/2016	<0.1%	0.09%

Erythritol	Foreign Material - COA	Arsenic	Lead	Less than 250 Micron	Mean Particle Size	Moisture	Nitrogen Content	pH
99.6	Pass Test			0	400	0	0	5
		1.3	0.5	20	700	0.15	2	7
%		ppm	ppm	%	Micron	%	ppm	
99.99	PASS TEST	0.1	0	7.3	540	0.04	0.5	5.4
99.99	PASS TEST	0	0	8.9	468	0.01	0.56	5.42
99.99	PASS TEST	0.1	0	7.6	535	0.06	0.22	5.4

Reducing Sugars	Ribitol + Glycerol	Sensory	Turbidity	Aerobic Plate Count	Yeast	Mold	Coliforms
0	0	PASS TEST	0	0	0	0	NEGATIVE
0.3	0.1		0.03	200	25	25	
%	%			cfu per gram	cfu per gram	cfu per gram	per 10 grams
0.01	0.01	PASS TEST	0	<10	<10	<10	NEGATIVE
0.02	0.01	PASS TEST	0	<10	<10	<10	NEGATIVE
0.01	0.01	PASS TEST	0	120	<10	<10	NEGATIVE

APPENDIX D

Human Intake Assessment

UPDATED ASSESSMENT OF THE ESTIMATED DAILY INTAKE OF ERYTHRITOL BY THE U.S. POPULATION FROM REVISED FOOD-USES AND USE-LEVELS (2013-2014 NHANES)

CONFIDENTIAL

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DATE:
04 May 2018

Updated Assessment of the Estimated Daily Intake of Erythritol by the U.S. Population from Revised Food-Uses and Use-Levels (2013-2014 NHANES)

TABLE OF CONTENTS

List of Tables

Updated Assessment of the Estimated Daily Intake of Erythritol by the U.S. Population from Revised Food-Uses and Use-Levels (2013-2014 NHANES)

1.0 INTRODUCTION

In 2015, Cargill proposed to expand the use of their ingredient erythritol to various food and beverage products marketed in the United States (U.S.). Exposure from the expanded uses were critically evaluated by an Expert Panel of scientists, who concluded that under the conditions of current and proposed conditions of use, erythritol is Generally Recognized as Safe[1]. Cargill has since updated the use-level of erythritol in various food and beverage categories previously assessed in 2015, including flavored quenchers, ready-to-eat cereals, fruit-based slushies, and yogurt- and fruit-based smoothies. In addition, for the following food categories, the expanded food-uses have been refined: reduced- and low-calorie carbonated and non-carbonated beverages (excluding soy-based drinks), imitation dairy drinks (soy, almond, cashew, coconut, and other plant-based), and frozen desserts (regular ice cream, soft serve, sorbet, frozen yogurt). Thus, an updated intakes assessment using the latest release of the U.S. National Health and Nutrition Examination Surveys (NHANES) 2013-2014 was conducted.

Estimates for the intake of erythritol were based on the proposed food-uses and use-levels for erythritol in conjunction with food consumption data included in the U.S. National Center for Health Statistics (NCHS)'s NHANES 2013-2014. Calculations for the mean and 90th percentile *per capita* and consumer-only intakes were performed for all proposed food-uses of erythritol and the percentage of consumers were determined. Similar calculations were used to estimate the intake of erythritol resulting from each individual proposed food-use, including the calculations of percent consumers. In both cases, the per person and per kilogram body weight intakes were reported for the following population groups:

- Infants and young children, up to and including 3 years;
- Children, ages 4 to 11;
- Female teenagers, ages 12 to 19;
- Male teenagers, ages 12 to 19;
- Female adults, ages 20 and up;
- Male adults, ages 20 and up; and
- Total population (all age and gender groups combined).

2.0 FOOD CONSUMPTION SURVEY DATA

2.1 Survey Description

NHANES for the years 2013-2014 are available for public use (USDA, 2014, 2016; CDC, 2015a,b, 2016). NHANES are conducted as continuous, annual surveys, and are released in 2-year cycles. During each year

[1] Cargill (2015) [unpublished]. *Expert Panel Consensus Statement Concerning the Generally Recognized as Safe (GRAS) Determination of Expanded Uses of Erythritol as an Ingredient in Food: Proprietary & Confidential.* Wayzata (MN):Cargill, Inc.

of the ongoing NHANES program, individuals from the U.S. are sampled from up to 30 different study locations in a complex multi-stage probability design intended to ensure the data are a nationally representative sample of the U.S. population.

NHANES 2013-2014 dietary survey data were collected from individuals and households *via* 24-hour dietary recalls administered on 2 non-consecutive days (Day 1 and Day 2) throughout all 4 seasons of the year. Day 1 data were collected in-person, and Day 2 data were collected by telephone in the following 3 to 10 days, on different days of the week, to achieve the desired degree of statistical independence. The data were collected by first selecting Primary Sampling Units (PSUs), which were counties throughout the U.S., of which 30 PSUs are visited per year. Smaller contiguous counties were combined to attain a minimum population size. These PSUs were segmented, and households were chosen within each segment. One or more participants within a household were interviewed. For NHANES 2013-2014, 14,332 individuals were selected for the sample, 10,175 were interviewed (71.0%), and 9,813 were examined (68.5%).

