GRAS Notice (GRN) No. 1141 with amendments
https://www.fda.gov/food/generally-recognized-safe-gras/gras-notice-inventory

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April 6, 2023

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

Dear Sir/Madam,

Pursuant to 21 CFR Part 170, Subpart E, Shenyang Gold Jyouki Technology Co., Ltd, through me as its agent, hereby provides the attached dossier to support their view that alpha-GPC under the conditions of intended use described in this Generally Recognized as Safe (GRAS) notice is not subject to premarket approval requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) based on Shenyang Gold Jyouki Technology Co., Ltd's conclusion through scientific procedures.

Shenyang Gold Jyouki Technology Co., Ltd proposes use of alpha-GPC as a nutrient in powdered beverage mixes, protein & nutritional powders, soft drinks, sport & energy drinks (21CFR 170.3(n)(2)), coffee and tea (21CFR 170.3(n)(7)), cereal, nutrition bars (21CFR 170.3(n)(4)), and soft candy (21CFR 170.3(n)(38)) at levels up to 600 mg/serving/day (reference amounts customarily consumed 21CFR 101.12). On a body weight (bw) basis, intake under the conditions of intended use is equivalent to approximately 1.12 mg/kg bw/day for an adult.

This is a resubmission of a notice sent on September 9, 2022 which FDA declined to file due to formatting errors and redaction, which have now been corrected.

I certify that the enclosed electronic files were scanned for viruses prior to submission and are thus certified as being virus-free using Symantec Endpoint Protection 12.1.5.

Please contact me at 631-670-3646 or Jimmy@summit-life-science.com if you have any questions or concerns regarding this GRAS notification. I look forward to receiving an acknowledgement of receipt of this notice.

Sincerely,

[redacted]

Jimmy Wang, Ph. D
Chief Scientific Officer
Summit Life Science, Inc.

SAFETY EVALUATION DOSSIER SUPPORTING A GENERALLY RECOGNIZED AS SAFE (GRAS) CONCLUSION FOR THE INTENDED USE OF

alpha-GPC

SUBMITTED TO:
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Campus Drive
College Park, MD 20740-3835

PREPARED FOR:
Shenyang Gold Jyouki Technology Co.,Ltd
Room 401, Building F8, No.860-1
Shenben Avenue, Hunnan District,
Shenyang, Liaoning, China
Post Code:110167
Tel: +86-24-31934012

PREPARED AND SUBMITTED BY:
Summit Life Science, Inc.
45 Adams Avenue
Hauppauge, NY, 11788
Tel: (631) 670 3646

DATE:
July 26, 2022

MODIFIED DATE:
March 30, 2023

Table of Contents

List of Figues

List of Tables

List of Exhibits

Part 1. § 170.225 Signed Statements and Certification

1.1 Claim of GRAS Notice

In accordance with 21 CFR §170 Subpart E consisting of §170.203 through 170.285, Shenyang Gold Jyouki Technology Co., Ltd (hereafter referred to as Jyouki or the Notifier), through its agent Summit Life Science, Inc., hereby informs the United States (U.S.) Food and Drug Administration (FDA) that alpha-GPC is not subject to premarket approval requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) based on Jyouki's conclusion, through scientific procedures, that the notified substance is Generally Recognized as Safe (GRAS) under the conditions of its intended use described in Section 1.4 below and fully described in Section 3, Dietary Exposure. In addition, as a responsible official of Jyouki, the undersigned hereby certifies that all data and information presented in this Notice represents a complete, representative, and balanced submission, and considered all unfavorable, as well as favorable, information known to Jyouki and pertinent to the evaluation of the safety and GRAS status of alpha-GPC as a food ingredient, as described herein.

Signed,

4/6/2023

Jimmy Wang, Ph.D.
Chief Scientific Officer
jimmy@summit-life-science.com
Summit Life Science, Inc., on behalf of
Shenyang Gold Jyouki Technology Co., Ltd

Date

1.2 Name and Address of the Notifier

Shenyang Gold Jyouki Technology Co., Ltd
Room 401, Building F8,
No.860-1 Shenben Avenue,
Hunnan District, Shenyang, Liaoning, China
Postal Code: 110167

1.3 Name and Address of the Agent of the Notifier

Jimmy Wang, Ph.D
Chief Scientific Officer
Jimmy@summit-life-science.com
Tel: (631) 670 3646
Summit Life Science, Inc.
45 Adams Ave, Hauppauge, NY 11788

1.4 Name of GRAS Substance

The subject of this GRAS Notification is alpha-GPC.

1.5 Intended Use and Consumer Exposure

alpha-GPC is proposed for use as a nutrient in powdered beverage mixes, protein & nutritional powders, soft drinks, sport & energy drinks (21CFR 170.3(n)(2)), coffee and tea (21CFR 170.3(n)(7)), cereal, nutrition bars (21CFR 170.3(n)(4)), and soft candy (21CFR 170.3(n)(38)) at levels up to 600 mg/serving/day (reference amounts customarily consumed 21CFR 101.12). In addition, under the applicable regulations, alpha-GPC is intended to be used in medical foods and dietary supplements. On a body weight (bw) basis, intake under the conditions of intended use is equivalent to approximately 1.12 mg/kg bw/day for an adult. The products containing alpha-GPC will be marketed to a general population for the technological function of nutrient (21CR 170.3 (o)(20)).

Foods that come under USDA jurisdiction are excluded from the list of food uses of alpha-GPC.

1.6 Basis for GRAS Conclusion

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 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 experiencebased 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 corroboratedby unpublished studies and other data and information.

The basis for the GRAS conclusion for alpha-GPC is scientific procedures in accordance with 21CFR §170.30(a) and (b).

The criteria stated above are applied herein in an analysis of whether the use of alpha-GPC is GRAS for the intended conditions of use.

The entire body of available information relevant to the safety of alpha-GPC, including identity, specifications, manufacturing process, probable consumer exposure, and toxicology/safety profile, provides a basis upon which to conclude that there is a reasonable certainty that alpha-GPC is not harmful under its intended conditions of use. In addition,because the information supporting safety is widely known and accepted by qualified experts (see Exhibit H, GRAS Panel Report), it is concluded that alpha-GPC is generally recognized as safe (GRAS) for the intended condition of use described herein.

1.7 Not Subject to Pre-market Approval

Jyouki concludes that alpha-GPC under the conditions of intended use described in this notice is GRAS and therefore does not fall under the definition of "food additive" and thus is not subject to the premarket

approval requirements outlined in section 201(s) of the FD&C Act.

1.8 Availability of Information

Jyouki's US Agent, Summit Life Science, Inc., will retain copies of all of the data and information that form the basis for the GRAS determination. Upon request, the US Agent will either provide the availability for the review and copying of the data and information during customary business hours at the address specified in Part 1.2 or will provide complete copies in an electronic or paper format.

Questions or requests for additional information may be directed to:

Jimmy Wang, Ph.D
Chief Scientific Officer
Summit Life Science, Inc.
45 Adams Ave,
Hauppauge, NY, 11788
Tel: (631) 670 3646
E-mail: Jimmy@summit-life-science.com

1.9 Exemption from Disclosure Under the Freedom of Information Act

None of the information in this GRAS notice is considered exempt from disclosure under the Freedom of Information Act, 5 U.S.C. 552, as trade secrets and/or commercial or financial information that is privileged or confidential.

1.10 Certification

Based upon our findings and knowledge of the information compiled in this Dossier, we conclude that alpha-GPC is GRAS for the intended conditions of use described herein. To the best of our knowledge, the current GRAS conclusion is a complete, representative, and balanced assessment that includes unfavorable information, as well as favorable information, known to us and pertinent to the evaluation of the safety and GRAS status for the use of alpha-GPC.

In consideration of the Food and Drug Administration Amendments Act of 2007 (FDAAA;Public Law 110-85) Section 912 of the FDAAA, codified as section 301(ll) of the FFDCA, alpha-GPC is neither an approved drug under section 505 of the Federal Food, Drug, and Cosmetic Act (FFDCA) nor a drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public.

Jyouki hereby concludes that the use of alpha-GPC described below is exempt from the pre-market approval requirements of the Federal Food, Drug, and Cosmetic Act. Jyouki has determined that such conditions of intended use are generally recognized as safe (GRAS) through scientific procedures.

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

2.1 Trade or Common Name

Common Name: alpha-GPC
Trade & Brand Name: PhoslipGPC™

2.2 Chemical Name

IUPAC: [(2R)-2,3-dihydroxypropyl] 2-(trimethylazaniumyl)ethyl phosphate

2.3 Synonyms

International Nonproprietary Name (INN): Choline Alfoscerate
USP: L-alpha-Glycerylphosphorylcholine
(R)-2,3-dihydroxypropyl 2-(trimethylammonio)ethyl phosphate
Alpha-Glyceryl phosphatidylcholine
Glycerophosphorylcholine
Glycerophosphocholine
Choline glycerophosphate
Cholinehydroxide
l-A-glyceryl phosphorylcholine
L-alphaglycerylphosphorylcholine

2.4 CAS Registry Numbers

28319-77-9

2.5 Physical Form, Taste and Odor

alpha-GPC is a white crystal or crystalline powder.
Slightly sweet and odorless.

2.6 Molecular and Structural Formula

Molecular weight: 257.22
Molecular formula: $C_8H_{20}NO_6P$

Structure:

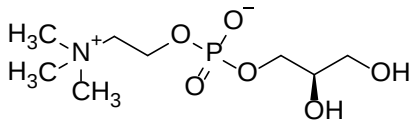


Figure 1: alpha-GPC Structure

2.7 Production Process

2.7.1 Method of Manufacture

The manufacturer of alpha-GPC, Shenyang Gold Jyouki Technology Co.,Ltd (hereafter referred to as "Jyouki") has provided the method of manufacture and all analytical data provided in the dossier.

Step 1：Preparation of Phosphorylcholine

Charge Polyphosphoric acid to a reactor and raise the temperature to 60˚C - 100°C by adding hot steam into the jacketed equipment.

Add Choline Chloride and stir for two (2) hours while maintaining the temperature.

Add Purified Water and continue stirring for two (2) hours. Cool it to room temperature.
Transfer to neutralization kettle.

Add Sodium Hydroxide aqueous solution drop by drop for three (3) hours.

Lower the temperature to 0˚C - 15℃, stir for crystallization for six (6) hours.

Filter by centrifugation. Transfer the filtrate to the concentration kettle pressure to remove part of the water under reduced pressure.

The aqueous solution of Phosphorylcholine is obtained for future use.

Step 2: Preparation of crude L-alpha-Glycerylphosphorylcholine

Feed R-3-Chloro-1,2-propanediol into reactor. Maintain temperature at -10˚C - +5°C. Keep stirring until dissolved.

Add Sodium Hydroxide solution drop by drop for one (1) to two (2) hours.

Add prepared aqueous solution of Phosphorylcholine from Step 1. Raise the temperature to 60˚C - 100°C and maintain it till alpha-GPC content is qualified.

Transfer the mixture to the de-colorization reactor. Add Medicinal Charcoal and stir for one (1) hour.

Filter to remove activated charcoal.

Transfer the filtrate to the distillation kettle, evaporate the water under reduced pressure, and control the mother liquor temperature not to exceed 90℃ for about ten (10) hours.

Cool down and add n-butanol. Stir for one (1) hour. Remove n-butanol after solution separation. Remove residual water by distilling the water phase under reduced pressure.

Add Anhydrous Ethanol and raise the temperature to 80℃ for dissolving.

Transfer the mixture into the crystallization reactor. Cool down to below 10℃, keep the constant temperature for crystallization for eight (8) hours.

Centrifuge and filter. Rinse the filtrate with cold Anhydrous Ethanol to obtain crude L-alpha-Glycerylphosphorylcholine

Step 3: Purification of L-alpha- glycerophosphoryl choline
Feed the crude L-alpha-Glycerylphosphorylcholine and Anhydrous Ethanol into reactor. Maintain the temperature at 70°C – 78°C and stir for one (1) hour.

Filter the mixture and transfer to crystallization reactor.

Cool down to below 0℃, stir for twelve (12) hours, centrifuge, wash with cold Anhydrous Ethanol.

Dry with double conical vacuum dryer at 60°C and ≥ -0.08mpa.

Pack the final product L-α- glycerophosphoryl choline in LDPE bag as a primary packaging and aluminum foil as a secondary packaging.

The flow chart of the manufacturing process is as follows:

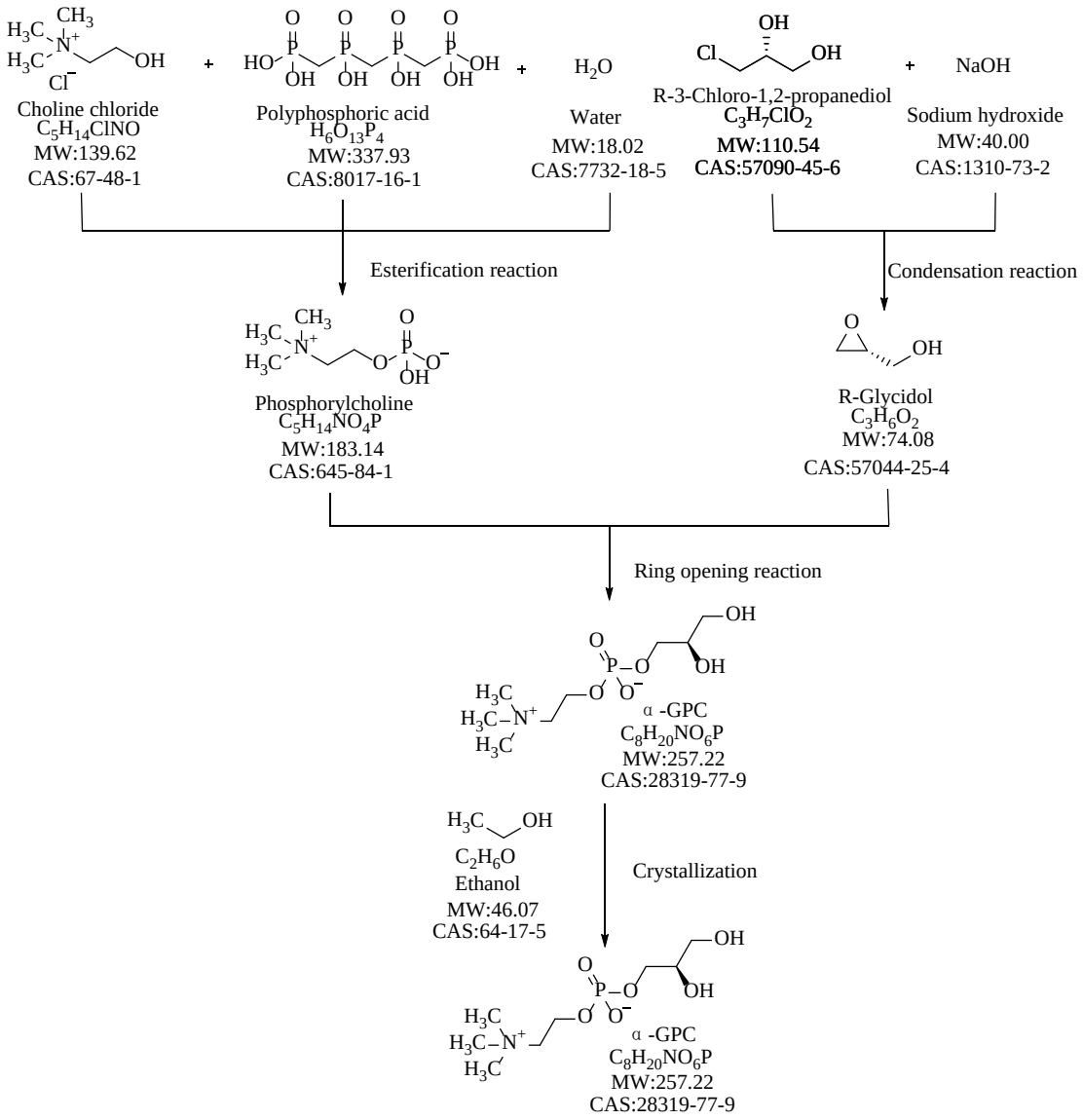


Figure 2: alpha-GPC Manufacturing Process Flow Chart

2.7.2 Raw Materials Used and Their Batch Analysis Results

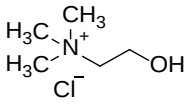
The manufacturer uses food grade raw materials and processing aids. The specifications for the critical ingredients are presented in the tables below (Tables 1 to 8). Certificates of Analysis (COA) of raw materials and processing aids are referenced in Exhibit A.