In addition to collecting information on the types and quantities of foods being consumed, NHANES 2013-2014 collected socio-economic, physiological, and demographic information from individual participants in the survey, such as sex, age, body weight, and other variables (including height and race-ethnicity) that may be useful in characterizing consumption. The inclusion of this information allows for further assessment of food intake based on consumption by specific population groups of interest within the total population. The primary sample design for NHANES 2013-2014 includes an oversample of non-Hispanic Asian persons, Hispanic persons, non-Hispanic black persons, older adults, and "low income whites/others"; however, sample weights were incorporated to allow estimates from these subgroups to be combined to obtain national estimates that reflect the relative proportions of these groups in the population as a whole (USDA, 2014, 2016; CDC, 2015a,b, 2016).

2.2 Statistical Methods

For the intake assessment, consumption data from individual dietary records, detailing food items ingested by each survey participant, were collated by computer and used to generate estimates for the intake of erythritol by the U.S. population[2]. Estimates for the daily intake of erythritol represent projected 2-day averages for each individual from Day 1 and Day 2 of NHANES 2013-2014; these average amounts comprised the distribution from which mean and percentile intake estimates were determined. Mean and percentile estimates were generated incorporating survey weights in order to provide representative intakes for the entire U.S. population. "*Per capita*" intake refers to the estimated intake of erythritol averaged over all individuals surveyed, regardless of whether they consumed food products in which erythritol is proposed for use, and therefore includes individuals with "zero" intakes (*i.e.*, those who reported no intake of food products containing erythritol during the 2 survey days). "Consumer-only" intake refers to the estimated intake of erythritol by those individuals who reported consuming food products in which the use of erythritol is currently under consideration. Individuals were considered "consumers" if they reported consumption of 1 or more food products in which erythritol is proposed for use on either Day 1 or Day 2 of the survey.

[2] Statistical analysis and data management were conducted in DaDiet Software (Dazult Ltd., 2018). DaDiet Software is a web-based software tool that allows accurate estimate of exposure to nutrients and to substances added to foods, including contaminants, food additives and novel ingredients. The main input components are concentration (use-level) data and food consumption data. Data sets are combined in the software to provide accurate and efficient exposure assessments.

Mean and 90th percentile intake estimates based on sample sizes of less than 30 and 80, respectively, may not be considered statistically reliable due to the limited sampling size (CDC, 2013). As such, the reliability of estimates for the intake of erythritol based on consumption estimates derived from individual population groups of a limited sample size should be interpreted with caution. These values are marked with an asterisk in the relevant data tables.

3.0 FOOD USAGE DATA

The proposed food-uses and use-levels for erythritol employed in the current intake analysis are summarized in Table 3-1. Food codes representative of each proposed food-use were chosen from the NHANES 2013-2014 (CDC, 2016). Food codes were grouped in food-use categories according to Title 21, Section §170.3 of the Code of Federal Regulations (CFR, 2017). Erythritol use-levels for the following food and beverage categories have been updated since the previous intakes assessment conducted in 2015: flavored quenchers, ready-to-eat cereals, fruit-based slushies, and yogurt and fruit-based smoothies (use-levels from the previous assessment are marked with ~~strikethrough~~ in Table 3-1). Additionally, the expanded food-uses from the 2015 assessment were further refined for the following food categories: reduced- and low-calorie carbonated and non-carbonated beverages, imitation dairy drinks, and frozen desserts (refinements are underlined in Table 3-1). If necessary, product-specific adjustment factors were developed for composite foods/mixtures based on data provided in the food and nutrient database for dietary studies (FNDDS) (USDA ARS, 2016) or the Food Commodity Intake Database (FCID) (U.S. EPA, 2018). All food codes included in the current intake assessment are listed in Appendix C.

Table 3-1 Summary of the Individual Proposed Food-Uses and Use-Levels for Erythritol in the U.S.

Food Category (21 CFR 170.3) (CFR, 2017)	Food-Uses	Erythritol Use-Levels (%)
Baked Goods and Baking Mixes	Baked Goods and Baking Mixes (excluding regular bread)	15
	Bars (Granola, High Protein)	15
	Cakes	25
	Cookies	15
Beverages, Alcoholic	Alcoholic Beverages (Lite Beer, Coolers)	3.5
Beverages and Beverage Bases	Flavored Quenchers	~~6~~ 3.5
	Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages (Excluding Soy-Based Drinks)	3.5
Breakfast Cereals	Hot Cereal – Oatmeal (Instant or Cooked)	3
	Ready-to-Eat Cereals	~~10~~ 30
Chewing Gum	Chewing Gum	75
Condiments and Relishes	BBQ Sauce	15
	Tomato Sauce	15
Dairy Product Analogs	Imitation Dairy Drinks (Soy, Almond, Cashew, Coconut, and Other Plant-Based Drinks)	6
	Non-Dairy Toppings	10
Fats and Oils	Low Calorie Salad Dressings	15
Frozen Dairy Desserts and Mixes	Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	10
Fruit and Water Ices	Fruit-Based Slushies	~~5~~ 3.5
Gelatins, Puddings, and Filings	Fillings (Fruit, Custard, Cream, Pudding)	15
	Puddings (Instant, Phosphate Set)	10
Hard Candy	Hard Candy (Mints, Pressed, Candies, Cough Drops)	99
Jams and Jellies	Jams and Jellies	15
Milk Products	Dairy drinks (Chocolate and Flavored Milks)	3.5
	Fat-Based Cream Used in Modified-Fat or Low-Calorie Cookies, Cakes and Pastries	60
	Yogurt	~~7.5~~ 5
Processed Fruits and Fruit Juices	Fruit-Based Smoothies	~~7~~ 3.5
Snack Foods	Salty Snacks	10
Soft Candy	Fruit Novelty Snacks (*e.g.*, Fruit Peel, Fruit Candy Bar, Fruit Leathers, Fruit Creams, Fruit Snack Candy, Gummy Fruits)	45
	Non-Chocolate Candies	45
	Soft Chocolate Candies	45
Sugar Substitutes	Sugar Substitutes	100
Sweet Sauces, Toppings, and Syrups	Canned Fruit (Syrup)	15
	Regular or Low-Calorie Syrups or Toppings	15

CFR = Code of Federal Regulations; U.S. = United States.

4.0 FOOD SURVEY RESULTS

Estimates for the total daily intakes of erythritol from proposed food-uses are provided in Tables 4.1-1 (g/person/day) and 4.1-2 (mg/kg body weight/day). Estimates for the daily intake of erythritol from individual proposed food-uses in the U.S. are summarized in Tables A-1 to A-7 and B-1 to B-7 of Appendices A and B, respectively. Tables A-1 to A-7 provide estimates for the daily intake of erythritol on an absolute basis (g/person/day), whereas Tables B-1 to B-7 provide estimates for the daily intake of erythritol on a per kilogram body weight basis (mg/kg body weight/day).

4.1 Estimated Daily Intake of Erythritol from All Proposed Food-Uses in the U.S.

Table 4.1-1 summarizes the estimated total intake of Erythritol (g/person/day) from all proposed food-uses in the U.S. population group. Table 4.1-2 presents this data on a per kilogram body weight basis (mg/kg body weight/day). The percentage of consumers was high among all age groups evaluated in the current intake assessment; more than 79.8% of the population groups consisted of consumers of food products in which erythritol is currently proposed for use (Table 4.1-1). Children had the greatest proportion of consumers at 99.9%. The consumer-only estimates are more relevant to risk assessments as they represent exposures in the target population; consequently, only the consumer-only intake results are discussed in detail herein.

Among the total population (all ages), the mean and 90th percentile consumer-only intakes of erythritol were determined to be 32.1 and 63.0 g/person/day, respectively. Of the individual population groups, male adults were determined to have the greatest mean and 90th percentile consumer-only intakes of erythritol on an absolute basis, at 35.6 and 69.6 g/person/day, respectively, while infants and young children had the lowest mean and 90th percentile consumer-only intakes of 20.6 and 41.3 g/person/day, respectively (Table 4.1-1).

Table 4.1-1 Summary of the Estimated Daily Intake of Erythritol from Proposed Food-Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants and Young Children	0 to <4	16.5	36.5	79.8	568	20.6	41.3
Children	4 to 11	34.2	58.1	99.9	1,155	34.2	58.1
Female Teenagers	12 to 19	28.1	52.3	99.0	571	28.3	53.3
Male Teenagers	12 to 19	33.7	62.1	97.1	552	34.7	62.9
Female Adults	20 and up	29.2	59.1	98.3	2,337	29.7	59.8
Male Adults	20 and up	34.6	69.1	97.2	2,035	35.6	69.6
Total Population	All ages	31.1	62.1	97.0	7,218	32.1	63.0

n = sample size; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

On a body weight basis, the total population (all ages) mean and 90th percentile consumer-only intakes of erythritol were determined to be 551 and 1,179 mg/kg body weight/day, respectively. Among the individual population groups, infants and young children were identified as having the highest mean and 90th percentile consumer-only intakes of any population group, of 1,512 and 2,816 mg/kg body weight/day, respectively. Female adults had the lowest mean consumer-only intakes of 405 mg/kg body weight/day,

whereas male adults had the lowest 90th percentile consumer-only intakes of 815 mg/kg body weight/day (Table 4.1-2).

Table 4.1-2 Summary of the Estimated Daily Per Kilogram Body Weight Intake of Erythritol from Proposed Food-Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (mg/kg bw/day)		Consumer-Only Intake (mg/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants and Young Children	0 to <4	1,206	2,681	79.7	563	1,512	2,816
Children	4 to 11	1,209	2,256	99.9	1,149	1,210	2,256
Female Teenagers	12 to 19	457	971	99.3	564	460	971
Male Teenagers	12 to 19	514	1,013	97.1	550	529	1,013
Female Adults	20 and up	398	815	98.3	2,323	405	817
Male Adults	20 and up	403	805	97.2	2,026	415	815
Total Population	All ages	535	1,159	97.0	7,175	551	1,179

bw = body weight; n = sample size; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.

4.2 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses in the U.S.

Estimates for the mean and 90th percentile daily intakes of erythritol from each individual food category are summarized in Tables A-1 to A-7 and B-1 to B-7 on a g/day and mg/kg body weight/day basis, respectively. The total U.S. population was identified as being significant consumers of baked goods and baking mixes (60 to 78% consumers), ready-to-eat cereals (29 to 59% consumers), salty snacks (32 to 51% consumers) and cookies (31 to 45% consumers).

In terms of contribution to total mean intake of erythritol, baked goods and baking mixes (which contributed 18 to 21% to total mean intakes), ready-to-eat cereals (which contributed 11 to 17% to total mean intakes), reduced- and low-calorie carbonated and non-carbonated beverages (which contributed 2 to 16% to total mean intakes) and flavored quenchers (which contributed 2 to 14% to total mean intakes) were the 4 main sources of intake across all population groups. Chewing gum, BBQ sauce, non-dairy toppings, low-calorie salad dressings, fillings, puddings, jam and jellies, sugar substitutes and regular or low-calorie syrups or toppings all individually contributed ≤1% to total mean erythritol intakes across all population groups (see Tables A-1 to A-7 for further details).