Table 1: Batch Analysis Results for Choline Chloride

Name: Choline Chloride CAS: 67-48-1

Molecular Weight: 139.62 Molecular Formula: $C_5H_{14}ClNO$

Structure:



Test parameter	Test Method	Acceptance Criteria	GC10-210802	GC10-210901	GC10-211001
Appearance	Visual	Colorless or white crystal, or crystalline powder	Conforms	Conforms	Conforms
Identification (IR)	ChP2020 Vol.4, Chap.0402	Conforms to reference material	Conforms	Conforms	Conforms
	ChP2020 Vol.4, Chap.0301	Positive Reaction	Conforms	Conforms	Conforms
Water Content	ChP2020 Vol.4, Chap.0832	≤ 1.0%	0.85%	0.87%	0.78%
Residue On Ignition	ChP2020 Vol.4, Chap.0841	≤ 0.10%	0.040%	0.042%	0.054%
Total Heavy Metal	ChP2020 Vol.4, Chap.0821	≤ 0.001%	Conforms	Conforms	Conforms
Residual Solvents	In-house (# SOP-QC2-503-00)				
1,4-dioxane		≤ 0.030%	Not Detected	Not Detected	Not Detected
Chloride Ethanol		≤ 0.030%	Not Detected	Not Detected	Not Detected
Assay (on anhydrous basis)	In-house (# SOP-QC2-503-00)	98.0 - 100.5%	98.7%	98.8%	99.1%

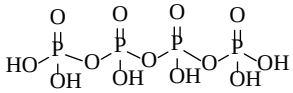
ChP: Chinese Pharmacopoeia

Table 2: Batch Analysis Results for Polyphosphoric Acid

Name: Polyphosphoric Acid CAS: Conforms to 8017-16-1

Molecular Weight: 337.93 Molecular Formula: $H_6O_{13}P_4$

Structure:



Test Parameter	Test Method	Acceptance Criteria	NP03-210701	NP03-210801	NP03-210901
Appearance	Visual	Colorless transparent or light-yellow viscous liquid	Conforms	Conforms	Conforms
Total Heavy metals	HG/T 4691-2014	≤ 0.003%	Conforms	Conforms	Conforms
Arsenic (Inorganic)	ChP2020 Vol.4, Chap.0822	≤ 0.008%	Conforms	Conforms	Conforms
Assay (calculated as phosphorus pentoxide)	HG/T 4691-2014	≥ 84.0%	84.6%	84.5%	84.8%

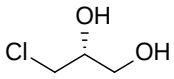
ChP: Chinese Pharmacopoeia HG/T: Chinese Industry Standard

Table 3: Batch Analysis Results for R-3-chloro-1,2-propanediol

Name: R-3-chloro-1,2-propanediol CAS: 57090-45-6

Molecular Weight: 110.54 Molecular Formula: $C_3H_7ClO_2$

Structure:



Test Parameter	Test Method	Acceptance Criteria	R201-PY-220202	R201-PY-220301	R201-PY-220401
Appearance	Visual	Colorless to light yellow liquid	Conforms	Conforms	Conforms
Specific Rotation	ChP2020 Vol.4, Chap.0621	-7.0° - -9.0°	-7.5°	-7.7°	-7.6°
Water Content	ChP2020 Vol.4, Chap.0832	≤ 0.10%	0.04%	0.03%	0.03%
Color	GB/T605-2006	≤ 30	15	15	15
Chemical Purity	In-house (# SOP-QC2-513-00)	≥ 99.0%	99.5%	99.4%	99.5%

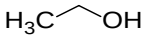
ChP: Chinese Pharmacopoeia GB/T: China National Standard (Recommended)

Table 4: Batch Analysis Results for Anhydrous Ethanol

Name: Anhydrous Ethanol CAS: 64-17-5

Molecular Weight: 46.07 Molecular Formula: C_2H_6O

Structure:



Test Parameter	Test Method	Acceptance Criteria	SW08-210802	SW08-210901	SW08-211002
Appearance	Visual	Colorless, transparent liquid, no visible impurities	Conforms	Conforms	Conforms
Identification	ChP2020 Vol.4, Chap. Pharmaceutical Excipients	Positive Reaction	Conforms	Conforms	Conforms
	ChP2020 Vol.4, Chap.0402	Conforms to reference material	Conforms	Conforms	Conforms
Water	ChP2020 Vol.4, Chap.0832	≤ 0.10%	0.08%	0.07%	0.05%

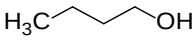
ChP: Chinese Pharmacopoeia

Table 5: Batch Analysis Results for N-butanol

Name: N-butanol CAS: 71-36-3

Molecular Weight: 74.12 Molecular Formula: $C_4H_{10}O$

Structure:



Test Parameter	Test Method	Acceptance Criteria	SZ16-220201	SZ16-220301	SZ16-220401
Appearance	Visual	Transparent liquid, no visible impurities	Conforms	Conforms	Conforms
Identification (IR)	ChP2020 Vol.4, Chap.0402	Conforms to reference material	Conforms	Conforms	Conforms
Color	GB/T605-2006	≤ 10	Conforms	Conforms	Conforms
Evaporation Residue	GB/T 6324.2	≤ 0.003%	0.003%	0.002%	0.003%

Water	ChP2020 Vol.4, Chap.0832	≤ 0.10%	0.04%	0.05%	0.06%
Assay	GB/T 6027-1998	≥ 99.5% (calculated with Area Normalization Method)	99.8%	99.7%	99.6%

ChP: Chinese Pharmacopoeia GB/T: China National Standard (Recommended)

Table 6: Batch Analysis Results for Sodium Hydroxide

Name: Sodium Hydroxide CAS: 1310-73-2

Molecular Weight: 40.00 Molecular Formula: NaOH

Structure: N/A

Test Parameter	Test Method	Acceptance Criteria	NH07-220201	NH07-220401	NH07-220501
Appearance	Visual	White shiny flakes, granular or lumpy, slight color allowed	Conforms	Conforms	Conforms
Identification	ChP2020 Vol.4, Chap.0402	Aqueous solution, showing the reaction phenomenon of Sodium salt	Conforms	Conforms	Conforms
Ferric oxide	GB/T 4348.3	≤ 0.008%	0.0002%	0.0005%	0.001%
Assay	ChP2020 Vol.4, Chap. Pharmaceutical Excipients				
Total Alkali Content		98.0% - 101.0%	99.4%	99.5%	99.5%
Sodium Carbonate		≤ 0.8%	0.7%	0.6%	0.7%

ChP: Chinese Pharmacopoeia GB/T: China National Standard (Recommended)

Table 7: Batch Analysis Results for Hydrochloric Acid

Name: Hydrochloric Acid CAS: 7647-01-0

Molecular Weight: 36.46 Molecular Formula: HCl

Structure: N/A

Test Parameter	Test Method	AcceptanceCriteria	NC01-210801	NC01-210901	NC01-211002
Appearance	Visual	Colorless or light-yellow transparent liquid	Conforms	Conforms	Conforms
Identification	ChP2020 Vol.4, Chap.0301	For Chlorides	Conforms	Conforms	Conforms

Iron	GB320-2006	≤ 0.008%	0.0001%	0.0002%	0.001%
Arsenic (Inorganic)	ChP2020 Vol.4, Chap.0822	≤ 0.0001%	Conforms	Conforms	Conforms
Assay	GB320-2006	≥ 31.0% (g/g)	36.4%	35.1%	36.1%

ChP: Chinese Pharmacopoeia GB: China National Standard (Mandatory)

Table 8: Batch Analysis Results for Medicinal Charcoal

Name: Medicinal Charcoal CAS: 64365-11-3

Molecular Weight: 12.00 Molecular Formula: C

Structure: N/A

Test Parameter	Test Method	Acceptance Criteria	GH21-210701	GH21-210801	GH21-210901
Appearance	Visual	Black powder; odorless; sand free	Conforms	Conforms	Conforms
Identification	ChP2020 Vol.4, Chap. Pharmaceutical Excipients	Formation of White precipitate is formed in calcium hydroxide test solution	Conforms	Conforms	Conforms
pH	ChP2020 Vol.4	Solution should be clear, and should not change color with blue and red litmus paper	Conforms	Conforms	Conforms
Acid Soluble Content	ChP2020 Vol.4, Chap. Pharmaceutical Excipients	Residue ≤ 10mg	3mg	2mg	5mg

ChP: Chinese Pharmacopoeia

2.8 Product Specifications

2.8.1 Physical and Chemical Specifications for alpha-GPC

Table 9: Physical and Chemical Specifications of alpha-GPC

Test	Specification	Test Method
Appearance	White crystal or crystalline powder	Visual method
Specific Rotation	-2.4° - -2.8°	USP43-NF38 (100mg/ml, 20℃, Calculated on anhydrous basis)
Identification	Conforms with reference material	USP43-NF38 (IR)
Particle size	≥ 85% passing through 80 mesh	ChP2020 Vol.4, Chap.0982
Bulk density	0.4 - 0.7g/mL	ChP2020 Vol.4, Chap.0993
Tap density	0.5 - 0.8g/mL	ChP2020 Vol.4, Chap.0993
pH	5.0 - 7.0	USP43-NF38 (85mg/mL solution)
Water	≤ 1.0%	USP43-NF38 (KF method)
Assay	98.0% - 102.0%	In-house method (on anhydrous basis) (# SOP-QC1-318-01)
Impurities		
Organic Impurities		USP43-NF38 (HPLC)
Beta-GPC	≤ 0.10%	
Any individual unspecified impurity	≤ 0.10%	
Total impurities	≤ 2.0%	
Other Impurities		
Chloride	≤ 0.02%	ChP2020 Vol.4, Chap.0801
Phosphate	≤ 0.005%	In-house method (# SOP-QC1-318-01)
Sulfate	≤ 0.02%	ChP2020 Vol.4, Chap.0802
Glycerol	≤ 0.50%	USP43-NF38 (HPLC)
Residual Solvents		In-house method (GC, # SOP-QC1-318-01)
Ethanol	≤ 0.50%	
N-Butanol	≤ 0.50%	

ChP: Chinese Pharmacopoeia

2.8.2 Microbiological Specifications for alpha-GPC

Table 10: Microbiological Specifications for alpha-GPC

Test	Specification	Test Method
Total bacterial count	≤ 1000 cfu/g	ChP2020 Vol.4, Chap.1105
Total combined molds and yeasts count	≤ 100 cfu/g	ChP2020 Vol.4, Chap.1105
Salmonella	Negative/10g	ChP2020 Vol.4, Chap.1106
Escherichia coli	Negative/10 g	ChP2020 Vol.4, Chap.1106
Staphylococcus	Negative/10 g	ChP2020 Vol.4, Chap.1106
Coliforms	Negative/1 g	GB4789.3-2016

ChP: Chinese Pharmacopoeia GB: China National Standard (Mandatory)

2.8.3 Heavy Metal Specifications for alpha-GPC

Table 11: Heavy Metal Specifications for alpha-GPC

Analyte	Specification	Test Method
Cadmium	≤ 0.5 µg/g	GB5009.268-2016
Arsenic (Inorganic)	≤ 1.0 µg/g	GB5009.268-2016
Lead	≤ 0.5 µg/g	GB5009.268-2016
Mercury	≤ 0.1 µg/g	GB5009.268-2016

GB: China National Standard (Mandatory)

2.8.4 Agricultural Residue Specifications for alpha-GPC

None of the materials used in the production of alpha-GPC are derived from agricultural commodities. Thus, the risk of presence of pesticides and other agricultural residues is non-existent. Therefore, Agricultural Residue for alpha-GPC is not required to be controlled and tested.

2.8.5 Specifications for Impurities of Potential Concern

Jyouki uses an impurity control strategy for a raw material and intermediates of potential concern, R-3-chloro-1,2-propanediol and glycidol, respectively. Using third-party testing agency to establish analytical methods for genotoxic impurities and perform analytical method validation in accordance with ICH Q2 guidelines, specifications have been set for these impurities of potential concern.

Table 12: Specifications for alpha-GPC Impurities of Concern

Analyte	Specification	LOQ	LOD	Test Method

Glycidol	1.25 ppm	0.625 ppm	0.313 ppm	ICAS “prior art” for test research or reference
R-3-chloro-1,2-propanediol	1.25 ppm	0.625 ppm	0.313 ppm	ICAS “prior art” for test research or reference
Epichlorohydrin	1.25 ppm	0.375 ppm	0.188 ppm	PVA-R-2020-078.01
1,3-Chloro-2-propanol	1.25 ppm	0.375 ppm	0.188 ppm	PVA-R-2020-078.01
2,3-Chloro-1-propanol	1.25 ppm	0.375 ppm	0.188 ppm	PVA-R-2020-078.01
2-Chloroethanol	1.25 ppm	0.625 ppm	0.313 ppm	PVA-R-2020-101.01

R-3-Chloro-1,2-propanediol is a suspect carcinogen and reproductive toxicant. Jyouki confirmed that R-3-chloro-1,2-propanediol may be surplus. As part of the in -process control, the manufacturer tested the residue of R-3-chloro-1,2-propanediol and indicates that the R-3-chloro-1,2-propanediol will be removed in the purification process. In addition, Jyouki has studied the residue of R-3-chloro-1,2-propanediol in the finished product of L-α-glycerylphosphorylcholine according to ICH M7. According to ICH M7, Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, the daily intake of an individual impurity should be controlled at 1.5µg/day. Jyouki has sent the limit of R-3-chloro-1,2-to no more than 1.25ppm.

Glycidol is an intermediate formed in the manufacturing process and is a probable human carcinogen. Jyouki confirmed that the glycidol is not totally reacted with the phosphorylcholine. During the reaction, because glycidol is unstable, the glycidol will break down to glycerol. The specifications control the amount of glycerol in the alpha-GPC to 0.5%. In addition, Jyouki has studied the residue of glycidol in the finished product according to ICH M7. Jyouki has set the limit of glycidol in alpha-GPC to no more than 1.25ppm, based on the TD50 of glycidol is, 4.28 mg/kg bw/day (rats) and 34.7 mg/kg bw/day (mice) (Carcinogenic Potency Database, CPDB).

2.9 Batch Analysis for alpha-GPC

Characterization analysis results for three non-consecutive lots of alpha-GPC are provided in the following tables (Tables 13 to 16). Supporting Certificates of Analysis are provided in Exhibit B.

Table 13: Batch Analysis Results for alpha-GPC

Test	Method	Specification	D01-GH-211101	D01-GH-211201	D01-GH-220101
Appearance	Visual	White crystal or crystalline powder	Conforms	Conforms	Conforms
Specific Rotation	USP43-NF38 (100mg/ml, 20°, anhydrous	-2.4° - -2.8°	-2.8°	-2.7°	-2.8°
Identification	USP43-NF38 (IR method)	Consistent with the reference standard	Conforms	Conforms	Conforms
Particle Size	ChP2020 Vol.4, Chap. 0982	≥85% passing 80 mesh	Conforms	Conforms	Conforms
Bulk density	ChP2020 Vol.4, Chap.0993	0.4 - 0.7g/mL	0.6g/ml	0.6g/ml	0.6g/ml

Tap density	ChP2020 Vol.4, Chap.0993	0.5 - 0.8g/mL	0.7g/ml	0.7g/ml	0.7g/ml
pH	USP43-NF38 (85mg/mL solution)	5.0 - 7.0	5.8	6.1	6.2
Water	USP43-NF38 (KF method)	≤ 1.0%	0.33%	0.32%	0.09%
Assay	In-house method (anhydrous basis)	98.0% - 102.0%%	99.9%	99.6%	100.4%
Impurities					
Organic Impurities	USP43-NF38 (HPLC)				
Beta-GPC		≤ 0.10%	0.056%	0.053%	0.056%
Any individual unspecified impurity		≤ 0.10%	0.069%	0.069%	0.083%
Total impurities		≤ 2.0%	0.12%	0.12%	0.14%
Other Impurities					
Chloride	ChP2020 Vol.4, Chap.0801	≤ 0.02%	Conforms	Conforms	Conforms
Phosphate`	In-house method (# SOP-QC1-318-01)	≤ 0.005%	Conforms	Conforms	Conforms
Sulfate	ChP2020 Vol.4, Chap.0802	≤ 0.02%	Conforms	Conforms	Conforms
Glycerol	USP43-NF38 (HPLC)	≤ 0.50%	Not Detected	Not Detected	Not Detected
Residual Solvents	In-house method (GC, # SOP-QC1-318-01)				
Ethanol		≤ 0.50%	0.11%	0.24%	0.12%
N-Butanol		≤ 0.50%	Not Detected	Not Detected	Not Detected

ChP: Chinese Pharmacopoeia

Table 14: Batch Microbiological Analysis Results for alpha-GPC

Test	Method	Specification	D01-GH-211101	D01-GH-211201	D01-GH-220101
Total bacterial count	ChP2020Vol.4 chap.1105	≤ 1000 cfu/g	< 1000cfu/g	< 1000cfu/g	< 1000cfu/g
Total combined molds and yeasts count	ChP2020 Vol.4 chap.1105	≤ 100 cfu/g	< 100cfu/g	< 100cfu/g	< 100cfu/g
Salmonella	ChP2020 Vol.4 chap.1106	Negative/10 g	Conforms	Conforms	Conforms
Escherichia coli	ChP2020 Vol.4 chap.1106	Negative/10 g	Conforms	Conforms	Conforms
Staphylococcus	ChP2020 Vol.4 chap.1106	Negative/10 g	Conforms	Conforms	Conforms
Coliforms	GB4789.3-2016	Negative/ 1 g	Conforms	Conforms	Conforms

ChP: Chinese Pharmacopoeia GB: China National Standard (Mandatory)

Table 15: Batch Heavy Metal Analysis Results for alpha-GPC

Analyte	Method	Specification	D01-GH-211101	D01-GH-211201	D01-GH-220101
Arsenic (Inorganic)	GB5009.268-2016	≤ 1.0µg/g	< 1.0µg/g	< 1.0µg/g	< 1.0µg/g
Lead	GB5009.268-2016	≤ 0.5µg/g	< 0.5µg/g	< 0.5µg/g	< 0.5µg/g
Mercury	GB5009.268-2016	≤ 0.1µg/g	< 0.1µg/g	< 0.1µg/g	< 0.1µg/g
Cadmium	GB5009.268-2016	≤ 0.5µg/g	< 0.5µg/g	< 0.5µg/g	< 0.5µg/g

GB: China National Standard (Mandatory)

Table 16: Batch Analysis Results for alpha-GPC Impurities of Concern

Analyte	Method	Specification	D01-GH-210301	D01-GH-210302	D01-GH-210303
Glycidol	ICAS "prior art" for test research or reference	1.25 ppm	ND	ND	ND
R-3-chloro-1,2-propanediol	ICAS "prior art" for test research or reference	1.25 ppm	ND	ND	ND
Epichlorohydrin	PVA-R-2020-078.01	1.25 ppm	ND	ND	ND
1,3-Chloro-2-propanol	PVA-R-2020-078.01	1.25 ppm	ND	ND	ND
2,3-Chloro-1-propanol	PVA-R-2020-078.01	1.25 ppm	ND	ND	ND
2-Chloroethanol	PVA-R-2020-101.01	1.25 ppm	ND	ND	ND

ND: Not detected

The impurity control strategy indicates, in analysis of 3 non-consecutive batches, that the levels of glycidol and R-3-chloro-1,2-propanediol are non-detected. Jyouki indicates that they will comply with ICH M7 (FDA CDER, 2018) impurity guidelines indicating periodic verification testing is justified when it can be shown that levels of the impurity in the substance is less than 30% of the acceptable limit for at least six consecutive pilot scale or three consecutive production scale batches. Therefore, the control strategy for the glycidol and R-3-chloro-1,2-propanediol is to perform verification testing in three consecutive production batches of samples per year.

2.10 Stability

Jyouki conducted accelerated stability tests with alpha-GPC (Exhibit E). The results of alpha-GPC held at 40°C, 75% RH for 1, 2, 3, and 6 months indicate that all the specifications parameters are met and comparable to data at time 0. The results of alpha-GPC held at 25°C, 60% RH for 3, 6, 9, 12, and 18, 24, and 36 months indicate that alpha-GPC is stable within 36 months. The changes observed were increase

water content (remains within specification), no significant changes in impurities, no significant changes in residual solvents, no change in conformity with microbiological specifications, and alpha-GPC 99.9% to 100.2% calculated on an anhydrous basis.

The manufacturer of alpha-GPC specifies a shelf-life of twenty-four (24) months from the date of production when preserved in well-closed containers at room temperature (Exhibit E). The shelf life of the products is twenty-four (24) months in the original unopened container. Jyouki stated that the retest date of two (2) years, as shown on the Certificate of Analysis for alpha-GPC is related to the fact that alpha-GPC is very stable.