4.3 Comparison of Intake Estimates from Updated Food-Uses and Use-Levels to Intake Estimates from 2015

A comparison of the intake estimates for erythritol from the current assessment to those from the previous assessment conducted in 2015 are provided in Tables 4.3-1 and 4.3-2 on an absolute basis (g/person/day) and body weight basis (mg/kg body weight/day), respectively. The direction of effect (*i.e.*, increase or decrease in intakes) and percent change are **bolded** in Tables 4.3-1 and 4.3-2. Generally, intake estimates from the current assessment increased slightly compared to those from the previous intakes assessment conducted in 2015.

Among the total population (all ages), on an absolute basis, consumer-only intakes of erythritol increased by 4.6% at the mean and 4.3% at the 90th percentile in the current intake assessment *versus* the previous intake assessment. Of the individual population groups, consumer-only mean intakes increased by 1.4 to 15.7%, except in infants and young children wherein intakes decreased by 1.0%, and consumer-only 90th percentile intakes increased by 1.5 to 15.4%, except in female teenagers wherein intakes remained unchanged (Table 4.3-1). Notably, changes in consumer-only intakes from the current assessment *versus* the previous assessment were greatest in male teenagers (intakes increased by 15.7 and 15.4% at the mean and 90th percentile, respectively).

Table 4.3-1 Comparison Between Current and Previous Estimated Daily Intakes: Consumer-Only Absolute Consumption (g/person/day)

Population Group	Age Group (Years)	Previous Results (2015) – NHANES 2011-2012				Updated Results (2018) – NHANES 2013-2014				Percent Change from 2015	
		%	n	Intake (g/day)		%	n	Intake (g/day)			
				Mean	90th Percentile			Mean	90th Percentile	Mean	90th Percentile
Infants and Young Children	0 to 3	82.6	677	20.8	39.6	79.8	568	20.6	41.3	↓ 1.0%	↑ 4.3%
Children	4 to 11	100.0	1,348	31.6	54.5	99.9	1,155	34.2	58.1	↑ 8.2%	↑ 6.6%
Female Teenagers	12 to 19	98.1	524	25.7	53.3	99.0	571	28.3	53.3	↑ 10.1%	nc
Male Teenagers	12 to 19	98.6	508	30.0	54.5	97.1	552	34.7	62.9	↑ 15.7%	↑ 15.4%
Female Adults	20 and up	97.8	2,158	28.3	56.4	98.3	2,337	29.7	59.8	↑ 4.9%	↑ 6.0%
Male Adults	20 and up	97.4	2,010	35.1	68.6	97.2	2,035	35.6	69.6	↑ 1.4%	↑ 1.5%
Total Population	All ages	97.1	7,225	30.7	60.4	97.0	7,218	32.1	63.0	↑ 4.6%	↑ 4.3%

↑ = increase in intake; ↓ = decrease in intake; n = sample size; nc = no change.

On a body weight basis (mg/kg body weight/day), the total population (all ages) mean and 90th percentile consumer-only intakes of erythritol increased by 2.4 and 3.3% in the current assessment *versus* the previous assessment, respectively. Among the individual population groups, consumer-only intakes increased by 0.8 to 12.3% at the mean and 1.5 to 6.0% at the 90th percentile, except in male adults wherein high-level intakes decreased by 1.9% (Table 4.3-2). Changes in consumer-only intakes from the current assessment *versus* the previous assessment were greatest in male teenagers at the mean (intakes increased by 12.3%) and in female teenagers and adults at the 90th percentile (intakes increased by 6.0% in both population groups).

Table 4.3-2 Comparison Between Current and Previous Estimated Daily Intakes: Consumer-Only Per Kilogram Body Weight Consumption (mg/kg bw/day)

Population Group	Age Group (Years)	Previous Results (2015) – NHANES 2011-2012				Updated Results (2018) – NHANES 2013-2014				Percent Change from 2015	
		%	n	Intake (mg/kg bw/day)		%	n	Intake (mg/kg bw/day)			
				Mean	90th Percentile			Mean	90th Percentile	Mean	90th Percentile
Infants and Young Children	0 to 3	82.5	674	1,500	2,775	79.7	563	1,512	2,816	↑ 0.8%	↑ 1.5%
Children	4 to 11	100.0	1,348	1,144	2,147	99.9	1,149	1,210	2,256	↑ 5.8%	↑ 5.1%
Female Teenagers	12 to 19	98.1	513	450	916	99.3	564	460	971	↑ 2.2%	↑ 6.0%
Male Teenagers	12 to 19	98.6	505	471	977	97.1	550	529	1,013	↑ 12.3%	↑ 3.7%
Female Adults	20 and up	97.8	2,135	392	771	98.3	2,323	405	817	↑ 3.3%	↑ 6.0%
Male Adults	20 and up	97.4	1,992	408	831	97.2	2,026	415	815	↑ 1.7%	↓ 1.9%
Total Population	All ages	97.1	7,167	538	1,141	97.0	7,175	551	1,179	↑ 2.4%	↑ 3.3%

↑ = increase in intake; ↓ = decrease in intake; bw = body weight; n = sample size; nc = no change.

5.0 SUMMARY AND CONCLUSIONS

Consumption data and information pertaining to the individual proposed food-uses of erythritol were used to estimate the *per capita* and consumer-only intakes of erythritol for specific demographic groups and for the total U.S. population. There were a number of assumptions included in the assessment which render exposure estimates that may be considered suitably conservative. For example, it has been assumed in both exposure assessments that all food products within a food category contain erythritol at the maximum specified level of use. In reality, the levels added to specific foods will vary depending on the nature of the food product and it is unlikely that erythritol will have 100% market penetration in all identified food categories.