Jyouki described alpha-GPC as governed by its chemical constituency as being very stable and nearly inert. Possible break down compounds of alpha-GPC consists primarily of glycerophosphoric acid (glycerophospholipid) and choline, and high levels of these compounds would have to be generated via forced hydrolysis caused by (intentional) extreme temperature, acid, and/ or catalytic induced conditions.

2.11 Physical or Technical Effect

Choline is critical for the normal function of all cells. It is an essential nutrient required for the structural integrity of cell membranes. It is used by the brain and nervous system to regulate memory, mood, muscle control and other functions. The main source of choline is food as many foods eaten by humans contain significant amounts of choline. However, the diets of most of the people in the USA do not provide recommended amount of choline (NIH, 2022). alpha-GPC is a choline containing compound which is used as a dietary source of choline. The technical effect of alpha-GPC for this GRAS review is as a nutrient ingredient.

Part 3. §170.235 Dietary Exposure

This section of the GRAS conclusion fulfills requirements of 21 CFR §170.235 in regard to the dietary exposure of the GRAS material as a result of its intended uses and use levels in a varietyof foods.

3.1 Intended Uses and Use Levels of alpha-GPC

The intended use of alpha-GPC is as a nutrient (21 CFR 170.3(o)(20)) in beverage, beverage bases and powders, coffee and tea, gummies, protein and nutrition bars and powders, (21CFR 170.3(n)). In addition, alpha-GPC is intended to be used, under the applicable regulations, in medical foods and as a dietary supplement ingredient. The proposed use levels of alpha-GPC in food, presented in the below table, is not intended to exceed 600 mg/serving per day.

Table 17: Intended Uses of alpha-GPC

Food Category	Serving Size *	Maximum IntendedUse Level (mg/serving)
Carbonated Soft Drinks	360 mL	20
Sports and Energy Drinks	360 mL	20
Un-reconstituted Powders	amount to make 240 – 360 mL	20
Coffee	360 mL	10
Tea	360 mL	10
Gummies (Candy not Chocolate)	15-30 g	20
Nutritional Beverages	240 mL	600
Nutritional Bars	40 g	100
Protein and Nutritional Powders	amount to make 240 – 360 mL	600

*Based on Reference Amounts Customarily Consumed (RACC) per Eating Occasion established in 21 CFR 101.12(b). (FDA CFSAN, 2018)

3.2 Estimated Daily Intake (EDI) of alpha-GPC

To estimate dietary exposure, the available USDA dietary exposure data were reviewed for the foods and the intended use levels. Exposure to alpha-GPC from the intended categories was estimated for the U.S. population using food consumption data from the What We Eat in America (WWEIA) component of the National Health and Nutrition Examination Surveys (NHANES). The most recent data available at the time of this writing (2017–2018) were analyzed using Creme Food Safety software 3.6 (www.cremeglobal.com).

These data were obtained from 6639 individuals who underwent two non-consecutive 24-hour dietary recall interviews (the first was collected in-person, the second by phone 3–10 days later).

WWEIA food codes that were considered most similar to the intended use categories were utilized in the assessment and were assigned the relevant intended use concentrations (Exhibit F). Creme software is a probabilistic modeling tool that uses high performance computing to predict intake, including total aggregate exposure, of food groups and/or individual food ingredients. Calculations are based on the calculated estimates on each individual's body weight from the survey, as opposed to averaged body weights. Calculations also incorporate the NHANES assigned sample weights for each individual in the survey, which measure the number of people in the population represented by that specific subject and help to ensure that the results statistically represent the entire U.S. population. Sample weights for NHANES participants incorporate adjustments for unequal selection probabilities and certain types of non-response, as well as an adjustment to independent estimates of population sizes for specific age, sex, and race/ethnicity categories.

The exposure is presented as an estimated daily intake on a "per capita" and "per user" basis at the mean and 90th percentile of intake. In this analysis, "per capita" estimates refer to the consumption based on the entire population of interest, whereas a "user" is anyone who reported consuming the food category of interest on either of the survey days. Results are stratified by age and gender and reported as both absolute exposure (mg/day) and exposure relative to body weight (mg/kg bw/day). Tables 18 and 19 show the population stratified estimated exposure to alpha-GPC at the proposed intended use levels in mg/day and mg/kg bw/day, respectively.

Table 18: Estimated Combined Daily Intake (mg/day) of alpha-GPC at Proposed Intended Use Levels in the U.S. by Population

Age (Years)	Gender	% Users	# Total Users	Per Capita Consumption (mg/day)				Per User Consumption (mg/day)			
				Mean	SE	90th Percentile	SE	Mean	SE	90th Percentile	SE
0-2	Female	22.1	45	3.3	1.2	4.4	2.8	14.9	5.3	25.9	6.4
	Male	25.8	57	3.5	1.2	9.3	3.3	13.5	4.1	26.6	4.6
3-12	Female	51.0	329	14.0	3.0	23.7	2.6	27.5	5.6	40.4	5.7
	Male	55.5	343	20.4	3.9	34.5	5.4	36.8	6.7	50.6	19.7
13-18	Female	74.2	249	40.1	13.8	55.4	28.9	54.1	18.3	77.1	42.6
	Male	75.7	249	48.1	9.6	59.7	20.4	63.6	12.5	91.5	36.6
19+	Female	92.2	1992	70.7	6.4	96.8	13.4	76.7	6.9	109.4	16.9
	Male	91.6	1854	91.6	10.6	120.5	22.1	100.1	11.6	134.3	30.3

Crème run 586

Table 19: Estimated Combined Daily (mg/kg bw/day) of alpha-GPC at Proposed Intended Use Levels in the US by Population

Age (Years)	Gender	% Users	# Total Users	Per Capita Consumption (mg/kg bw/day)				Per User Consumption (mg/kg bw/day)			
				Mean	SE	90th Percentile	SE	Mean	SE	90th Percentile	SE

0-2	Female	22.1	45	0.3	0.9	0.4	0.2	1.2	0.4	2.0	0.5
	Male	25.8	57	0.3	0.1	0.8	0.2	1.1	0.4	1.7	0.3
3-12	Female	51.0	329	0.6	0.1	0.8	0.1	1.1	0.2	1.5	0.2
	Male	55.5	343	0.6	0.1	1.1	0.2	1.2	0.2	2.0	0.7
13-18	Female	74.2	249	0.8	0.3	0.9	0.5	1.0	0.4	1.2	0.7
	Male	75.7	249	0.7	0.1	1.0	0.3	0.9	0.2	1.3	0.5
19+	Female	92.2	1992	1.0	0.1	1.5	0.3	1.1	0.1	1.7	0.3
	Male	91.6	1854	1.1	0.1	1.4	0.3	1.2	0.1	1.6	0.4

Crème run 586

The relative standard error (RSE) is a statistical criterion that can be used to determine the reliability of estimates as it pertains to the population. RSE values, calculated by dividing the standard error of the estimate by the estimate itself and multiplying by 100, greater than 25-30% may be considered reasonable cut-offs by which to consider a value unreliable (Wright et al., 2003; Klein et al., 2002). RSE values are shown for the 90th percentile values only, as the 90th percentile values are the most pertinent for the exposure estimates used for safety evaluation conclusions. The alpha-GPC per user exposure estimates from the intended use categories are shown for the total population (ages 2 years and older) below in Tables 20 and 21. All of the values were considered reasonably reliable using the RSE 25% cut-off.

Table 20: Total U.S. Population "User" Estimated Daily Intake (mg/day) of alpha-GPC at Proposed Intended Use Levels

Age (Years)	Gender	% Users	# Total Users	Per User Consumption (mg/ day)				90th Percentile RSE Value
				Mean	SE	90th Percentile	SE	
2+	Both	85.0	5016	80.1	5.7	113.3	11.3	10.0

Crème run 586

Table 21: Total U.S. Population "User" Estimated Daily Intake (mg/kg bw/day) of alpha-GPC at Proposed Intended Use Levels

Age (Years)	Gender	% Users	# Total Users	Per User Consumption (mg/kg bw/day)				90th Percentile RSE Value
				Mean	SE	90th Percentile	SE	
2+	Both	85.0	5016	1.1	0.1	1.6	0.2	12.5

Crème run 586

The tables above indicate that approximately 85% of the U.S. total population, ages 2 and above, was identified as potential consumers of alpha-GPC from the proposed food use. The mean intake for users of foods with consumption data available is estimated to be 80.1 mg/day (1.1 mg/kg bw/day). The user 90th percentile is 113.3 mg/day (1.6 mg/kg bw/day). It should be noted that these estimates are considered extremely conservative, as they assume that 100% of the numerous intended use food products in the market will contain the maximum intended use levels of the ingredient.

3.3 Dietary Exposure to Choline

Many foods contain choline. The main dietary sources of choline in the United States consist primarily of animal-based products that are particularly rich in choline; including meat, poultry, fish, dairy products, and eggs (Zeisel, 2014; Hollenbeck, 2012; Chester et al., 2011). Cruciferous vegetables and certain beans are also rich in choline, and other dietary sources of choline include nuts, seeds, and whole grains. About half the dietary choline consumed in the United States is in the form of phosphatidylcholine (Leermakers et al., 2015; Sanders, 2007). Many foods also contain lecithin, a substance rich in phosphatidylcholine that is prepared during commercial purification of phospholipids; lecithin is a common food additive used as an emulsifying agent in processed foods, such as gravies, salad dressings, and margarine (Zeisel et al., 2012; Zeisel, 2010).

The Food Nutrition Board (FNB) of the Institute of Medicine (IOM) determined that there was insufficient data available to establish an estimated average requirement (EAR), the average daily level of intake estimated to meet the requirements of 50% of healthy individuals. Therefore, the FNB established adequate intake (AI) levels, the level assumed to ensure nutritional adequacy. The AIs are based on the prevention of liver damage, as measured by serum alanine aminotransferase levels. The amount of choline that individuals need is influenced by the amount of methionine, betaine, and folate in the diet, gender, pregnancy, lactation, stage of development, ability to produce choline endogenously, and genetic mutations that affect choline needs. The current AIs for choline are presented in the Table 22, below, indicate 550 mg/day for adult males, 425 mg/day for adult females, 450 mg/day for pregnant women and 550 mg/d for nursing mothers based on the amount necessary to prevent liver damage and fatty liver (IOM, 1998; Zeisel et al., 1991). These levels are equivalent to 7-9 mg/kg bw/day for men and women based on 60 kg human adult reference body weight (FDA CDER 2005).

Table 22: Adequate Intakes for Choline

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	125 mg/day	125 mg/day		
7 - 12 months	150 mg/day	150 mg/day		
1 – 3 years	200 mg/day	200 mg/day		
4 – 8 years	250 mg/day	250 mg/day		
9 – 13 years	375 mg/day	375 mg/day		
14 – 18 years	550 mg/day	400 mg/day	450 mg/day	550 mg/day
19+ years	550 mg/day	425 mg/day	450 mg/day	550 mg/day

Choline consumption has been shown to increase production of trimethylamine-N-oxide (TMAO), a substance that has been linked to a higher risk of cardiovascular disease, in a dose-dependent manner in adults. High intakes of choline are associated with a fishy body odor, vomiting, excessive sweating and salivation, hypotension, and liver toxicity (Zeisel et al., 2012; IOM, 1998). The FNB has established upper limits (UL) for choline from food and supplements based on the amounts of choline that are associated with hypotension and fishy body odor. The ULs apply to healthy children and adults, but not to those taking high

doses of choline under medical supervision. The FNB was unable to establish ULs for infants due to the lack of data on adverse effects in this age group. The ULs are presented in the following Table 23 (IOM, 1998).

Table 23: Upper Limits for Choline

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months				
7 - 12 months				
1 – 3 years	1000 mg/day	1000 mg/day		
4 – 8 years	1000 mg/day	1000 mg/day		
9 – 13 years	2000 mg/day	2000 mg/day		
14 – 18 years	3000 mg/day	3000 mg/day	3000 mg/day	3000 mg/day
19+ years	3500 mg/day	3500 mg/day	3500 mg/day	3500 mg/day

Because choline is consumed in the diet, the total amount of choline from diet and contribution from the proposed conditions of intended use of a-GPC was calculated and compared against the AI and UL levels. NHANES 2017-2018 was used for the choline mean amount consumed per individual (USDA ARS, 2020). For a conservative analysis, the 90th percentile consumption of choline was estimated as a pseudo 90th percentile, twice the mean (FDA CFSAN, 2018).

The choline content of alpha-GPC is approximately 40% choline by weight. Therefore, a factor of 40% was applied to the mean and 90th percentile per capita and user consumption from the Crème 586 run data for total population (2+) to determine the contribution of alpha-GPC. The table below indicates that the additional choline consumption from the proposed uses of alpha-GPC will be effective in augmenting the diet towards achieving the adequate intake level of choline proposed by the Institute of Medicine (1998).

Table 24: Mean Choline Consumption, mg/day, from Foods and Proposed Use of alpha-GPC

Age (Years)	Gender	Choline Consumption from Foods (mg/day)		Mean Choline Consumption from Proposed alpha-GPC Uses (mg/day)*		Mean Total Choline (mg/day)		AI Choline (mg/day)
		Mean	**SE**	**Per Capita**	**Users**	**Per Capita**	**Users**	
2-19	Both	246	4.5	25	37	271	283	200-375
19+	Both	332	4.6	32	35	364	367	425-550
2+	Both	312	3.4	27	32	339	344	200-550
	Female	267	5.7	24	28	291	295	200-425
	Male	359	3.5	31	36	390	395	200-550

* Choline consumption adjusted as 40% of alpha-GPC

The table below confirms that the additional choline consumption from the proposed uses of alpha-GPC does not result in total choline consumption in excess of the upper levels of choline proposed by the Institute of Medicine. The 90th percentile total choline consumption of users/eaters, age 2+, from all sources, diet, and alpha-GPC, was estimated to be 669 mg/day. This is well below the upper limit of 1000 mg/day (1-8 years), 2000 mg/day (9-13 years), 3000 mg/day (14-18 years) and 3500 mg/day (19+ years) (IOM, 1998).

Table 25: 90th Percentile Choline Consumption, mg/day, from Foods and Proposed Use of alpha-GPC

Age (Years)	Gender	90th Percentile Choline Consumption from Foods (mg/day)	90th Percentile Choline Consumption from Proposed alpha-GPC Uses (mg/day)*		90th Percentile Total Choline Consumption (mg/day)		UL Choline (mg/day)
			Per Capita	**Users**	**Per Capita**	**Users**	
2-19	Both	492	35	50	527	542	1000-3500
19+	Both	664	45	48	709	712	3500
2+	Both	624	37	45	661	669	1000-3500
	Female	534	33	39	567	573	1000-3500
	Male	718	41	50	759	768	1000-3500

* Choline consumption adjusted as 40% of alpha-GPC

3.4 Discussion and Conclusion

alpha-GPC is intended for use as a nutrient ingredient in various foods and drinks such as beverage and beverage powder (carbonated, sports, and energy), coffee, tea, gummies, nutritional beverages and bars, and protein and nutritional powders; at levels not to exceed 600 mg/serving. Additionally, within the applicable regulations, alpha-GPC will be used in medical foods and dietary supplements.

The 90th percentile "user" consumption of alpha-GPC under the conditions of intended use is 1.6 mg/kg bw/day. Because alpha-GPC is used to supply the nutrient choline, the total choline consumption from both the diet and the choline contribution from the proposed conditions of use of alpha-GPC was calculated and compared to the upper limit of consumption determined by the Institute of Medicine (1998). The 90th percentile total choline consumption of users/eaters from all sources, diet, and alpha-GPC, was estimated to be 669 mg/day. This is well below the tolerable upper limit of 3500 mg/day. alpha-GPC consumption from the proposed intended use will provide additional choline needed to achieve the adequate daily intake published by the Institute of Medicine (1998).

Part 4. §170.240 Self-Limiting Levels of Use

This section of the GRAS conclusion fulfills requirements of 21 CFR §170.240 by providing information about any self-limiting characteristics of the GRAS material.

There are no known inherent self-limiting levels of use associated with alpha-GPC.

Part 5. §170.245 Experience Based on Common Use in Food Before 1958

General recognition of safety for the reviewed substance is established through scientific procedures in accordance with the Code of Federal Regulations 21 CFR §170.30(a) and (b). Therefore, information regarding experience based on common use of the notified substance in food prior to 1958 is not applicable.

Part 6. §170.250 Narrative and Safety Information

This section of the GRAS conclusion fulfills the requirements of 21 CFR §170.250 by providing a narrative regarding the generally available and accepted scientific data, information, methods, or principles that are relied on to establish safety.

6.1. Introduction

The totality of the evidence provides a basis upon which to conclude that the uses of alpha-GPC described in this GRAS Conclusion satisfy the safety standard of Reasonable Certainty of No Harm. In addition, these data and information are known and accepted by a consensus of qualified experts in the general scientific community. Thus, this information base not only assures that the intended uses of alpha-GPC described herein are safe, but also comprises common knowledge that alpha-GPC is also generally recognized as safe under its intended conditions of use. The following subsections of this Safety Narrative provide an overview of the data and information that support the above conclusions. In addition, the conclusions reached by the Expert Panel are presented in Exhibit H and are considered to be accurate.

6.2. Authorizations and Safety Evaluations by Authoritative Bodies

6.2.1. United State

6.2.1.1. FDA Generally Recognized as Safe

In accordance with 21 CFR §170 Subpart E, ChemiNutra Inc., through its agent the Life Sciences Research Organization, informed the FDA of their view that the use of alpha-glyceryl phosphoryl choline (A-GPC) as described in GRAS Notice 419 is not subject to the premarket approval requirements of the Federal Food, Drug and Cosmetic Act (FD&C Act) based on ChemiNutra's conclusion through scientific procedures that this use is Generally Recognized as Safe (GRAS). In the letter of November 20, 2012, the FDA indicated that the agency had no questions that A-GPC is GRAS under the intended conditions of use. GRN419 stated the conditions of intended use for A-GPC as a source of choline in conventional beverage and beverage bases, including coffee, tea, milk (fluid), powdered milk, flavored milk/milk drinks, carbonated beverages, powdered beverages, meal replacement liquids, foods including yogurt, grain-based bars, protein bars, ready-to-eat breakfast cereals, and snack foods including chocolates, candies, and chewing gum at levels ranging from 10-100 milligrams.