In summary, on a consumer-only basis, the resulting mean and 90th percentile intakes of erythritol by the total U.S. population from all proposed food-uses were estimated to be 32.1 and 63.0 g/person/day, respectively. The estimated intake of erythritol among the total U.S. population increased by 4.6% at the mean and 4.3% at the 90th percentile in the current intake assessment *versus* the previous intake assessment conducted in 2015. Among the individual population groups, the highest mean and 90th percentile consumer-only intakes of erythritol were determined to be 35.6 g/person/day (415 mg/kg body weight/day) and 69.6 g/person/day (815 mg/kg body weight/day), respectively, as identified among male adults. Infants and young children had the lowest mean and 90th percentile consumer-only intakes of 20.6 and 41.3 g/person/day, respectively. Compared to the previous assessment, consumer-only intakes in the current assessment were most affected in male teenagers, increasing by 15.7 and 15.4% at the mean and 90th percentile, respectively.

When intakes were expressed on a body weight basis, infants and young children had the highest mean and 90th percentile consumer-only intake of 1,512 mg/kg body weight/day (20.6 g/person/day) and 2,816 mg/kg body weight/day (41.3 g/person/day), respectively. Nonetheless, intake estimates for this population group increased by only 0.8% at the mean and 1.5% at the 90th percentile in the current assessment *versus* the previous assessment. Although younger populations were identified as the groups having higher exposures to erythritol on a body weight basis, it should be noted that products containing erythritol will not be targeted towards infants and young children, and estimates described herein assume *all* products, including those consumed by younger individuals, would contain the ingredient at the maximum intended use-levels. In actuality, these products would, in the worst case, only be consumed incidentally and intakes described in the older populations (*i.e.*, not more than 529 and 1,013 mg/kg body weight/day at the mean and 90th percentile, respectively) are expected to be more accurate estimates of dietary exposure among the intended population.

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Appendix A
Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Different Population Groups within the U.S. (2013-2014 NHANES Data)

Table A-1 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Infants and Young Children Aged Up to 3 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***16.5***	***36.5***	***79.8***	***568***	***20.6***	***41.3***
Baked Goods and Baking Mixes (excluding regular bread)	17.8	2.9	7.6	60.2	419	4.9	11.2
Bars (Granola, High Protein)	1.4	0.2	na	6.6	36	3.6	7.6*
Cakes	2.6	0.4	na	7.5	51	5.8	18.7*
Cookies	6.7	1.1	4.4	37.2	238	3.0	6.5
Alcoholic Beverages (Lite Beer, Coolers)	0	na	na	0	0	na	na
Flavored Quenchers	2.2	0.4*	na	4.6	22	7.9*	15.5*
Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages	2.3	0.4	na	9.4	61	4.1	8.4*
Hot Cereal – Oatmeal (Instant or Cooked)	1.8	0.3	0.9*	10.6	68	2.7	5.3*
Ready-to-Eat Cereals	14.4	2.4	7.6	46.0	302	5.2	10.4
Chewing Gum	0.2	<0.1*	na	1.2	13	2.1*	3.0*
BBQ Sauce	0.1	<0.1*	na	3.0	21	0.8*	1.6*
Tomato Sauce	1.1	0.2	0.7	17.6	110	1.1	2.3
Imitation Dairy Drinks (Soy, almond, cashew, coconut, and other plant-based)	5.4	0.9	na	6.3	30	14.2	39.0*
Non-Dairy Toppings	0	na	na	0	0	na	na
Low Calorie Salad Dressings	0.1	<0.1*	na	1.6	15	0.6*	1.1*
Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	3.8	0.6	2.5	16.9	119	3.7	7.4
Fruit-Based Slushies	0.4	0.1	na	7.1	48	1.0	1.9*
Fillings (Fruit, Custard, Cream, Pudding)	0	na	na	0	0	na	na
Puddings (Instant, Phosphate Set)	0.4	0.1*	na	1.2	10	4.8*	5.7*
Hard Candy (Mints, Pressed, Candies, Cough Drops)	5.4	0.9	na	9.0	46	9.8	29.7*
Jams and Jellies	1.0	0.2	0.5	13.9	80	1.2	2.1
Dairy drinks (Chocolate and Flavored Milks)	6.3	1.0	3.3	16.2	104	6.4	13.6
Yogurt	6.0	1.0	3.1	25.8	158	3.8	8.0
Fruit-Based Smoothies	0.7	0.1*	na	3.0	23	4.1*	4.9*
Salty Snacks	3.0	0.5	1.6	32.1	206	1.5	2.7
Fruit Novelty Snacks (*e.g.*, fruit peel, fruit candy bar, fruit leathers, fruit creams, fruit snack candy, gummy fruits)	8.2	1.3	na	9.5	58	14.2	68.6*
Non-Chocolate Candies	3.3	0.5	1.6*	10.9	57	5.0	10.8*
Soft Chocolate Candies	2.3	0.4	na	9.2	59	4.2	7.9*

Table A-1 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Infants and Young Children Aged Up to 3 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Sugar Substitutes	0.1	<0.1*	na	0.5	2	2.1*	2.9*
Canned Fruit (Syrup)	2.7	0.5	1.8*	12.3	70	3.7	6.7*
Regular or Low-Calorie Syrups or Toppings	0.3	<0.1	na	4.6	32	1.0	1.8*

n = sample size; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements (mean n<30; 90th percentile n<80).