6.2.1.2. Hydrolysis Products of Lecithin

alpha-GPC is a hydrolysis product of lecithin (Marinetti, 1962). Lecithin is described by the FDA as a mixture of phosphatides of choline, ethanolamine, and inositol and is isolated from many sources of human food, including soy, safflower, and corn oils, and is approved as a food substance directly added to human food affirmed as generally recognized as safe (21CFR 184.1400). Both lecithin and bleached lecithin were reviewed by the Select Committee on GRAS Substances (SCOGS) with the conclusion that there was no evidence to demonstrate or suggest a hazard to the public when used at levels that were current or might reasonably be expected in the future (LSRO, 1979). Several GRAS Notifications (939, 533, and 226), for various sources of lecithin, were determined to be GRAS based on scientific procedures and have received an indication that FDA has no questions. The lecithin in these

notifications is described as natural complex mixture of acetone-insoluble phospholipids that consists mainly of phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, and phosphatidic acid, as well as various amounts of other substances, such as triglycerides, fatty acids, and carbohydrates. The presence of alpha-GPC in these GRAS conclusions was noted with no questions. In addition, hydrolyzed lecithin (GRN134), and soy lecithin phosphatidylserine (GRN186) were determined to be GRAS by scientific procedures.

6.2.1.3. Dietary Supplements

In accordance with the requirements of Section 413(b) of the FD&C Act and Section 8 of the Dietary Supplement Health and Education Act, Lucas Meyer Inc. filed a 75-day premarket notification with the FDA (Docket Number 95S-0316, filing date September 20, 1999) for choline alfoscerate-enriched phospholipid (Leci-GHA) as a new dietary ingredient for use in dietary supplements. Leci-GHA is a phospholipid that is enriched with choline alfoscerate (also known as glycerophosphorylcholine). Although choline alfoscerate products were referenced as sold in multiple countries, the FDA concluded that the safety of Leci-GHA could not be based solely on choline alfoscerate. The submission did not contain adequate information on the phospholipid.

The National Institutes of Health's Office of Dietary Supplements includes 274 products "on market" that include alpha-GPC on the label. The amount of alpha-GPC in the products is as high as 600 mg/serving in a range of products from tablets and capsules to beverages and powders (DSLD, 2022). A search of FDA Warning Letters did not indicate any warning letters issued with respect to alpha-GPC safety. Additionally, a search of FDA Adverse Events Reporting System (FAERS) Public Dashboard did not indicate any adverse events with respect to alpha-GPC.

6.2.1.4. United States Pharmacopeia (USP)

A monograph for L-alpha-glycerophosphorylcholine has been included in the USP Dietary Supplements Compendium (Exhibit G).

6.3. Metabolic Fate of alpha-GPC

6.3.1. Role of Choline

A dietary requirement for choline was first demonstrated in healthy men participating in a depletion-repletion metabolic study (Zeisel, 1991). The critical role of choline in neurotransmitter synthesis (acetylcholine), cell membrane signaling (phospholipids), lipid transport (lipoproteins), and methyl group metabolism (homocysteine reduction) is demonstrated by its official classification an essential nutrient (Zeisel let al., 1991; Institute of Medicine, 1998).

Humans can produce choline endogenously in the liver, mostly as phosphatidylcholine, but the amount that the body naturally synthesizes is not sufficient to meet human needs (Zeisel et al., 2014). As a result, humans must obtain some choline from the diet. When a diet is deficient in folate, a B-vitamin that is also a methyl donor, the need for dietary choline rises because choline becomes the primary methyl donor (Zeisel et al., 2012).

Free choline, phosphocholine, and glycerophosphocholine are absorbed in the small intestine, enter the portal circulation, and are stored in the liver, where they are subsequently phosphorylated and distributed throughout the body to make cell membranes (Zeisel et al., 2012; IOM, 1998; Zeisel et al., 2010).

In healthy adults, the concentration of choline in plasma ranges from 7 to 20 mcmol/L (IOM, 1998). According to one study, the range is 7–9.3 mcmol/L in fasting adults (Holm et al., 2003). Plasma choline levels do not decline below 50% of normal, even in individuals who have not eaten for more than a week (Zeisel et al. 2010). This may be due to the hydrolysis of membrane phospholipids, a source of choline, to maintain plasma choline concentrations above this minimal level, or to endogenous synthesis.

Most people in the United States consume less than the AI for choline. An analysis of data from the 2013–2014 National Health and Nutrition Examination Survey (NHANES) found that the average daily choline intake from foods and beverages among children and teens is 256 mg for ages 2–19. In adults, the average daily choline intake from foods and beverages is 402 mg in men and 278 mg in women. The groups most at risk for choline inadequacy include pregnant women, people with genetic alterations, and patients requiring total parenteral nutrition. Approximately 90-95% of pregnant women consume less than the choline AI (Brunst et al., 2014) and evidence suggests an association with increased neural tube defects in offspring (Wu et al., 2012; Shaw et al., 2009). Humans have variations in the DNA sequences for the genes involved in the metabolism of choline, folate, and methionine. Single nucleotide polymorphisms (SNPs) in the genes alter the requirements for choline and the prevalence of SNPs increase the risk of organ dysfunction when a low choline diet is consumed (daCosta et al., 2014). At present, choline is not routinely added to commercial parenteral solutions for infants and adults. The American Society for Parenteral and Enteral Nutrition recommends the routine addition of choline to adult and pediatric parenteral nutrition formulations and calls for the development of a commercially available parenteral product that contains choline (Vaneck et al., 2012).

Choline may play a role in cardiovascular and peripheral artery disease, neurological disorders, and nonalcoholic fatty liver disease (NAFLD). Choline is involved in functions that overlap with those of folate and other B vitamins. Many studies do not assess the status of all B vitamins, which can confound results and obscure the true relationship between choline and the observed outcome, and more research is recommended to further clarify the role of choline in each of these conditions (NIH, 2022).

6.3.2. Phospholipid Hydrolysis Pathway and Metabolism

Phosphatidylcholine (PtdCho) is the most abundant phospholipid in all mammalian cell types and subcellular organelles, comprising, in general, 40-50% of total cellular phospholipids. PtdCho is also the principal phospholipid circulating in plasma, serving as an integral part of the lipoproteins. The second most abundant phospholipid in mammalian membranes is phosphatidylethanolamine (PE).

PtdCho and PE can contain acyl-, ether-, or vinyl-ether bonds at the sn-1 bonds and are sub-classified into diacyl-, alkylacyl-, or alkenylacyl-phospholipids, respectively. In animal tissues, phosphatidylcholine tends to exist in mainly in the diacyl form.

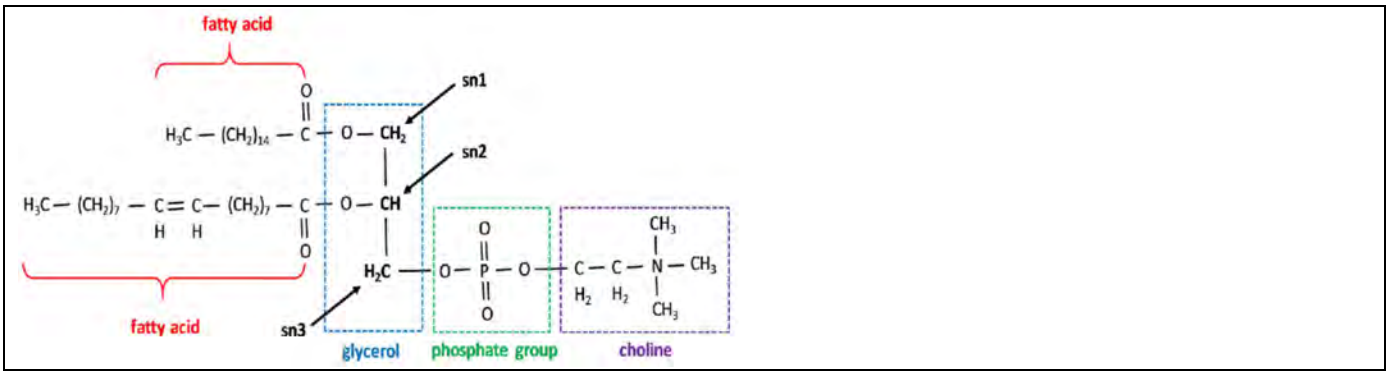


Figure 3: Phosphatidylcholine structure

Several *in vitro* studies demonstrate that PtdCho can be degraded by pancreatic phospholipase A1 to produce alpha-GPC (Bang 2016, Song 2020, Van den Bosch 1974, Zhao 2014). As a major component of the mammalian cell membrane (Van der Veen 2017), PtdCho is a source of alpha-GPC in an omnivorous diet.

PtdCho is a major lipid constituent in both the cortex and medulla of the mammalian kidney. PtdCho synthesis in mammalian kidney cells occurs through the Kennedy pathway with choline as one of the starting materials. The synthesis of GPC could involve sequential activity of a phospholipase A and a lysophospholipase or, alternatively, activity of a single phospholipase B. The GPC that results is water soluble and is degraded by hydrolysis to glycerol-3- phosphate (G-3-P) and choline, catalyzed by GPC:choline phosphodiesterase (GCPD) activity. The choline that results can be used for resynthesis of PC.

6.3.3. Metabolism and Distribution of alpha-GPC

The metabolic pathway of alpha-GPC is presented in Figure 4 .

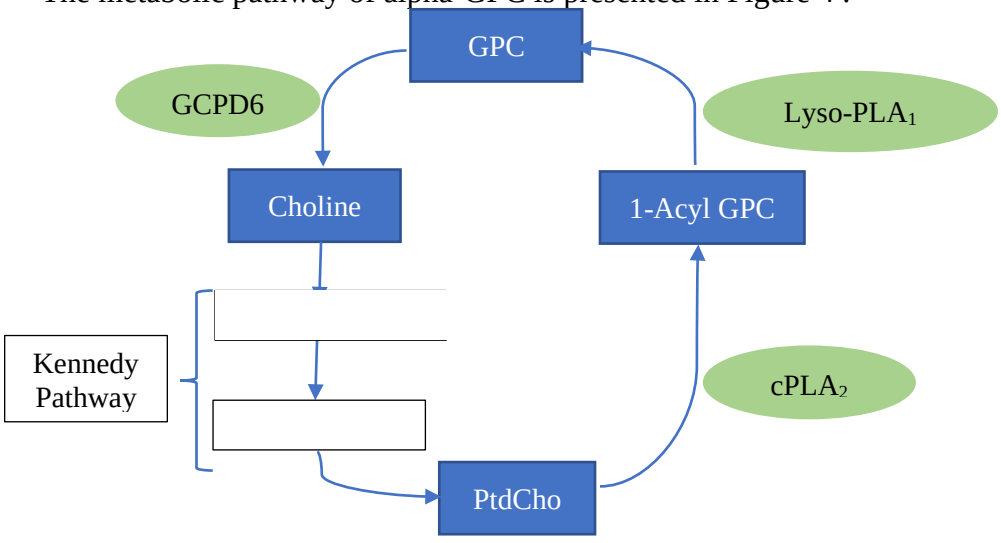


Figure 4 : Glycerophosphocholine metabolic pathway.
Enzymes are shown in green ovals and metabolites in blue boxes.
Abbreviations: CDP, cytidine diphosphate; $cPLA_2$, cytoplasmic phosphatidylcholine-specific lipase A2; GCPD, glycerophosphodiester phosphodiesterase; GPC, glycerophosphocholine; Lyso-PLA_1, lysophospholipase A1; PtdChol, phosphatidylcholine; (Adapted from Sonkar et al., 2019)

Phosphatidylcholine (PtdCho) is the most abundant phospholipid in mammalian cell membranes. PtdCho is synthesized from free choline through the Kennedy pathway (Kennedy and Weiss, 1956) in which free choline is phosphorylated to phosphocholine which is then converted to cytidine diphosphate choline. Using diacylglycerol as a lipid anchor, diacylglycerol-cholinephosphotransferase catalyzes the reaction to produce PtdCho. In a catabolic pathway, PtdCho is broken down to 1-acyl-GPC and GPC, which is subsequently converted to free choline, thus completing the choline cycle. There are three enzymes that are contributing to the GPC pathway that breaks down PtdCho to free choline. The first step in the GPC breakdown pathway is the hydrolysis of PtdCho by the enzyme cytosolic phospholipase A2 (cPLA2), which removes one fatty acid to produce 1-acyl-GPC (Morash et al., 1988). This is followed by a second hydrolysis step by the enzyme lysophospholipase A1 (lyso-PLA1), which removes the second fatty acid to produce GPC (Strauss et al., 1976;Loo et al., 1997). GPC is then converted to free choline and glycerol-3-phosphate by the enzyme glycerophosphocholine phosphodiesterase (GPC-PDE, EC 3.1.4.2). These three key enzymes directly regulate GPC levels in mammalian cells (Cao et al., 2012; Corda et al., 2014; Okazaki et al.,2010).

After oral consumption, alpha-GPC is converted to the metabolically active phosphorylcholine which travels to the cholinergic synaptic endings and can elevate acetylcholine synthesis and release (Lopez et al., 1991). Normal, human volunteers given an i.m. dose of alpha-GPC demonstrated a rapid rise in plasma choline, peaking between 0.25 and 0.5 hours. Thereafter, the concentration of choline declined gradually and returned to near baseline values at the end of the 6-hour observation period (Gatti et al., 1992).

The pharmacological action of alpha-GPC is believed to result from enhancement of central cholinergic functions through a stimulation of acetylcholine and phosphatidylcholine synthesis or an indirect activation of post synaptic cholinergic receptors (Trabucchi et al., 1986; Lopez et al., 1991). Rats have been extensively used in neurochemical studies with alpha-GPC. In a study on the absorption, distribution, and excretion of alpha-GPC (Abbiati et al., 1991; Abbiati et al., 1993), alpha-GPC was labeled in the glycerol part ([14C]-glycerol-GPC) and in the choline part ([14C]-choline-GPC) of the molecule. Sprague Dawley rats received the labeled compound either by iv into the tail vein at 10 mg/kg or orally by gastric intubation at 100 mg/kg.

The study demonstrated that the different labelled metabolites have different kinetic properties of absorption, distribution, and clearance, leading to different blood concentration-time curves of total radioactivity. Both labelled compounds gave a wide distribution of radioactivity, particularly concentrated in the liver, kidney, lung, and spleen compared to blood. Tissue distribution studies showed that alpha-GPC and its metabolites do not accumulate in particular organs and tissues after oral administration. Choline was incorporated into brain phospholipids in increasing amounts within 24 h of dosing. In all cases renal and fecal excretion of radioactivity was low and comparable for [14C]-glycerol-GPC and [14C]-choline -GPC. Mostly the administered radioactivity was exhaled as 14CO2, this degradation being faster and more pronounced for the glycerol-labelled metabolites than for the choline-labelled metabolites.

6.4. Bioequivalence and Bioavailability

Based on the radiolabeled alpha-GPC studies described above GPC (Abbiati et al., 1991; Abbiati et al., 1993), after oral administration, the main circulating metabolite was choline and intact alpha-GPC was not

present after either labelled compound. With both i.v. and oral administration, at least two unidentified metabolites for each labelling position could be detected. It is assumed that a-GPC is hydrolyzed in the rat intestinal mucosa by a specific enzyme system degrading a-GPC to choline and glycerol-3-phosphate. This enzyme system has been shown not only in the gut mucosa but also in liver, brain, and kidney. Based on the studies, the amount of available choline can be estimated on a molecular weight basis. alpha-GPC contains 40.8% of choline and has a produrig structure and separated by a precursor of choline and nerve cell membrane precursor of acetylcholine glycerophosphate (Clinical Trials. 2013 NCT 02395926).

6.5. Information Pertaining to Safety

6.5.1. Preclinical Studies

Pre-clinical studies including in vitro and in vivo mutagenicity assays, acute, sub-chronic, and chronic oral toxicity were conducted in accordance with OECD Guidelines for Testing Chemicals and GLP regulations were conducted using alpha-GPC supplied by Italafarmaco S.p.A.. The studies, published by Brownawell et al. (2011), on 90% active alpha-GPC provide the data for publicly available, peer-reviewed data in support of a GRAS determination.

An overview of the toxicity studies performed with alpha-GPC is presented in Table 26. Details of each of the studies are provided in the following sections of the dossier.

Table 26: Summary of Pre-Clinical Studies with a-GPC*

Study Type	Test System/Species	Concentrations/Dosages	Results
***In vitro* studies**			
Bacterial reverse mutation, direct plate incorporation	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	100, 300, 1000, 3000, or 10,000 ug/plate +/- S9	Non-mutagenic
Yeast forward mutation, standard plate method	Schizosacchoromyces Pombe (strain P1)	30, 100, 300, 1000, or 3000 ug/ml +/- S9	Non-mutagenic
Gene conversion, standard plate method	Saccharomyces cerevisiae (strain D4)	100, 300, 1000, or 3000 ug/ml +/- S9	Non-mitotic gene conversion
Gene conversion, host-mediated technique	S. cerevisiae (strain D4)		Non-mitotic gene conversion
***In vivo* studies**			
Mammalian erythrocyte micronucleus test	Male and female Swiss mice	30, 100, or 300 mg/kg was administered twice, via subcutaneous injection, at a 24 h intervals	Non-genotoxic
Acute toxicity	Male and female Swiss mice	521, 729, 1,020, 1,429, or 2,000 mg/kg, intravenous via tail vein	LD50 Males: 1267 mg/kg LD50 Females: 1027 mg/kg
		781, 1,093, 1,531, 2,143, or 3,000 mg/kg, intraperitoneal	LD50 Males: 2053mg/kg LD50 Females: 1809 mg/kg
		2500, 5000, or 10000 mg/kg by oral gavage	LD50 Males: >10,000 mg/kg LD50 Females: 10,000 mg/kg
	Male and female Sprague-	781, 1,093, 1,531, 2,143,	LD50 Males: 1621 mg/kg

	Dawley rats	and 3,000, intravenous via tail vein	LD50 Females: 1531 mg/kg
		781, 1,093, 1,531, 2,143, or 3,000 mg/kg intraperitoneal	LD50 Males: 2215 mg/kg LD50 Females: 2017 mg/kg
		2,500, 5,000 or 10,000 mg/kg by oral gavage	LD50 Males: >10,000 mg/kg LD50 Females: >10,000 mg/kg
	Male and female Beagle dogs	200 or 500 mg/kg, intramuscular	LD50 >500 mg/kg
		1000 or 3000 mg/kg by oral gavage	LD50 >3000
13-Week sub-chronic oral toxicity test with 4-week recovery period	Male and female Sprague-Dawley rats	100, 300, or 1000 mg/kg/day by oral gavage	No treatment-related adverse effects. NOAEL at highest level tested, 1000 mg/kg
26-Week chronic oral toxicity test with 4-week recovery period	Male and female Sprague-Dawley rats	100, 300, or 1000 mg/kg/day by oral gavage	Reversible reduced activity and body weight gain at highest dose, no histopathological correlates. NOAEL 300 mg/kg
	Male and female Beagle dogs	75, 150 mg, or 300 mg/kg/day by oral gavage	Reduced activity and body weight gain at highest dose, suggested reduced liver function. NOAEL 150 mg/kg

*Brownawell et al. (2011)

6.5.1.1. Genotoxicity

6.5.1.2. Acute Toxicity

6.5.1.2.1. Mice

The acute oral toxicity of alpha-GPC was investigated in male and female Swiss mice (6 mice/sex/group) at doses of 2,500, 5,000 or 10,000 mg/kg. Behavior was observed for 6 hours post-administration and then once *per* day. Post-mortems were performed on all dead animals and survivors sacrificed at the end of the two-week observation period. Mice in the 10,000 mg/kg group experienced severe prolonged reduced activity for 12-36 hours. Reduced activity was low and transient for the low dose and was generally mild in animals receiving the intermediate dose. Lethality in mice (33% males, 50% females) was seen at 10,000 mg/kg body weight, the highest dose administered. No deaths occurred in the 2,500 and 5,000 mg/kg groups.