Table A-2 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Children Aged 4 to 11 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***34.2***	***58.1***	***99.9***	***1,155***	***34.2***	***58.1***
Baked Goods and Baking Mixes (excluding regular bread)	20.9	7.2	17.9	77.5	896	9.2	19.7
Bars (Granola, High Protein)	1.1	0.4	1.6	12.1	117	3.0	6.0
Cakes	4.5	1.5	5.8	16.1	163	9.6	18.8
Cookies	5.3	1.8	6	44.8	498	4.1	9.0
Alcoholic Beverages (Lite Beer, Coolers)	0	na	na	0	0	na	na
Flavored Quenchers	3.8	1.3	3.3	13.0	120	10.0	19.8
Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages	3.8	1.3	4.8	24.5	247	5.4	8.7
Hot Cereal – Oatmeal (Instant or Cooked)	0.5	0.2	na	5.3	73	2.9	4.6*
Ready-to-Eat Cereals	13.9	4.8	12.7	59.3	701	8.0	16.1
Chewing Gum	0.3	0.1	na	4.7	55	2.1	4.5*
BBQ Sauce	0.4	0.1	na	6.8	100	1.8	4.2
Tomato Sauce	2.1	0.7	2.3	38.6	437	1.8	4.5
Imitation Dairy Drinks (Soy, almond, cashew, coconut, and other plant-based)	0.8	0.3	na	3.0	31	8.7	15.4*
Non-Dairy Toppings	<0.1	<0.1*	na	0.3	3	1.5*	1.8*
Low Calorie Salad Dressings	0.2	0.1	na	3.6	42	2.1	4.6*
Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	7.3	2.5	7.5	35.7	348	7.0	13.9
Fruit-Based Slushies	0.5	0.2	1.0	14.2	124	1.3	2.2
Fillings (Fruit, Custard, Cream, Pudding)	<0.1	<0.1*	na	<0.1	1	5.0*	5.0*
Puddings (Instant, Phosphate Set)	0.4	0.1*	na	1.7	24	7.6*	15.1*
Hard Candy (Mints, Pressed, Candies, Cough Drops)	4.9	1.7	3.5	15.5	157	10.9	20.8
Jams and Jellies	0.8	0.3	1.1	18.0	205	1.4	2.8
Dairy drinks (Chocolate and Flavored Milks)	7.2	2.5	8.7	39.2	463	6.3	12.6
Yogurt	2.9	1.0	4.3	21.9	233	4.5	8.8
Fruit-Based Smoothies	0.7	0.2	na	4.7	58	5.1	8.6*
Salty Snacks	3.4	1.2	3.3	50.8	566	2.3	5.0
Fruit Novelty Snacks (*e.g.*, fruit peel, fruit candy bar, fruit leathers, fruit creams, fruit snack candy, gummy fruits)	3.2	1.1	4.7	14.5	143	7.6	11.7
Non-Chocolate Candies	4.2	1.4	4.1	18.3	203	7.9	18.2
Soft Chocolate Candies	4.3	1.5	4.1	21.5	220	6.9	16.1

Table A-2 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Children Aged 4 to 11 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Sugar Substitutes	<0.1	<0.1*	na	0.9	7	0.4*	0.6*
Canned Fruit (Syrup)	1.6	0.5	1.84	12.3	151	4.4	11.6
Regular or Low-Calorie Syrups or Toppings	1.0	0.3	0.38	10.9	125	3.2	7.9

n = sample size; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements (mean n<30; 90th percentile n<80).

Table A-3 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***28.1***	***52.3***	***99.0***	***571***	***28.3***	***53.3***
Baked Goods and Baking Mixes (excluding regular bread)	17.9	5.0	13.5	61.5	354	8.1	15.8
Bars (Granola, High Protein)	2.4	0.7	3.2*	17.0	68	4.0	6.3*
Cakes	5.5	1.5	1.8*	11.5	74	13.3	27.0*
Cookies	5.1	1.4	4.5	34.1	205	4.2	9.5
Alcoholic Beverages (Lite Beer, Coolers)	0.3	0.1*	na	0.9	2	8.4*	8.4*
Flavored Quenchers	3.7	1.1	na	9.2	55	11.4	20.6*
Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages	8.0	2.2	6.0	14.8	91	15.1	62.1
Hot Cereal – Oatmeal (Instant or Cooked)	0.6	0.2*	na	3.5	28	4.9*	7.7*
Ready-to-Eat Cereals	14.8	4.2	13.8	43.0	230	9.7	18.4
Chewing Gum	0.1	<0.1*	na	2.9	22	1.2*	1.5*
BBQ Sauce	0.9	0.2	na	7.5	48	3.2	10.3*
Tomato Sauce	1.6	0.4	1.1	26.7	134	1.7	4.5
Imitation Dairy Drinks (Soy, almond, cashew, coconut, and other plant-based)	0.7	0.2*	na	2.0	22	9.2*	20.2*
Non-Dairy Toppings	0	na	na	0	0	na	na
Low Calorie Salad Dressings	0.8	0.2*	na	8.4	23	2.6*	5.0*
Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	6.1	1.7	6.0	24.3	125	7.1	12.0
Fruit-Based Slushies	0.3	0.1*	na	2.6	13	2.9*	4.8*
Fillings (Fruit, Custard, Cream, Pudding)	0	na	na	0	0	na	na
Puddings (Instant, Phosphate Set)	0.5	0.1*	na	1.8	9	8.1*	11.3*
Hard Candy (Mints, Pressed, Candies, Cough Drops)	5.3	1.5	na	8.5	54	17.6	52.7*
Jams and Jellies	0.5	0.2	na	9.6	44	1.6	2.1*
Dairy drinks (Chocolate and Flavored Milks)	5.0	1.4	6.1	20.2	114	7.0	12.7
Yogurt	2.4	0.7	2.3*	14.8	61	4.5	9.5*
Fruit-Based Smoothies	1.8	0.5*	na	5.7	24	9.0*	19.1*
Salty Snacks	3.8	1.1	3.2	40.9	262	2.6	5.6
Fruit Novelty Snacks (*e.g.*, fruit peel, fruit candy bar, fruit leathers, fruit creams, fruit snack candy, gummy fruits)	1.8	0.5	na	6.4	39	7.8	15.4*
Non-Chocolate Candies	4.3	1.2	na	9.5	51	12.6	26.3*
Soft Chocolate Candies	3.9	1.1	3.7	18.3	110	6.0	15.4

Table A-3 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Sugar Substitutes	<0.1	<0.1*	na	1.1	5	1.1*	1.3*
Canned Fruit (Syrup)	1.4	0.4	0.7*	10.6	32	3.6	6.6*
Regular or Low-Calorie Syrups or Toppings	0.5	0.1*	na	4.8	22	3.0*	6.0*

n = sample size; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements (mean n<30; 90th percentile n<80).

Table A-4 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***33.7***	***62.1***	***97.1***	***552***	***34.7***	***62.9***
Baked Goods and Baking Mixes (excluding regular bread)	20.8	7.0	18.5	60.2	346	11.7	24.5
Bars (Granola, High Protein)	1.5	0.5	1.8*	12.3	52	4.1	10.2*
Cakes	3.5	1.2	na	8.7	54	13.6	29.8*
Cookies	5.6	1.9	5.3	34.5	197	5.5	12.1
Alcoholic Beverages (Lite Beer, Coolers)	0.1	<0.1*	na	0.2	2	18.9*	18.9*
Flavored Quenchers	14.4	4.9	13.0	19.8	92	24.6	34.7
Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages	3.6	1.2	4.2	13.1	84	9.2	14.4
Hot Cereal – Oatmeal (Instant or Cooked)	0.5	0.2*	na	3.0	20	5.9*	12.2*
Ready-to-Eat Cereals	16.8	5.7	17.3	45.5	252	12.4	24.4
Chewing Gum	0.1	<0.1*	na	1.7	20	2.3*	4.1*
BBQ Sauce	0.9	0.3	0.6*	11.1	72	2.6	6.4*
Tomato Sauce	1.9	0.6	2.1	35.0	193	1.8	4.5
Imitation Dairy Drinks (Soy, almond, cashew, coconut, and other plant-based)	0.5	0.2*	na	1.2	12	13.4*	22.7*
Non-Dairy Toppings	0	na	na	0	0	na	na
Low Calorie Salad Dressings	0.3	0.1*	na	3.2	16	3.5*	4.9*
Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	6.1	2.0	7.9	19.8	109	10.4	19.0
Fruit-Based Slushies	<0.1	<0.1*	na	0.5	7	2.6*	4.0*
Fillings (Fruit, Custard, Cream, Pudding)	0	na	na	0	0	na	na
Puddings (Instant, Phosphate Set)	0.3	0.1*	na	0.8	5	12.6*	13.1*
Hard Candy (Mints, Pressed, Candies, Cough Drops)	2.0	0.7	na	5.9	42	11.4	14.9*
Jams and Jellies	0.6	0.2	na	6.3	48	3.0	5.7*
Dairy drinks (Chocolate and Flavored Milks)	5.6	1.9	6.0	24.3	143	7.8	15.5
Yogurt	0.7	0.2	na	5.3	34	4.4	7.4*
Fruit-Based Smoothies	0.6	0.2*	na	1.7	14	11.7*	18.8*
Salty Snacks	4.1	1.4	4.2	41.9	241	3.3	6.1
Fruit Novelty Snacks (*e.g.*, fruit peel, fruit candy bar, fruit leathers, fruit creams, fruit snack candy, gummy fruits)	0.6	0.2*	na	3.3	24	6.0*	11.7*
Non-Chocolate Candies	4.5	1.5	2.1*	10.7	65	14.2	27.5*
Soft Chocolate Candies	3.4	1.1	4.2	16.8	80	6.9	11.8

Table A-4 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Sugar Substitutes	<0.1	<0.1*	na	1.1	4	0.8*	1.2*
Canned Fruit (Syrup)	0.7	0.2	na	5.9	31	3.9	5.7*
Regular or Low-Calorie Syrups or Toppings	0.3	0.1*	na	3.1	20	3.6*	6.7*

n = sample size; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements (mean n<30; 90th percentile n<80).