The acute toxicity of intravenous administration of 521, 729, 1,020, 1,429, or 2,000 mg/kg doses of alpha-GPC delivered *via* the tail vein was studied in male and female Swiss mice (6 mice/sex/dose group). The 2,000 mg/kg dose was lethal to all animals within 24 hr of dosing. The mortality for both male and female mice was 0% at the 521 mg/kg dose; 0% (male), 16.6% (female) and 8.3% (combined mortality) at the 729 mg/kg dose; 33.3% (male), 66.6% (female) and 50% (combined mortality) at the 1,020 mg/kg dose; and 50% (male), 66% (female) and 58.3% (combined mortality) at the 1,429 mg/kg. Some animals experienced convulsions prior to their death. For survivors, symptoms of toxicity included dose-dependent in severity and duration reduced or absent motility, reduced activity, and bradypnea or dyspnea, which was. The signs lasted up to 48 hours for animals that received the higher doses. Weight loss or retardation of growth was observed in the first week, but recuperation occurred the next week. The LD50 was 1,267 mg/kg for males

(C.I. = 1,056-1,520) and 1,027 mg/kg for females (C.I. = 837-1,260).

The acute toxicity of intraperitoneal administration of 781, 1,093, 1,531, 2,143, or 3,000 mg/kg doses of alpha-GPC was studied in male and female Swiss mice (6 mice/sex/dose group). Dose-dependent symptoms include reduced activity. Some animals demonstrated writhing movements, indicative of local pain. Within 14 days of receiving alpha-GPC, the mortality for both male and female mice was 0% at 781 mg/kg dose; 0% (male), 16.6% (female) and 8.3% (combined mortality) at 1093 mg/kg; 33.3% (male), 33.3% (female) and 33.3% (combined mortality at 1531 mg/kg; 50% (male), 50% (female) and 50% (combined mortality) at 2,143 mg/kg; and 83.3% (male), 100% (female), and 91.6% (combined mortality) at 3,000 mg/kg. The LD50 was 2,053 mg/kg for males (C.I. = 1644–2564) and 1,809 mg/kg for females (C.I. = 1459–2243).

6.5.1.2.2. Rats

The acute oral toxicity of alpha-GPC was investigated in male and female Sprague Dawley rats (6 rats/sex/group) at doses of 2,500, 5,000 or 10,000 mg/kg. Oral dosing of rats with 10 g/kg resulted in 16% mortality in males and 33% in females. No deaths occurred at lower doses. Reduced mobility and activity were severe at the lethal dose lasting from 3 to 24 h. The effects were less severe and of a shorter duration (1–6 h) at the lower doses. Necropsies on animals dying or after 2 weeks did not reveal any alpha-GPC related changes.

The acute toxicity of intravenous administration of 781, 1,093, 1,531, 2,143, and 3,000 mg/kg doses of alpha-GPC delivered *via* the tail vein was studied in male and female Sprague Dawley rats (6 rats/sex/dose group). Symptoms of toxicity and the timing of death were similar to those for mice. Mortality rates were 0% for male and female rats at 781 mg/kg; 16.6% for males and females at 1,093 mg/kg; 50% for males and females 1,531 mg/kg; 66.6% (males), 83.3% (females), and 75% (combined mortality) at 2,143 mg/kg; and 100% for both sexes at 3,000 mg/kg. The LD 50 for male rats was 1,621 mg/kg (C.I. = 1,323-1,986) and 1,531 mg/kg for female rats (C.I. = 1,269-1,848). and 1,575 mg/kg for both sexes (C.I. = 1,372-1,809). Necropsies did not indicate any alpha-GPC related changes.

The acute toxicity of intraperitoneal administration of 781, 1,093, 1,531, 2,143, or 3,000 mg/kg doses of alpha-GPC was studied in male and female Sprague Dawley rats (6 rats/sex/dose group). Mortality rates were 0% for males and females at both 781 and 1093 mg/kg; 16.6% for males and females at 1531 mg/kg; 33% (males) and 50% (females) at 2,143 mg/kg; and 100% for both males and females at 3, 000 mg/kg. The LD50 was 2,125 (C.I. = 1,797-2,513) mg/kg for male rats and 2,017 (C.I. = 1,722-2,362) mg/kg for female rats. Necropsies did not indicate any alpha-GPC related changes.

6.5.1.2.3. Dogs

The acute toxicity of intramuscular or oral administration at the maximum tolerated dose (MTD) was studied in male and female, young Beagle dogs. The animals were observed for 6 h following dosing and then daily for 2 weeks. Intramuscular administration of alpha-GPC at 200 or 500 mg/kg did not cause any deaths. Oral administration of alpha-GPC at 1000 or 3000 mg/kg did not cause any deaths. At the lowest doses mild to no reduced activity was observed. At the highest doses, mild reduced activity, lasting between 3 and 24 hours, was observed. The intramuscular and oral LD50 values were estimated to be >500 mg/kg and >3000 mg/kg, respectively.

6.5.1.3. Subchronic Toxicity

Eighty Sprague–Dawley rats (10 rats/sex/group) were administered 100, 300 or 1000 mg/kg doses of alpha-GPC by oral gavage. Daily clinical observation and weekly body weight measurements were conducted during the pre-treatment and active phases of the study. After 4 weeks of treatment, urine samples were collected, and blood drawn from the abdominal aorta under fasting conditions and general anesthesia. Hematology and limited clinical chemistry analyses were performed on all animals. A post-mortem examination including organ weights and histopathology was conducted on all animals at termination. Oral administration of 100 and 300 mg/kg AGPC for 4 weeks did not alter animal behavior or produce any signs of general toxicity. Reduced activity, with intensity varying from animal to animal, was generally observed in the groups of rats administered the highest dose (1000 mg/kg). There were no significant differences in body weights, in hematology, clinical chemistry, organ weights or histopathology. Treatment of rats at a dose up to 1000 mg/kg/day for 4 weeks did not produce any toxicological changes.

GRAS Notification 419 references a subchronic, subcutaneous study in Sprague Dawley rats. These are referenced as unpublished toxicology studies performed on alpha-GPC and provided by ChemiNutra. Rats (10/sex/group) were administered 50, 150, or 500 mg/kg subcutaneously. GRN419 concluded no differences between controls and A-GPC treated rats were observed.

6.5.1.4. Chronic Toxicity and Carcinogenicity

6.5.1.4.1. Rats

One-hundred forty-four Sprague–Dawley rats (18 rats/sex/dose) were administered 100, 300 or 1000 mg/kg doses of alpha-GPC by oral gavage. Individual daily clinical observations were performed during both the pre-test and dosing phases of the study. Body weights were measured weekly during the first 3 months of treatment, and every 2 weeks thereafter. Food consumption was measured every 2 weeks during the first 3 months, and every 4 weeks thereafter. During the 13th week of treatment, blood samples were drawn from the retro-orbital plexus under fasting conditions for limited hematology and clinical chemistry evaluations. Blood and urine were collected from 10/sex/group after 26 weeks of treatment. Recovery animals (controls and high dose) were observed for 4 additional weeks. A full necropsy was performed following sacrifice under general anesthesia. The parameters evaluated included: body weight, organ weight, hematology (hematocrit, hemoglobin, erythrocyte count, platelet count (13th and 26th week), total and differential leukocytes, prothrombin time (26th week), clinical chemistry (glucose, BUN, creatinine, AST, ALT, alkaline phosphatase, total serum proteins, bilirubin, cholesterol, triglycerides, sodium, and potassium), and urinalysis (specific weight, pH, protein, bilirubin, blood). Histopathologic examinations were performed on all high dose and control animals and those showing gross lesions in the mid- and low-dose groups.

There were 10 deaths during the study: 2 controls (pulmonary infection and perforated gastric ulcer); 4 in the 100 mg/kg group (2 gavage errors and 2 with renal necrosis); 2 in the 300 mg/kg group (gavage error and unknown cause); and 2 in the 1000 mg/kg group (both pulmonary infection). None of the deaths were attributed to treatment.

Reduction in spontaneous motor activity and of reactivity to stimulation was observed in animals receiving 1000 mg/kg, starting after 3–4 weeks of treatment. The symptoms appeared within 1–2 h of dosing and continued for 3–5 h thereafter. There was considerable variability from one animal to another but the severity was only mild to moderate in all cases. Food

consumption and body weight gain were reduced in the high dose group starting at week 4. In contrast, animals in the 100 mg/kg and 300 mg/kg groups showed no reduction in activity. Body weight gain and food consumption were not affected in the low and mid dose groups.

Hematology and clinical chemistry evaluations at 13 weeks did not reveal any treatment related effects except for a slight reduction in creatinine in the high dose females. After 26 weeks, changes in the high dose group were limited to a decrease in plasma triglycerides in males and females; a reduction in plasma bilirubin, ALT, and creatinine in females. Triglycerides were reduced in the mid dose males after 26 weeks. Urinalysis did not show any treatment related effects. The heart weight was reduced in the mid- and high-dose females, but the relative weight (to bodyweight) was unchanged.

Necropsy and histopathological evaluations did not reveal any treatment related effects. The nature and frequency of the observed pathology was essentially similar in all experimental groups. By the end of the 4-week recovery period, the high dose animals' body weights were the same as the controls and reduction of spontaneous motor activity resolved.

Dosing of rats for 26 weeks with 300 mg/kg AGPC did not produce any toxic effects. The high dose (1000 mg/kg) induced postdosing reduced activity lasting for 3–5 h. Food consumption and body weight gains were reduced. Changes in clinical chemistry were limited to reductions which may be related to inactivity and reduced body weight. There were no histopathological correlates. Reduced activity and body weight gain returned to normal during the recovery period.

6.5.1.4.2. Dogs

Twenty-four beagle dogs (3 dogs/sex/group) were administered 75, 150, or 300 mg/kg/day by oral gavage for 26 consecutive weeks. The dogs were dosed in the morning and fed in the afternoon. The animals were observed daily, and body weights were measured at monthly intervals during the first 3 months of treatment, and then at the end of the study. Venous blood samples were collected under fasting conditions before study initiation and at the end of the 13th and 26^{th} week for hematology and clinical chemistry evaluations. Urine samples were also collected at the same time points. A full necropsy was performed on all animals at study termination. The parameters examined included: body weight, organ weight, hematology (hematocrit, hemoglobin, erythrocyte count, platelet count, total and differential leukocytes, and prothrombin time), clinical chemistry (glucose, BUN, creatinine, AST, ALT, alkaline phosphatase, total serum proteins, bilirubin, cholesterol, triglycerides, sodium, and potassium), and urinalysis (specific weight, pH, protein, bilirubin, and blood). Necropsy and select histopathological examination of certain tissues were also performed on all animals.

There were no deaths during the 26-week study. Administration of 75 and 150 mg/kg for 26 weeks had no effect on behavior or body weight gain. Mild reduced activity lasting 2 to 5 h after dosing began the second week of the study in the high-dose animal group (300 mg/kg daily). Body weight gain was reduced at 13 weeks but not at 26 weeks. No hematological changes were observed during the 26-week treatment period. Clinical chemistry evaluations performed at week 13 showed a significant increase in plasma cholesterol and decreased alkaline phosphatase levels in the mid-dose group. These changes were absent at week 26. In the high-dose group significant changes were observed in plasma bilirubin, plasma triglycerides, and alkaline phosphatase, which were

reduced 34%, 56%, and 9%, respectively, relative to controls. No significant urinalysis abnormalities were observed. The weights of the liver and of the heart showed a dose-related decrease that did not achieve statistical significance. Histopathological evaluation of the tissues did not reveal any treatment related effects. There were no changes associated with the decrease in liver enzymes and liver and heart weight. Treatment of dogs for 26 weeks with 300 mg/kg AGPC resulted in reduced activity after dosing lasting up to 5 h. Body weight gain was reduced in the males at 13 weeks. Clinical chemistry evaluations suggested a reduced liver function. Liver and heart weights were reduced. There were no histopathological correlates. These changes may be the result of reduced body weight and activity. Treatment with 75 or 150 mg/kg alpha-GPC had no untoward effects.

6.5.1.5. Developmental and Reproductive Toxicity

GRAS Notification 419 references a reproductive study in Sprague Dawley rats. These are referenced as unpublished toxicology studies performed on alpha-GPC and provided by ChemiNutra. Rats (24 rats/sex/dose) were administered 50, 150, or 500 mg/kg subcutaneously. Males were dosed for 9 weeks and throughout the mating period. Females were dosed for 4 weeks before mating and until pregnancy was confirmed. GRN419 reported all female F 1 rats had normal pregnancies except one in the control group and another in the 500 mg/kg group. F 1 females sacrificed after delivery were not significantly different in terms of the number of *corpora lutea,* implant sites, reabsorbed embryos, and total fetuses. F2 litters showed no significant differences regarding the number of live and still births, sex distribution or fetal weight. One malformation was found in the low-dosage group and the intermediate-dosage group.

GRAS Notification 419 references a teratogenicity study in Sprague Dawley rats. These are referenced as unpublished toxicology studies performed on alpha-GPC and provided by ChemiNutra. Mated females (24 rats/dose) were administered 50, 150, or 500 mg/kg subcutaneously during the organogenesis period, from the 6^{th} to 15^{th} day of pregnancy. GRN419 reported no significant differences in *corpora lutea* and implant sites and in pre- and post-implants losses between groups. alpha-GPC did not appear to affect the course of pregnancy post-implantation. One fetus died in the control and 50 mg/kg groups, as did three in the 150 mg/kg group. No fetuses in the high-dose group died. There were no significant differences in fetal weight between the various treatment groups. Major fetal malformation was observed in the control and the 150 mg/kg groups (n = 1/group) and there was no significant difference in the frequency of minor malformations of skeletal formation. There was no significant difference across treatment groups in the number of fetuses with minor defects.

GRAS Notification 419 references a perinatal and postnatal study in Sprague Dawley rats. These are referenced as unpublished toxicology studies performed on alpha-GPC and provided by ChemiNutra. Pregnant rats (15 rats/dose) were administered 50, 150, or 500 mg/kg subcutaneously from day 15 of pregnancy to day 21 postpartum. GRN419 reported no significant difference between treatment groups and controls regarding litter size, sex distribution, and mean weight *per* litter. There appeared to be no effect of alpha-GPC on prenatal mortality. Caesarean section of F 1 females showed no significant differences in number of corpora lutea, implant sites, or reabsorbed embryos. There were also no significant differences in the total number of fetuses extracted, the number of live and dead fetuses, the mean fetal weight, or the sex distribution of fetuses. There was no correlation between pre- and post-implant losses and treatments given to F 1 mothers.

6.5.1.6. Neurotoxicity and Behavioral Toxicity

GRAS Notification 419 references a neurotoxicity study in Sprague Dawley rats. These are referenced as unpublished toxicology studies performed on alpha-GPC and provided by ChemiNutra. Sprague Dawley rats (5 rats/sex/dose) were administered 50, 100, 200, or 400 mg/kg alpha-GPC orally or subcutaneously 60 minutes before each test. Before testing, rats were trained to walk on a particular region of the rota-rod device while it was turning at 10 rpm, for 60 seconds without falling. Animals that did not learn to navigate the rota-rod without falling off in the first 5 seconds were replaced. After the required number of animals was trained they received their allotted treatment and were retested. The number of rats falling off the rota-rod before the defined period of time had elapsed was recorded in order to calculate a neurotoxic dose for 50% of the animals. There were no neurotoxic effects of any doses of A-GPC for either route of administration.

6.5.2. Human Studies

As a result of the function of alpha-GPC as a contributor of the nutrient choline, human clinical studies have primarily focused on evaluation of efficacy. The National Institutes of Health Office of Dietary Supplements provides a fact sheet on choline for health professionals (NIH 2022) which the focuses on 3 conditions in which choline may play a role: (1) cardiovascular and peripheral artery disease (2) neurological disease and (3) nonalcoholic fatty liver disease (NAFLD). More recently, there are human studies investigating the efficacy of choline on markers of physical performance, e.g. power, speed, and agility.

The Choline Fact Sheet for Health Professionals concludes that choline is involved in functions that overlap with those of folate and other B vitamins. Many studies do not assess the status of all B vitamins, which can confound results and obscure the true relationship between choline and the observed outcome. Although there are some data that suggest an increased risk of mortality in those consuming higher levels of choline possibly due to increased product of trimethylamine-N-oxide (TMAO) (Zheng et al., 2016), the Fact Sheet indicates that the hypothesis was not proven as the researchers did not directly measure TMAO.

6.5.2.1. Clinical Safety Data

The major objective in clinical testing of food and food additives is to assess aspects of safety that cannot be addressed adequately by non-human studies or by existing data on population exposure. (FDA, 1993).

Under the proposed conditions of intended use, alpha-GPC is not intended to substitute for a major nutrient. The consumption of choline from the use of alpha-GPC under the proposed conditions of use does not result in human choline consumption greater than the UL published by the Institute of Medicine (IOM, 1998). In addition, the non-human studies described above provide adequate information to assess safety. The review of clinical studies on efficacy was intended to demonstrate alpha-GPC tolerance and absence of adverse events to provide information corroborative of the safety of alpha-GPC.