Table A-5 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Female Adults Aged 20 Years and Over within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***29.2***	***59.1***	***98.3***	***2,337***	***29.7***	***59.8***
Baked Goods and Baking Mixes (excluding regular bread)	16.2	4.7	13.3	62.5	1,502	7.6	17.9
Bars (Granola, High Protein)	1.5	0.4	1.6	10.6	209	4.2	7.7
Cakes	6.6	1.9	7.3	15.7	392	12.2	24.9
Cookies	5.1	1.5	4.7	33.4	768	4.4	8.9
Alcoholic Beverages (Lite Beer, Coolers)	3.3	1.0	na	4.5	95	21.7	50.4
Flavored Quenchers	1.6	0.5	na	3.3	72	14.0	21.7*
Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages	18.6	5.4	18.3	27.7	552	19.6	45.6
Hot Cereal – Oatmeal (Instant or Cooked)	1.6	0.5	na	9.9	285	4.6	7.5
Ready-to-Eat Cereals	9.7	2.8	10.2	31.0	711	9.2	16.7
Chewing Gum	0.3	0.1	na	2.9	84	3.0	6.0
BBQ Sauce	0.7	0.2	na	8.4	204	2.4	4.7
Tomato Sauce	1.1	0.3	1.1	21.4	452	1.5	2.9
Imitation Dairy Drinks (Soy, almond, cashew, coconut, and other plant-based)	2.5	0.7	na	7.7	183	9.7	20.1
Non-Dairy Toppings	<0.1	<0.1*	na	1.2	27	0.8*	1.5*
Low Calorie Salad Dressings	0.7	0.2	na	8.8	178	2.3	4.6
Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	5.7	1.7	6.0	24.9	549	6.7	14.5
Fruit-Based Slushies	0.1	<0.1	na	1.1	37	1.6	2.9*
Fillings (Fruit, Custard, Cream, Pudding)	0	na	na	0	0	na	na
Puddings (Instant, Phosphate Set)	0.6	0.2	na	2.9	59	6.4	12.2*
Hard Candy (Mints, Pressed, Candies, Cough Drops)	2.4	0.7	na	7.0	137	10.2	28.3
Jams and Jellies	0.5	0.1	0.1	10.1	227	1.4	2.8
Dairy drinks (Chocolate and Flavored Milks)	2.1	0.6	na	8.7	222	7.1	13.7
Yogurt	3.8	1.1	4.3	20.2	411	5.5	9.9
Fruit-Based Smoothies	1.4	0.4	na	4.8	99	8.8	13.7
Salty Snacks	3.0	0.9	2.9	35.6	728	2.5	5.0
Fruit Novelty Snacks (*e.g.*, fruit peel, fruit candy bar, fruit leathers, fruit creams, fruit snack candy, gummy fruits)	0.4	0.1*	na	1.2	25	10.6*	25.0*
Non-Chocolate Candies	2.7	0.8	na	9.2	218	8.5	22.7
Soft Chocolate Candies	5.3	1.5	5.1	25.9	543	5.9	12.4
Sugar Substitutes	1.3	0.4	1.3	18.5	413	2.1	4.3

Table A-5 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Female Adults Aged 20 Years and Over within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Canned Fruit (Syrup)	0.8	0.2	na	6.4	150	3.8	7.1
Regular or Low-Calorie Syrups or Toppings	0.4	0.1	na	3.7	75	3.4	6.0*

n = sample size; na = not available; NHANES = National Health and Nutrition Examination Survey; U.S. = United States.
* Indicates an intake estimate that may not be statistically reliable, as the sample size does not meet the minimum reporting requirements (mean n<30; 90th percentile n<80).

Table A-6 Estimated Daily Intake of Erythritol from Individual Proposed Food-Uses by Male Adults Aged 20 Years and Over within the U.S. (2013-2014 NHANES Data)

Food-Use Category	% Contribution to Total Mean Intake	*Per Capita* Intake (g/day)		Consumer-Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
All	***100***	***34.6***	***69.1***	***97.2***	***2,035***	***35.6***	***69.6***
Baked Goods and Baking Mixes (excluding regular bread)	17.7	6.1	17.6	62.1	1,274	9.9	22.8
Bars (Granola, High Protein)	1.4	0.5	1.8	12.1	185	4.0	8.3
Cakes	5.8	2.0	6.8	15.0	323	13.4	28.0
Cookies	4.5	1.6	5.3	31.1	632	5.1	10.1
Alcoholic Beverages (Lite Beer, Coolers)	8.2	2.9	6.3	11.1	223	25.7	50.4
Flavored Quenchers	3.9	1.3	na	8.0	162	16.8	33.6
Reduced- and Low-Calorie Carbonated and Non-Carbonated Beverages	15.5	5.4	19.6	26.7	465	20.1	40.64
Hot Cereal – Oatmeal (Instant or Cooked)	1.3	0.4	na	7.3	197	6.0	12.07
Ready-to-Eat Cereals	11.2	3.9	14.2	28.5	574	13.6	25.5
Chewing Gum	0.2	0.1	na	2.9	48	2.0	4.5*
BBQ Sauce	1.0	0.4	0.9	12.1	215	2.9	6.52
Tomato Sauce	1.4	0.5	1.4	24.4	529	2.0	4.5
Imitation Dairy Drinks (Soy, almond, cashew, coconut, and other plant-based)	1.3	0.5	na	4.6	100	10.1	22.0
Non-Dairy Toppings	<0.1	<0.1*	na	1.3	11	1.3*	2.8*
Low Calorie Salad Dressings	0.4	0.1	na	3.9	103	3.2	7.7
Frozen Desserts (Regular Ice Cream, Soft Serve, Sorbet, Frozen Yogurt)	6.2	2.2	8.3	24.5	448	8.8	17.1
Fruit-Based Slushies	0.1	<0.1*	na	2.1	26	1.3*	1.9*
Fillings (Fruit, Custard, Cream, Pudding)	<0.1	<0.1*	na	0.2	1	1.7*	1.7*
Puddings (Instant, Phosphate Set)	0.7	0.2	na	2.3	30	10.9	19.5*
Hard Candy (Mints, Pressed, Candies, Cough Drops)	1.0	0.3	na	2.9	75	11.8	23.8*
Jams and Jellies	0.6	0.2	0.5	11.4	235	1.9	4.2
Dairy drinks (Chocolate and Flavored Milks)	1.9	0.7	na	8.7	175	7.6	14.2
Yogurt	1.9	0.7	2.7	11.5	224	5.9	12.3
Fruit-Based Smoothies	0.8	0.3	na	3.1	61	9.2	15.1*
Salty Snacks	3.1	1.1	3.6	31.5	569	3.4	7.3
Fruit Novelty Snacks (*e.g.*, fruit peel, fruit candy bar, fruit leathers, fruit creams, fruit snack candy, gummy fruits)	0.5	0.2*	na	1.3	25	12.8*	22.2*
Non-Chocolate Candies	2.9	1.0	na	7.7	139	13.3	31.5
Soft Chocolate Candies	4.8	1.7	5.6	21.2	413	7.9	15.4