GRAS Notification 419 L-alpha-glycerylphosphorylcholine (ChemiNutra, 2012) provides a thorough summary of the human studies conducted prior to 2012. The majority of the studies summarized in GRN419 were with unhealthy populations with oral administration of doses as high as 1200 mg/day for as long as 6 months. Some minor adverse effects such as insomnia, gastralgia, restlessness, headache, constipation, or nervousness were noted but none warranted discontinuation of treatment or withdrawal

from the study. A study in healthy volunteers orally administered alpha-GPC 1200 mg/day for 10 days had no reported adverse effects.

GRN419 reported on Gliatilin® , choline alfoscerate product of Italfarmaco S.p.A.. GRN419 indicated that there were an estimated 705,000 individuals treated with Gliatilin® between 1990 and 1996 and there were no reports of adverse events by individuals prescribed the medication.

US National Library of Medicine (clinicaltrials.gov) indicated 13 completed studies with choline alfoscerate (alpha-GPC). None of the records provide any study results.

An updated literature search (2012 to present) of alpha-GPC used in human clinical studies did not indicate any unexpected adverse events. The studies are summarized below:

Table 27: Summary of Human Clinical Studies (2012 to Present)

Citation	Cohort	Route	Dose	Duration	Endpoint	Adverse Events
Pizova, 2014	Unhealthy, males/females, n=25	Oral	1000 mg	3 months	Cognition	Well tolerated
Bellar et al., 2015	Healthy, males, n=13	Oral	600 mg	6 days	Isometric strength	None reported
Erichev and Mazurova, 2016	Unhealthy, males/female, n=120	IV and Oral	1000 mg	4 months	Glaucoma	None reported
Carotenuto et al., 2017	Unhealthy, male/female, n=113	Oral	1200 mg	24 months	Dementia	None reported
Marcus et al., 2017	Healthy, males, n= 48	Oral	500mg, 200 mg	7 days	Physical and psychomotor performance	None reported
Min et al., 2019	Healthy, male	Oral	1200 mg	Single dose	Formulation Bioequivalence	No adverse events; Well tolerated
Tamura et al., 2021	Healthy, males/females, n=40	Oral	400 mg	2 weeks	Motivation	None reported

6.5.2.2. Allergenicity

There is no data to indicate that alpha-GPC manufactured according to the process described in this dossier would elicit an oral allergenic response.

6.5.3. Safety Conclusions

The safety of use of alpha-GPC as a nutrient ingredient in beverage, beverage bases and powders, coffee and tea, gummies, protein and nutrition bars and powders has been thoroughly assessed as described above. Following ingestion, alpha-GPC is converted to phosphorylcholine, a metabolically active form of choline. By weight, 40% of alpha-GPC is choline. Choline is an essential nutrient needed for cell membrane structural integrity, to produce the important neurotransmitter acetylcholine, and for other important roles in modulating gene expression, cell membrane signaling, lipid transport and metabolism and early brain development. Consequently, there is a wealth of information available in the public domain on the absorption, distribution, metabolism, excretion, safety and efficacy of choline and alpha-GPC.

The scientific data, information and methods that form the technical element of this conclusion are:

- The Institute of Medicine has determined the adequate and upper-level intakes for choline. Because the amount the body needs cannot be obtained by endogenous synthesis, humans must obtain some choline in the diet. Most people in the US consume less than the AI for choline. alpha-GPC can function as a nutrient ingredient supplying choline.
- The establishment of the identity of alpha-GPC
- The method of manufacture and specifications demonstrating the safe production and high-quality control of the process and final product which ensure purity of the product and prevention of contamination
- The body of literature available to describe the ADME of alpha-GPC and choline
- The suite of published genotoxicity and toxicity studies establishing the lack of genotoxic and toxic potential of alpha-GPC, as well as low toxicity in the repeated dose studies in rats and dogs
- The NOAEL of 150 mg/kg bw/d established in the chronic dog study provides a margin of safety of 95 at the highest 90th percentile user intake of alpha-GPC.
- The 90th percentile user consumption of alpha-GPC plus the pseudo 90th percentile consumption of choline from foods and beverages is below the upper limit for choline as established by the Institute of Medicine.
- The pivotal data establishing the safety of alpha-GPC is published and peer-reviewed (Brownawell et al., 2011)

In summary, the totality of scientific evidence from publicly available information relevant to the safety of alpha-GPC, including identity, specifications, manufacturing process, probable consumer exposure, and toxicology profile, provides a basis upon which to conclude that there is a reasonable certainty that alpha-GPC, produced in accordance with current Good Manufacturing Practices, is not harmful under the proposed intended conditions of use. The safety data supporting this conclusion is known and accepted by a consensus of qualified experts in the general scientific community. This not only assures that the intended uses of alpha-GPC described herein are safe, but also corroborates the conclusion that alpha-GPC is generally recognized as safe under the proposed conditions of use.

Shenyang Gold Jyouki Technology Co.,Ltd is not aware of any information that would be inconsistent with the conclusion that the proposed uses of alpha-GPC, meeting appropriate specifications and used according to current Good Manufacturing Practices, are GRAS.

Part 7. §170.255 List of Supporting Data and Information

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Exhibits

EXHIBIT A

Certificates of Analysis for Raw Materials and Processing Aids

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZY21073002

Sample Name	Choline Chloride	Sample Source	Jinan Asia Pharmaceutical Co., Ltd
Manufacturer Batch Number	421210711	Incoming Batch Number	GC10-210802
Quantity	3160kg	Storage Condition	Dark, dry and ventilated place
Test Date	2021.07.30	Report Date	2021.08.05
Test Reference	SOP for GC10 Testing (SOP-QC2-503-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless or white crystal, or crystalline powder	White crystalline powder
【Identification】		
IR method	The IR spectrum of the test sample is consistent with that of the reference	Conforms
Chemical method	Should be positive reaction	Positive reaction
【test】		
Water content	Not more than 1.0%	0.85%
Residue on Ignition	Not more than 0.10%	0.040%
Total Heavy Metal	Not more than 0.001%	Conforms
Residual solvent	1,4-dioxane shall be not more than 0.030% chloride ethanol shall be not more than 0.030%	1,4-dioxane: not detected chloride ethanol :not detected
【Assay】		
Assay	Content of Choline chloride: 98.0 % to 100.5% , calculated on anhydrous basis.	98.7%
Remarks	None	
Test Conclusion	It is tested according to SOP for GC10 Testing (SOP-QC2-503-00), the results are conformed	

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZY21090501

Sample Name	Choline Chloride	Sample Source	Jinan Asia Pharmaceutical Co., Ltd
Manufacturer Batch Number	421210713	Incoming Batch Number	GC10-210901
Quantity	3240kg	Storage Condition	Dark, dry and ventilated place
Test Date	2021.09.05	Report Date	2021.09.10
Test Reference	SOP for GC10 Testing (SOP-QC2-503-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless or white crystal, or crystalline powder	White crystalline powder
【Identification】		
IR method	The IR spectrum of the test sample is consistent with that of the reference	Conforms
Chemical method	Should be positive reaction	Positive reaction
【test】		
Water content	Not more than 1.0%	0.87%
Residue on Ignition	Not more than 0.10%	0.042%
Total Heavy Metal	Not more than 0.001%	Conforms
Residual solvent	1,4-dioxane shall be not more than 0.030% chloride ethanol shall be not more than 0.030%	1,4-dioxane: not detected chloride ethanol :not detected
【Assay】		
Assay	Content of Choline chloride: 98.0 % to 100.5% , calculated on anhydrous basis.	98.8%
Remarks	None	
Test Conclusion	It is tested according to SOP for GC10 Testing (SOP-QC2-503-00), the results are conformed	

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZY2110010

Sample Name	Choline Chloride	Sample Source	Jinan Asia Pharmaceutical Co., Ltd
Manufacturer Batch Number	421210811	Incoming Batch Number	GC10-211001
Quantity	3150kg	Storage Condition	Dark, dry and ventilated place
Test Date	2021.10.01	Report Date	2021.10.06
Test Reference	SOP for GC10 Testing (SOP-QC2-503-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless or white crystal, or crystalline powder	White crystalline powder
【Identification】		
IR method	The IR spectrum of the test sample is consistent with that of the reference	Conforms
Chemical method	Should be positive reaction	Positive reaction
【test】		
Water content	Not more than 1.0%	0.78%
Residue on Ignition	Not more than 0.10%	0.054%
Total Heavy Metal	Not more than 0.001%	Conforms
Residual solvent	1,4-dioxane shall be not more than 0.030% chloride ethanol shall be not more than 0.030%	1,4-dioxane: not detected chloride ethanol :not detected
【Assay】		
Assay	Content of Choline chloride: 98.0 % to 100.5% , calculated on anhydrous basis.	99.1%
Remarks	None	
Test Conclusion	It is tested according to SOP for GC10 Testing (SOP-QC2-503-00), the results are conformed	

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1 No.: SOP-QC-004-R01-00

COA No.: ZY21072803

Sample Name	Polyphosphoric Acid	Sample Source	Chuan Lin Chemical Co., Ltd
Manufacturer Batch Number	20210722	Incoming Batch Number	NP03-210701
Quantity	8760kg	Storage Condition	Cool and ventilated place
Test Date	2021.08.02	Report Date	2021.08.03
Test Reference	SOP for NP03 Testing (SOP-QC2-501-00)		

Test item	Specification	Test result
【Character】		
Appearance	Colorless transparent or light yellow,viscous liquid	light yellow,viscous liquid
【Test】		
Total Heavy metals	NMT 0.003%	conforms
Arsenic (Inorganic)	NMT0.008%	conforms
【Assay】		
Assay(calculated as phosphorus pentoxide)	Polyphosphoric acid shall be not less than 84.0%	84.6%

Remarks	None
Test conclution	It is tested according to SOP for NP03 Testing (SOP-QC2-501-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1 No.: SOP-QC-004-R01-00

COA No.: ZY2108250l

Sample Name	Polyphosphoric Acid	Sample Source	Chuan Lin Chemical Co., Ltd
Manufacturer Batch Number	20210728	Incoming Batch Number	NP03-210801
Quantity	9000kg	Storage Condition	Cool and ventilated place
Test Date	2021.08.25	Report Date	2021.08.25
Test Reference	SOP for NP03 Testing (SOP-QC2-501-00)		

Test item	Specification	Test result
【Character】		
Appearance	Colorless transparent or light yellow,viscous liquid	light yellow,viscous liquid
【Test】		
Total Heavy metals	NMT 0.003%	conforms
Arsenic (Inorganic)	NMT0.008%	conforms
【Assay】		
Assay(calculated as phosphorus pentoxide)	Polyphosphoric acid shall be not less than 84.0%	84.5%

Remarks	None
Test conclution	It is tested according to SOP for NP03 Testing (SOP-QC2-501-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1 No.: SOP-QC-004-R01-00

COA No.: ZY21091802

Sample Name	Polyphosphoric Acid	Sample Source	Chuan Lin Chemical Co., Ltd
Manufacturer Batch Number	20210805	Incoming Batch Number	NP03-210901
Quantity	8000kg	Storage Condition	Cool and ventilated place
Test Date	2021.09.18	Report Date	2021.09.18
Test Reference	SOP for NP03 Testing (SOP-QC2-501-00)		

Test item	Specification	Test result
【Character】		
Appearance	Colorless transparent or light yellow,viscous liquid	light yellow,viscous liquid
【Test】		
Total Heavy metals	NMT 0.003%	conforms
Arsenic (inorganic)	NMT 0.008%	conforms
【Assay】		
Assay(calculated as phosphorus pentoxide)	Polyphosphoric acid shall be not less than 84.0%	84.8%

Remarks	None
Test conclution	It is tested according to SOP for NP03 Testing (SOP-QC2-501-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZC22022305

Sample Name	R-3-chloro-1,2-propanediol	Sample Source	Self- production
Manufacturer Batch Number	——	Incoming Batch Number	R201（for API）-PY-220202
Quantity	3250 kg	Storage Condition	Dark and dry place, sealed
Test Date	2022.02.23	Report Date	2022.02.24
Test Reference	SOP for R201 Testing (SOP-QC2-513-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless to light yellow liquid	Light yellow liquid
Specific rotation	-7.0° ~-9.0°	-7.5 °
【Tests】		
Water content	Not more than 0.10%	0.04%
Color	Not more than 30	15
Chemical purity	Not less than 99.0%	99.5%

Remarks	None
Test conclusion	It is tested according to SOP for R201 Testing (SOP-QC2-513-00), and the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZC22031001

Sample Name	R-3-chloro-1,2-propanediol	Sample Source	Self- production
Manufacturer Batch Number	——	Incoming Batch Number	R201（for API）-PY-220301
Quantity	3100kg	Storage Condition	Dark and dry place, sealed
Test Date	2022.03.10	Report Date	2022.03.10
Test Reference	SOP for R201 Testing (SOP-QC2-513-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless to light yellow liquid	Light yellow liquid
Specific rotation	-7.0° ~-9.0°	-7.7 °
【Tests】		
Water content	Not more than 0.10%	0.03%
Color	Not more than 30	15
Chemical purity	Not less than 99.0%	99.4%

Remarks	None
Test conclusion	It is tested according to SOP for R201 Testing (SOP-QC2-513-00), and the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZC22041502

Sample Name	R-3-chloro-1,2-propanediol	Sample Source	Self- production
Manufacturer Batch Number	——	Incoming Batch Number	R201（for API）-PY-220401
Quantity	3500kg	Storage Condition	Dark and dry place, sealed
Test Date	2022.04.15	Report Date	2022.04.15
Test Reference	SOP for R201 Testing (SOP-QC2-513-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless to light yellow liquid	Light yellow liquid
Specific rotation	-7.0° ~-9.0°	-7.6 °
【Tests】		
Water content	Not more than 0.10%	0.03%
Color	Not more than 30	15
Chemical purity	Not less than 99.0%	99.5%

Remarks	None
Test conclusion	It is tested according to SOP for R201 Testing (SOP-QC2-513-00), and the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-024-R01-00

COA No.: ZY21081601

Sample Name	Anhydrous ethanol	Sample Source	Meihekou Fukang alcohol Co., Ltd/Liaoning Meilong economic and Trade Co., Ltd
Manufacturer Batch Number	2021062905	Incoming Batch Number	SW08-210802
Quantity	3915	Storage Condition	Sealed in a cool and ventilated place
Test Date	2021.08.16	Report Date	2021.08.16
Test Reference	SOP for SW08 Testing (SOP-QC2-504-00)		

Test item	Specification	Test result
【Character】		
appearance	Colorless ,transparent liquid , no visible impurities	Colorless ,transparent liquid , no visible impurities
【Identification】		
Chemical method	Positive reaction	Positive reaction
IR method	The infrared absorption spectrum should be consistent with that of reference substance	conforms
【Test】		
Water	NMT 0.10%	0.08%

Remarks	None
Test method	It is tested according to SOP for SW08 Testing (SOP-QC2-504-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-024-R01-00

COA No.: ZY21090102

Sample Name	Anhydrous ethanol	Sample Source	Meihekou Fukang alcohol Co., Ltd/Liaoning Meilong economic and Trade Co., Ltd
Manufacturer Batch Number	2021080511	Incoming Batch Number	SW08-210901
Quantity	4000	Storage Condition	Sealed in a cool and ventilated place
Test Date	2021.09.01	Report Date	2021.09.01
Test Reference	SOP for SW08 Testing (SOP-QC2-504-00)		

Test item	Specification	Test result
【Character】		
appearance	Colorless ,transparent liquid , no visible impurities	Colorless ,transparent liquid , no visible impurities
【Identification】		
Chemical method	Positive reaction	Positive reaction
IR method	The infrared absorption spectrum should be consistent with that of reference substance	conforms
【Test】		
Water	NMT 0.10%	0.07%

Remarks	None
Test method	It is tested according to SOP for SW08 Testing (SOP-QC2-504-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-024-R01-00

COA No.: ZY21102503

Sample Name	Anhydrous ethanol	Sample Source	Meihekou Fukang alcohol Co., Ltd/Liaoning Meilong economic and Trade Co., Ltd
Manufacturer Batch Number	2021080512	Incoming Batch Number	SW08-211002
Quantity	4000	Storage Condition	Sealed in a cool and ventilated place
Test Date	2021.10.25	Report Date	2021.10.25
Test Reference	SOP for SW08 Testing (SOP-QC2-504-00)		
Test item	Specification		Test result
【Character】			
appearance	Colorless ,transparent liquid , no visible impurities		Colorless ,transparent liquid , no visible impurities
【Identification】			
Chemical method	Positive reaction		Positive reaction
IR method	The infrared absorption spectrum should be consistent with that of reference substance		conforms
【Test】			
Water	NMT 0.10%		0.05%
Remarks	None		
Test method	It is tested according to SOP for SW08 Testing (SOP-QC2-504-00), the results are conformed		

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1 No.: SOP-QC-024-R01-00

COA No.: ZY22022103

Sample Name	N-butanol	Sample Source	Shenyang dike Chemical Co., Ltd
Manufacturer Batch Number	0113	Incoming Batch Number	SZ16-220201
Quantity	500ml	Storage Condition	Dry, sealed and protected from light
Test Date	2022.02.17	Report Date	2022.02.21
Test Reference	SOP for SZ16 Testing (SOP-QC2-505-00)		

Test item	Specification	Test result
【Character】		
Appearance	Transparent liquid, no visible impurities	Transparent liquid, no visible impurities
【Identification】		
IR method	The infrared absorption spectrum should be consistent with that of reference substance	conforms
【Test】		
Color	NMT 10	conforms
Evaporation residue	NMT 0.003%	0.003%
Water	NMT 0.10%	0.04%
【Assay】		
Assay	N-butanol :NLT 99.5% ,calculated with Area Normalization Method.	99.8%

remarks	None
Test conclusion	It is tested according to SOP for SZ16 Testing (SOP-QC2-505-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-024-R01-00

COA No.: ZY22031501

Sample Name	N-butanol	Sample Source	Shenyang dike Chemical Co., Ltd
Manufacturer Batch Number	0115	Incoming Batch Number	SZ16-220301
Quantity	500ml	Storage Condition	Dry, sealed and protected from light
Test Date	2022.03.15	Report Date	2022.03.17
Test Reference	SOP for SZ16 Testing (SOP-QC2-505-00)		

Test item	Specification	Test result
【Character】		
Appearance	Transparent liquid, no visible impurities	Transparent liquid, no visible impurities
【Identification】		
IR method	The infrared absorption spectrum should be consistent with that of reference substance	conforms
【Test】		
Chroma	NMT 10	conforms
Evaporation residue	NMT 0.003%	0.002%
Water	NMT 0.10%	0.05%
【Assay】		
Assay	N-butanol :NLT 99.5% ,calculated with Area Normalization Method.	99.7%

remarks	None
Test conclusion	It is tested according to SOP for SZ16 Testing (SOP-QC2-505-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-024-R01-00

COA No.: ZY22042201

Sample Name	N-butanol	Sample Source	Shenyang dike Chemical Co., Ltd
Manufacturer Batch Number	0117	Incoming Batch Number	SZ16-220401
Quantity	500ml	Storage Condition	Dry, sealed and protected from light
Test Date	2022.04.22	Report Date	2022.04.23
Test Reference	SOP for SZ16 Testing (SOP-QC2-505-00)		

Test item	Specification	Test result
【Character】		
Appearance	Transparent liquid, no visible impurities	Transparent liquid, no visible impurities
【Identification】		
IR method	The infrared absorption spectrum should be consistent with that of reference substance	conforms
【Test】		
Chroma	NMT 10	conforms
Evaporation residue	NMT0.003%	0.003%
Water	NMT0.10%	0.06%
【Assay】		
Assay	N-butanol :NLT 99.5% ,calculated with Area Normalization Method.	99.6%

remarks	None
Test conclusion	It is tested according to SOP for SZ16 Testing (SOP-QC2-505-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1

No.: SOP-QC-004-R01-00

COA No.: ZY21071601

Sample Name	Sodium Hydroxide	Sample Source	Shandong Binhua Dongrui Chemical Co., Ltd
Manufacturer Batch Number	DR01000220 21080422	Incoming Batch Number	NH07-220201
Quantity	2900kg	Storage Condition	sealed to avoid light and moisture,in dry place
Test Date	2022.02.16	Report Date	2022.02.17
Test Reference	SOP for NH07 Testing (SOP-QC2-502-00)		

Test item	Specification	Test result
【Character】		
Appearance	White shiny flakes, granular or lumpy, slight color allowed	White glossy granular
【Identification】		
Chemical method	Aqueous solution, showing the reaction phenomenon of sodium salt	positive reaction
【Test】		
Ferric oxide	NMT 0.008%	0.0002%
【Assay】		
Total Alkali Content	The total alkali content should be 98.0% ~ 101.0%	total alkali content： 99.4%
Sodium Carbonate	Content of sodium carbonate should not exceed 0.8%.	sodium carbonate： 0.7%

Remarks	None
Test conlusion	It is tested according to SOP for NH07 Testing (SOP-QC2-502-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZY22040501

Sample Name	Sodium Hydroxide	Sample Source	Shandong Binhua Dongrui Chemical Co., Ltd
Manufacturer Batch Number	DR01000220 21080512	Incoming Batch Number	NH07-220401
Quantity	3000kg	Storage Condition	sealed to avoid light and moisture,in dry place
Test Date	2022.04.05	Report Date	2022.04.06
Test Reference	SOP for NH07 Testing (SOP-QC2-502-00)		

Test item	Specification	Test result
【Character】		
Appearance	White shiny flakes, granular or lumpy, slight color allowed	White glossy granular
【Identification】		
Chemical method	Aqueous solution, showing the reaction phenomenon of sodium salt	positive reaction
【Test】		
Ferric oxide	NMT 0.008%	0.0005%
【Assay】		
Total Alkali Content	The total alkali content should be 98.0% ~ 101.0%	total alkali content： 99.5%
Sodium Carbonate	Content of sodium carbonate should not exceed 0.8%.	sodium carbonate： 0.6%

Remarks	None
Test conlusion	It is tested according to SOP for NH07 Testing (SOP-QC2-502-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1

No.: SOP-QC-004-R01-00

COA No.: ZY22051801

Sample Name	Sodium Hydroxide	Sample Source	Shandong Binhua Dongrui Chemical Co., Ltd
Manufacturer Batch Number	DR01000220 21090601	Incoming Batch Number	NH07-220501
Quantity	3000kg	Storage Condition	sealed to avoid light and moisture,in dry place
Test Date	2022.05.18	Report Date	2022.05.19
Test Reference	SOP for NH07 Testing (SOP-QC2-502-00)		

Test item	Specification	Test result
【Character】		
Appearance	White shiny flakes, granular or lumpy, slight color allowed	White glossy granular
【Identification】		
Chemical method	Aqueous solution, showing the reaction phenomenon of sodium salt	positive reaction
【Test】		
Ferric oxide	NMT 0.008%	0.001%
【Assay】		
Total Alkali Content	The total alkali content should be 98.0% ~ 101.0%	total alkali content : 99.5%
Sodium Carbonate	Content of sodium carbonate should not exceed 0.8%.	sodium carbonate: 0.7%

Remarks	None
Test conlusion	It is tested according to SOP for NH07 Testing (SOP-QC2-502-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1 No.: SOP-QC-004-R01-00

COA No.: ZY21080501

Sample Name	Hydrochloric Acid	Sample Source	Liaoning Meilong Technology Co., Ltd Tangshan Sanyou chlor alkali Co., Ltd
Manufacturer Batch Number	20210727	Incoming Batch Number	NC01-210801
Quantity	4000kg	Storage Condition	Dark, dry and ventilated place
Test Date	2021.08.05	Report Date	2021.08.06
Test Reference	SOP for NC01 Testing (SOP-QC2-506-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless or light yellow transparent liquid	Colorless transparent liquid
【Identification】		
For Chlorides	Positive reaction	Positive reaction
【Test】		
Iron	Not more than 0.008%	0.0001%
Arsenic (Inorganic)	Not more than 0.0001%	conforms
【Assay】		
Assay	Content of HCl shall be not less than 31.0% (g/g)	36.4%

remarks	None
Test conclusion	It is tested according to SOP for NC01 Testing (SOP-QC2-506-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

Page 1/1 No.: SOP-QC-004-R01-00

COA No.: ZY21091101

Sample Name	Hydrochloric Acid	Sample Source	Liaoning Meilong Technology Co., Ltd Tangshan Sanyou chlor alkali Co., Ltd
Manufacturer Batch Number	20210728	Incoming Batch Number	NC01-210901
Quantity	4000kg	Storage Condition	Dark, dry and ventilated place
Test Date	2021.09.11	Report Date	2021.09.12
Test Reference	SOP for NC01 Testing (SOP-QC2-506-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless or light yellow transparent liquid	Colorless transparent liquid
【Identification】		
For Chlorides	Positive reaction	Positive reaction
【Test】		
Iron	Not more than 0.008%	0.0002%
Arsenic (Inorganic)	Not more than 0.0001%	conforms
【Assay】		
Assay	Content of HCl shall be not less than 31.0% (g/g)	35.1%

remarks	None
Test conclusion	It is tested according to SOP for NC01 Testing (SOP-QC2-506-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI

Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

COA No.: ZY21101501

Sample Name	Hydrochloric Acid	Sample Source	Liaoning Meilong Technology Co., Ltd Tangshan Sanyou chlor alkali Co., Ltd
Manufacturer Batch Number	20210730	Incoming Batch Number	NC01-211002
Quantity	3500kg	Storage Condition	Dark, dry and ventilated place
Test Date	2021.10.15	Report Date	2021.10.16
Test Reference	SOP for NC01 Testing (SOP-QC2-506-00)		

Test item	Specification	Test result
【Characters】		
Appearance	Colorless or light yellow transparent liquid	Colorless transparent liquid
【Identification】		
For Chlorides	Positive reaction	Positive reaction
【Test】		
Iron	Not more than 0.008%	0.001%
Arsenic (Inorganic)	Not more than 0.0001%	conforms
【Assay】		
Assay	Content of HCl shall be not less than 31.0% (g/g)	36.1%

remarks	None
Test conclusion	It is tested according to SOP for NC01 Testing (SOP-QC2-506-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

Page1/1

COA No.: ZY21071601

Sample Name	Medicinal charcoal	Sample Source	SHHXTC
Manufacturer Batch Number	2152054	Incoming Batch Number	GH21-210701
Quantity	100kg	Storage Condition	Store in a cool and dry place , avoid sun and rain
Test Date	2021.07.16	Report Date	2021.07.19
Test Reference	SOP for GH21 Testing (SOP-QC2-507-00)		

Test item	Specification	Test result
【Character】		
Appearance	black powder; odorless; sand free	black powder; odorless; sand free
【Identification】		
Identification	White precipitate is formed in calcium hydroxide test solution	Positive reaction
【Test】		
pH	Solution should be clear, and should not change color with blue and red litmus paper	confroms
Acid Soluble Content	Residue ≤ 10mg	3mg

Remarks	None
Conclusion	It is tested according to SOP for GH21 Testing (SOP-QC2-507-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

Page1/1

COA No.: ZY21080501

Sample Name	Medicinal charcoal	Sample Source	SHHXTC
Manufacturer Batch Number	2152060	Incoming Batch Number	GH21-210801
Quantity	100kg	Storage Condition	Store in a cool and dry place , avoid sun and rain
Test Date	2021.08.05	Report Date	2021.08.08
Test Reference	SOP for GH21 Testing (SOP-QC2-507-00)		

Test item	Specification	Test result
【Character】		
Appearance	black powder; odorless; sand free	black powder; odorless; sand free
【Identification】		
Identification	White precipitate is formed in calcium hydroxide test solution	Positive reaction
【Test】		
pH	Solution should be clear, and should not change color with blue and red litmus paper	confroms
Acid Soluble Content	Residue ≤ 10mg	2mg

Remarks	None
Conclusion	It is tested according to SOP for GH21 Testing (SOP-QC2-507-00), the results are conformed

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

JYOUKI Jyouki Pharmaceutical Co., Ltd.

Certificate of Analysis for Material

No.: SOP-QC-004-R01-00

Page1/1

COA No.: ZY21090601

Sample Name	Medicinal charcoal	Sample Source	SHHXTC
Manufacturer Batch Number	2152103	Incoming Batch Number	GH21-210901
Quantity	100kg	Storage Condition	Store in a cool and dry place , avoid sun and rain
Test Date	2021.09.06	Report Date	2021.09.09
Test Reference	SOP for GH21 Testing (SOP-QC2-507-00)		

Test item	Specification	Test result
【Character】		
Appearance	black powder; odorless; sand free	black powder; odorless; sand free
【Identification】		
Identification	White precipitate is formed in calcium hydroxide test solution	Positive reaction
【Test】		
pH	Solution should be clear, and should not change color with blue and red litmus paper	confroms
Acid Soluble Content	Residue ≤ 10mg	5mg
Remarks	None	
Conclusion	It is tested according to SOP for GH21 Testing (SOP-QC2-507-00), the results are conformed	

Analyzed by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

EXHIBIT B
Certificates of Analysis for alpha-GPC

JYOUKI

CERTIFICATE OF ANALYSIS

编号：SOP-QC-004-R03-00

Product Name	L-alpha-Glycerylphosphorylcholine Powder		
CAS No.	28319-77-9	Batch	D01-GH-211201
Quantity	331.25kg	Storage	Preserve in well-closed containers
Manufacturing Date	2021.11.29	Retest Date	2023.11.28
Test Date	2021.12.06	Standard	Enterprise Standard

Tests	Limits	Results	Method
【Description】			
Appearance	White crystal or crystalline	White crystalline	Visual method
Specific rotation	-2.4°~-2.8°	-2.7°	USP43-NF38
【Identification】			
IR	Conforms to the standard	Conforms	USP43-NF38 (IR)
【Test】			
pH value	5.0~7.0	6.1	USP43-NF38 (85mg/mL solution)
Water	≤1.0%	0.32%	USP43-NF38 (KF method)
Chloride	≤0.02%	Conforms	ChP2020 Vol.4, Chap.0801
Sulfate	≤0.02%	Conforms	ChP2020 Vol.4, Chap.0802
Phosphate	≤0.005%	Conforms	In-house method (# SOP-QC1-318-01)
Glycerol	≤0.50%	Not Detected	USP43-NF38 (HPLC)
Related substances	Beta-GPC：≤0.10%； Any individual unspecified impurity：≤0.10%； Total impurities：≤2.0%	Beta-GPC：0.053%； Any individual unspecified impurity：0.069%； Total impurities：0.12%	USP43-NF38 (HPLC)

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CERTIFICATE OF ANALYSIS

编号：SOP-QC-004-R03-00

Product Name	L-alpha-Glycerylphosphorylcholine Powder		
CAS No.	28319-77-9	Batch	D01-GH-211201
Tests	Limits	Results	Method
Residual Solvents	Ethanol：≤0.50%； N-butanol：≤0.50%	Ethanol：0.24%； N-butanol：Not Detected	In-house method (GC, # SOP-QC1-318-01)
Arsenic	≤1.0μg/g	<1.0μg/g	GB5009.268-2016
Lead	≤0.5μg/g	<0.5μg/g	GB5009.268-2016
Mercury	≤0.1μg/g	<0.1μg/g	GB5009.268-2016
Cadmium	≤0.5μg/g	<0.5μg/g	GB5009.268-2016
Particle size	≥85% passing through 80 mesh	Conforms	ChP2020 Vol.4, Chap.0982
Bulk density	0.4-0.7g/ml	0.6g/ml	ChP2020 Vol.4, Chap.0993
Tap density	0.5-0.8g/ml	0.7g/ml	ChP2020 Vol.4, Chap.0993
Total plate count	≤1000cfu/g	<1000cfu/g	ChP2020 Vol.4, Chap.1105
Yeast and mold	≤100cfu/g	<100cfu/g	ChP2020 Vol.4, Chap.1105
Escherichia coliform	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Salmonella	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Staphylococcus	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Coliforms	Absent in 1 g	Conforms	GB4789.3-2016
【Assay】	98.0%-102.0%	99.6%	In-house method (on anhydrous basis) (# SOP-QC1-318-01)
Conclusion	Complies with specification		

Analyzed by [redacted] Checked by [redacted] Approved by [redacted]

金久奇(抚顺)药业有限公司
JYOUKI PHARMACEUTICAL CO., LTD.

JYOUKI

CERTIFICATE OF ANALYSIS

编号：SOP-QC-004-R03-00

Product Name	L-alpha-Glycerylphosphorylcholine Powder		
CAS No.	28319-77-9	Batch	D01-GH-211101
Quantity	336.90kg	Storage	Preserve in well-closed containers
Manufacturing Date	2021.11.01	Retest Date	2023.10.31
Test Date	2021.11.08	Standard	Enterprise Standard

Tests	Limits	Results	Method
【Description】			
Appearance	White crystal or crystalline	White crystalline	Visual method
Specific rotation	-2.4°~-2.8°	-2.8°	USP43-NF38
【Identification】			
IR	Conforms to the standard	Conforms	USP43-NF38 (IR)
【Test】			
pH value	5.0~7.0	5.8	USP43-NF38 (85mg/mL solution)
Water	≤1.0%	0.33%	USP43-NF38 (KF method)
Chloride	≤0.02%	Conforms	ChP2020 Vol.4, Chap.0801
Sulfate	≤0.02%	Conforms	ChP2020 Vol.4, Chap.0802
Phosphate	≤0.005%	Conforms	In-house method (# SOP-QC1-318-01)
Glycerol	≤0.50%	Not Detected	USP43-NF38 (HPLC)
Related substances	Beta-GPC：≤0.10%； Any individual unspecified impurity：≤0.10%； Total impurities：≤2.0%	Beta-GPC：0.056%； Any individual unspecified impurity：0.069%； Total impurities：0.12%	USP43-NF38 (HPLC)

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CERTIFICATE OF ANALYSIS

编号：SOP-QC-004-R03-00

Product Name	L-alpha-Glycerylphosphorylcholine Powder		
CAS No.	28319-77-9	Batch	D01-GH-211101
Tests	Limits	Results	Method
Residual Solvents	Ethanol：≤0.50%； N-butanol：≤0.50%	Ethanol：0.11%； N-butanol：Not Detected	In-house method (GC, # SOP-QC1-318-01)
Arsenic	≤1.0μg/g	<1.0μg/g	GB5009.268-2016
Lead	≤0.5μg/g	<0.5μg/g	GB5009.268-2016
Mercury	≤0.1μg/g	<0.1μg/g	GB5009.268-2016
Cadmium	≤0.5μg/g	<0.5μg/g	GB5009.268-2016
Particle size	≥ 85% passing through 80 mesh	Conforms	ChP2020 Vol.4, Chap.0982
Bulk density	0.4-0.7g/ml	0.6g/ml	ChP2020 Vol.4, Chap.0993
Tap density	0.5-0.8g/ml	0.7g/ml	ChP2020 Vol.4, Chap.0993
Total plate count	≤1000cfu/g	<1000cfu/g	ChP2020 Vol.4, Chap.1105
Yeast and mold	≤100cfu/g	<100cfu/g	ChP2020 Vol.4, Chap.1105
Escherichia coliform	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Saimonella	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Staphylococcus aureus	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Coliforms	Absent in 1 g	Conforms	GB4789.3-2016
【Assay】	98.0%-102.0%	99.9%	In-house method (on anhydrous basis) (# SOP-QC1-318-01)
Conclusion	Complies with specification		

Analyzed by [redacted] Checked by [redacted] Approved by [redacted]

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JYOUKI

Page 1/2

CERTIFICATE OF ANALYSIS

编号：SOP-QC-004-R03-00

Product Name	L-alpha-Glycerylphosphorylcholine Powder		
CAS No.	28319-77-9	Batch	D01-GH-220101
Quantity	337.10kg	Storage	Preserve in well-closed containers
Manufacturing Date	2021.12.30	Retest Date	2023.12.29
Test Date	2022.01.06	Standard	Enterprise Standard

Tests	Limits	Results	Method
【Description】			
Appearance	White crystal or crystalline	White crystalline	Visual method
Specific rotation	-2.4°~-2.8°	-2.8°	USP43-NF38
【Identification】			
IR	Conforms to the standard	Conforms	USP43-NF38 (IR)
【Test】			
pH value	5.0~7.0	6.2	USP43-NF38 (85mg/mL solution)
Water	≤1.0%	0.09%	USP43-NF38 (KF method)
Chloride	≤0.02%	Conforms	ChP2020 Vol.4, Chap.0801
Sulfate	≤0.02%	Conforms	ChP2020 Vol.4, Chap.0802
Phosphate	≤0.005%	Conforms	In-house method (# SOP-QC1-318-01)
Glycerol	≤0.50%	Not Detected	USP43-NF38 (HPLC)
Related substances	Beta-GPC：≤0.10%； Any individual unspecified impurity：≤0.10%； Total impurities：≤2.0%	Beta-GPC：0.056%； Any individual unspecified impurity：0.083%； Total impurities：0.14%	USP43-NF38 (HPLC)

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CERTIFICATE OF ANALYSIS

编号：SOP-QC-004-R03-00

Product Name	L-alpha-Glycerylphosphorylcholine Powder		
CAS No.	28319-77-9	Batch	D01-GH-220101
Tests	Limits	Results	Method
Residual Solvents	Ethanol：≤0.50%； N-butanol：≤0.50%	Ethanol：0.12%； N-butanol：Not Detected	In-house method (GC, # SOP-QC1-318-01)
Arsenic	≤1.0μg/g	<1.0μg/g	GB5009.268-2016
Lead	≤0.5μg/g	<0.5μg/g	GB5009.268-2016
Mercury	≤0.1μg/g	<0.1μg/g	GB5009.268-2016
Cadmium	≤0.5μg/g	<0.5μg/g	GB5009.268-2016
Particle size	≥ 85% passing through 80 mesh	Conforms	ChP2020 Vol.4, Chap.0982
Bulk density	0.4-0.7g/ml	0.6g/ml	ChP2020 Vol.4, Chap.0993
Tap density	0.5-0.8g/ml	0.7g/ml	ChP2020 Vol.4, Chap.0993
Total plate count	≤1000cfu/g	<1000cfu/g	ChP2020 Vol.4, Chap.1105
Yeast and mold	≤100cfu/g	<100cfu/g	ChP2020 Vol.4, Chap.1105
Escherichia coliform	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Salmonella	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Staphylococcus aureus	Absent in 10 g	Conforms	ChP2020 Vol.4, Chap.1106
Coliforms	Absent in 1 g	Conforms	GB4789.3-2016
【Assay】	98.0%-102.0%	100.4%	In-house method (on anhydrous basis) (# SOP-QC1-318-01)
Conclusion	Complies with specification		

Analyzed by [redacted] Checked by [redacted] Approved by: [redacted]

金久奇(抚顺)药业有限公司
JYOUKI PHARMACEUTICAL CO., LTD.

EXHIBIT C

Certificates of Analysis for alpha-GPC Impurities

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Test Report

Report No.	SHP20010040-05.01
Applicant	Jinjiuqi (Fushun) Pharmaceutical Co., Ltd.
Type of Test	Commission Test

ICAS Testing Technology Service (Shanghai) CO.,LTD.

Prepared by [redacted] Reviewed by [redacted] Approved by [redacted]

英格尔检测技术服务（上海）有限公司
ICAS TESTING TECHNOLOGY SERVICE (SHANGHAI) CO., LTD
NCA0494134
Hotline:400-182-9001 Tel:0086 21-51682918 www.icas.org.cn Add:155 Pingbei Rd,Minhang District,Shanghai 上海市闵行区瓶北路155号

ICAS®
英格尔集团

Test Report

Report No.: SHP20010040-05.01

Applicant Details	
Company Name:	Jinjiuqi (Fushun) Pharmaceutical Co., Ltd.
Address:	No.3 Tongyi Shihua South, Nian Pan Road, Dongzhou District, Fushun City, Liaoning Province, China

Sample Information			
Sample No.:	P20010040-05	Sample Type/Specification:	50 g/Bag
Batch No.:	D01-GH-210301	Sample Qty:	100 g
Sample Name:	L-α-Glycerophosphorylcholine	Sample Preservation:	Seal drying
Sample Description:	Solid	Date of sample received:	2021.05.14/2021.05.31

Test Results

No.	Test Items	Test Method(s)	Limit (ppm)	LOQ	LOD	Results
1	Glycidol	In-house laboratory method<1>	1.25 ppm	0.625 ppm	0.313 ppm	N.D
2	3-Chloro-1,2-propanediol		1.25 ppm	0.625 ppm	0.313 ppm	N.D
3	Epichlorohydrin	PVA-R-2020-078.01	1.25 ppm	0.375 ppm	0.188 ppm	N.D
4	1,3-Dichloro-2-propanol		1.25 ppm	0.375 ppm	0.188 ppm	N.D
5	2,3-Dichloro-1-propanol		1.25 ppm	0.375 ppm	0.188 ppm	N.D
6	2-Chloroethanol	PVA-R-2020-101.01	1.25 ppm	0.625 ppm	0.313 ppm	N.D

Note:
<1> This test data is the test result under the condition of prior art and is only for test research or reference.
N.D=Not detected.

ICAS®
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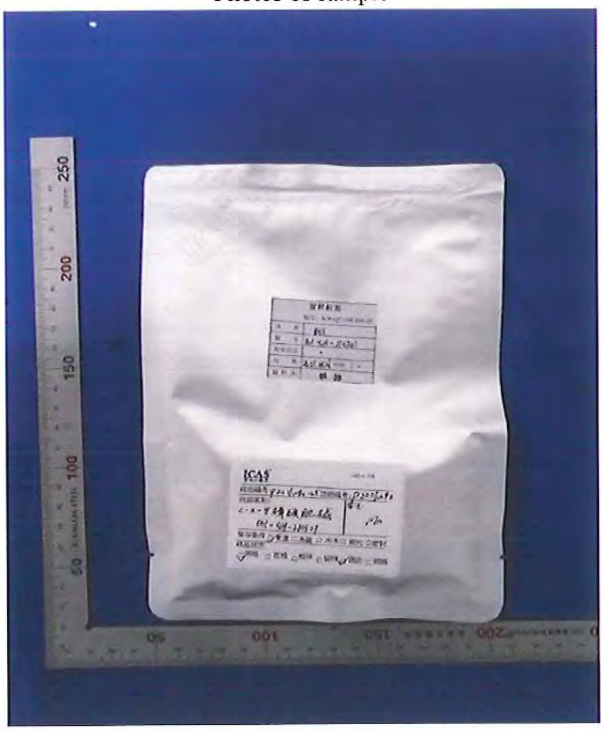
Test Report

Report No.：SHP20010040-05.01

Photos of sample



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End of the report

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Test Report

Report No.	SHP20010040-06.01
Applicant	Jinjiuqi (Fushun) Pharmaceutical Co., Ltd.
Type of Test	Commission Test

ICAS Testing Technology Service (Shanghai) CO.,LTD.

Prepared by [redacted] Reviewed by [redacted] Approved by [redacted]

ICAS®
英格尔集团

Test Report

Report No.: SHP20010040-06.01

Applicant Details	
Company Name:	Jinjiuqi (Fushun) Pharmaceutical Co., Ltd.
Address:	No.3 Tongyi Shihua South, Nian Pan Road, Dongzhou District, Fushun City, Liaoning Province, China

Sample Information			
Sample No.:	P20010040-06	Sample Type/Specification:	50 g/Bag
Batch No.:	D01-GH-210302	Sample Qty:	100 g
Sample Name:	L-α-Glycerophosphorylcholine	Sample Preservation:	Seal drying
Sample Description:	Solid	Date of sample received:	2021.05.14/2021.05.31

Test Results

No.	Test Items	Test Method(s)	Limit (ppm)	LOQ	LOD	Results
1	Glycidol	In-house laboratory method<1>	1.25 ppm	0.625 ppm	0.313 ppm	N.D
2	3-Chloro-1,2-propanediol		1.25 ppm	0.625 ppm	0.313 ppm	N.D
3	Epichlorohydrin	PVA-R-2020-078.01	1.25 ppm	0.375 ppm	0.188 ppm	N.D
4	1,3-Dichloro-2-propanol		1.25 ppm	0.375 ppm	0.188 ppm	N.D
5	2,3-Dichloro-1-propanol		1.25 ppm	0.375 ppm	0.188 ppm	N.D
6	2-Chloroethanol	PVA-R-2020-101.01	1.25 ppm	0.625 ppm	0.313 ppm	N.D

Note:
<1> This test data is the test result under the condition of prior art and is only for test research or reference.
N.D=Not detected.

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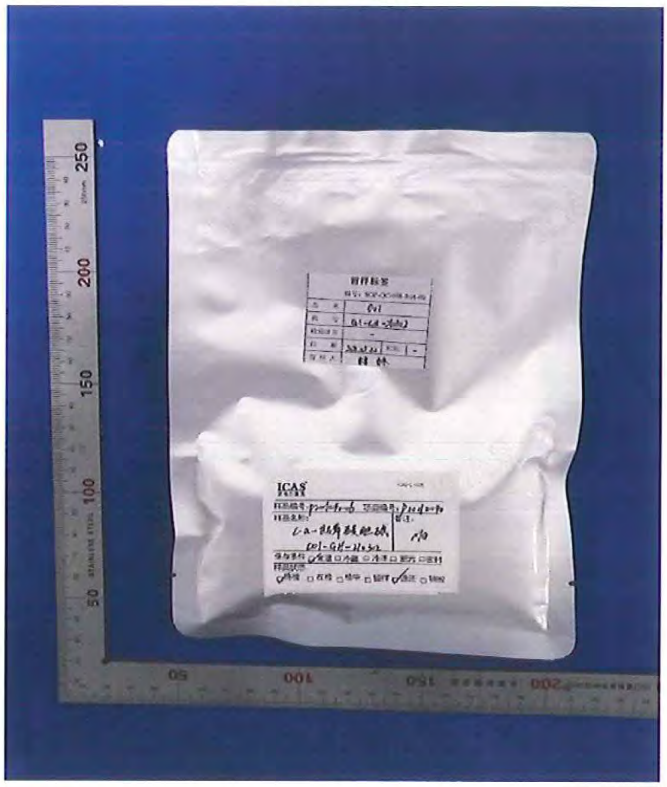
Test Report

Report No.：SHP20010040-06.01

Photos of sample



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End of the report

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Test Report

Report No.	SHP20010040-07.01
Applicant	Jinjiuqi (Fushun) Pharmaceutical Co., Ltd.
Type of Test	Commission Test

ICAS Testing Technology Service (Shanghai) CO.,LTD.

Prepared by [redacted] Reviewed by [redacted] Approved by [redacted]

英格尔检测技术服务（上海）有限公司
ICAS TESTING TECHNOLOGY SERVICE (SHANGHAI) CO., LTD
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Test Report

Report No.: SHP20010040-07.01

Applicant Details	
Company Name:	Jinjiuqi (Fushun) Pharmaceutical Co., Ltd.
Address:	No.3 Tongyi Shihua South, Nian Pan Road, Dongzhou District, Fushun City, Liaoning Province, China

Sample Information			
Sample No.:	P20010040-07	Sample Type/Specification:	50 g/Bag
Batch No.:	D01-GH-210303	Sample Qty:	100 g
Sample Name:	L-α-Glycerophosphorylcholine	Sample Preservation:	Seal drying
Sample Description:	Solid	Date of sample received:	2021.05.14/2021.05.31

Test Results

No.	Test Items	Test Method(s)	Limit (ppm)	LOQ	LOD	Results
1	Glycidol	In-house laboratory method<1>	1.25 ppm	0.625 ppm	0.313 ppm	N.D
2	3-Chloro-1,2-propanediol		1.25 ppm	0.625 ppm	0.313 ppm	N.D
3	Epichlorohydrin	PVA-R-2020-078.01	1.25 ppm	0.375 ppm	0.188 ppm	N.D
4	1,3-Dichloro-2-propanol		1.25 ppm	0.375 ppm	0.188 ppm	N.D
5	2,3-Dichloro-1-propanol		1.25 ppm	0.375 ppm	0.188 ppm	N.D
6	2-Chloroethanol	PVA-R-2020-101.01	1.25 ppm	0.625 ppm	0.313 ppm	N.D

Note:
<1> This test data is the test result under the condition of prior art and is only for test research or reference.
N.D=Not detected.

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Test Report

Report No.：SHP20010040-07.01

Photos of sample

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End of the report

EXHIBIT D
Analytical Method for alpha-GPC

JYOUKI

Analytical Procedures

1.Character

1.1.Appearance

Take the test sample and observe visually under natural light.It should be white crystalline or crystalline powder

1.2 Specific Rotation

Take an appropriate amount of the test sample, dissolve it in water and quantitatively dilute it to make a solution of about 100 mg, measure its optical rotation at 20°C, and calculate the specific rotation according to the following formula. The specific rotation $[\alpha]_D^{20}$ should between -2.4° to -2.8°.

$$[\alpha]_D^{20} = \frac{100\alpha}{L \times c \times (1 - mo)}$$

In the formula,

α is the measured optical rotation;

D means measure under wavelength ($\lambda = 589.3nm$);

L is the length of the measuring tube (1dm);

c is the weight (g) of the substance to be tested per 100ml of solution;

mo is moisture refer to water content

1.3 Identification

Take about 1 to 1.5mg of the test sample, put it in an agate mortar and grind it into fine. Add 200 ~ 300mg dry potassium bromide fine powder (the ratio with the test sample is about 200:1) as diluent, fully grind and mix. Prepare the potassium bromide plates and it shall be transparent by visual inspection . In potassium bromide plates,the test sample shall be evenly distributed without obvious particles. The full scan was carried out in the wave number range of 4000cm^{-1} to 400cm^{-1}, and the control test was carried out. the infrared spectrum of this product should be consistent with that of the reference substance

2.Test

2.1 pH

Take this product, dissolve it with water and dilute it to make a solution containing about 85mg per 1ml. Test it according to the method. The pH value should be 5.0 to 7.0.

2.2 Water

Take the test sample, weigh it accurately,, use methanol as solvent and use Karl Fischer method to determine the water content. According to the following formula,the water content of the test sample shall not exceed 1.0%

$$water = \frac{(A-B) \times F \times 100\%}{1000 \times W}$$

Where,

A is the volume of Fisher's solution consumed by the test sample, ml;

B is the volume of Fisher's solution consumed by blank solution, ml;

F is the weight of water equivalent to 1 ml of Fisher's solution, mg;

W is the weight of the test sample,g .

2.3 Chloride

Preparation of standard sodium chloride solution :weigh 0.165g of sodium chloride, put it into a 1000ml volumetric flask. Add water to dilute it to the scale, and shake it well to get the stock solution. Before use, accurately measure 10ml of standard sodium chloride stock solution, put it into a 100ml volumetric flask, add water to dilute it to the scale, and shake it well to get the solution (every 1ml is equivalent to 10μg CL).

Preparation of test solution:Take 0.25g of the test sample, put it into a 50ml Nessler colorimetric tube and add water to dissolve it into 25ml. Then add 10ml diluted nitric acid(take 105ml of nitric acid and dilute it to 1000ml with water), add water to make it into 40ml solution, shake well and get the test solution.

Preparation of control solution:accurately measure 5.00ml of standard sodium chloride solution

and put it into a 50ml Nessler colorimetric tube, add 10ml of diluted nitric acid and add water to make it into 40ml solution, and shake well and get the control solution.

Add 1.0ml silver nitrate solution(take 17.5g of silver nitrate, dilute it to 1000ml with water, and shake it well) into test solution and control solution respectively, and dilute with water to make 50ml. Shake well, place in dark place for 5 minutes and place on same black background, observe and compare from up to down of colorimetric tube.Any opalescence in the test solution is not more intense than that in the control solution (0.02%).

2.4.Sulfate

Preparation of standard potassium sulfate solution: weigh 0.181g of potassium sulfate, put it into a 1000ml volumetric flask, add appropriate amount of water to dissolve it, dilute it to the scale, and shake it evenly (every 1ml is equivalent to 100 μ g of SO_4)

Preparation of test solution:Take 1.0g of the test sample, put it into a 50ml Nessler colorimetric tube and add water to make it into 40ml solution . Add 2.0ml diluted hydrochloric acid (take 234ml of hydrochloric acid and dilute it to 1000ml with water) and shake well to get the test solution.

Preparation of control solution:accurately measure 2.00ml of standard potassium sulfate solution and put it into a 50ml Nessler colorimetric tube and add water to make it into 40ml solution .Add 2.0ml of diluted hydrochloric acid and shake well to get control solution.

Add 5.0ml 25% barium chloride solution into the test solution and the control solution respectively, and dilute to 50ml with water. Shake well, place them for 10 minutes, and place them on the same black background. Observe and compare from the top to the bottom of the colorimetric tube.Any opalescence in the test solution is not more intense than that in the control solution (0.02%).

2.5.Phosphate

Preparation of standard phosphate solution: accurately weigh 0.286g of potassium dihydrogen phosphate dried to constant weight at 105 °C, put it into a 1000ml volumetric flask, add water to dissolve and dilute to the scale as standard phosphate stock solution.

Before use, take 5.00 ml of the above standard phosphate stock solution, put it into 100ml volumetric flask, add water to dilute to the scale, shake well and use it as phosphate standard

solution.(Every 1ml of this solution is equivalent to 10 μg of PO_4^{3-})

Preparation of test solution :take 1.0g of test sample, put it into 25ml Nessler colorimetric tube, and add 10ml of water to dissolve it.

Preparation of control solution :take 5.0ml of standard phosphate solution, put it into 25ml Nessler colorimetric tube, and add water to 10ml.

Preparation of ammonium molybdate solution :weigh 1g of ammonium molybdate and dissolve it with 40ml of 0.5mol/L sulfuric acid solution.

Preparation of 1-amino-2-naphthol-4-sulfonic acid solution: take 5g of anhydrous sodium sulfite, 94.3g of sodium bisulfite and 0.7g of 1-amino-2-naphthol-4-sulfonic acid, and mix well, before use , take the 1.5 g of above mixture, dissolve it with 10ml of water.and filter it if necessary)

Add 1.0ml of ammonium molybdate and 0.5ml of 1-amino-2-naphthol-4-sulfonic acid solution to to the test solution and the control solution respectively. Dilute them with water to 25ml respectively. Shake well, place them for 10 minutes, and place them on the same white background. Observe and compare from the top to the bottom of the colorimetric tube. The color of test solution should not be deeper than the color of control solution (0.005%).

2.6.Glycerol

Take 4g of the test sample, put it into a 10ml volumetric flask,, add water to dissolve and dilute to the scale, shake well, and use it as the test solution. Take an appropriate amount of glycerol reference substance and dilute it with water to form a solution containing 2mg glycerol per 1ml as the control solution.Take appropriate amount of control solution and test solution respectively, and dilute them with water to get one solution containing 2mg glycerol per 1mland anther solution containing 400mg of choline alfoscerate per 1ml, as the System suitability solution. Use Zorbax Sax column (4.6mm × 25cm, 5μm) as the analytical column, acetonitrile-water (55:45) as the mobile phase, the flow rate : 0.5 ml per minute, the column temperature : 40°C, and the detector: the differential detector. Injection volume: 20μl.

Take the blank solution (water) and the system suitability solution for injection once respectively,

and record the chromatogram. The resolution of Glycerol and L-α- glycerophosphoryl choline in the chromatogram of the system suitability solution shall not be less than 2.0.Take the control solution for 6 consecutive injections, and calculate from the last injection of the control solution. the bracketing standard solution (that is, System suitability solution) is respectively injected once after every 12 times injection and ending the sequence. and record the chromatogram.The RSD should not exceed 5.0%, base on the chromatographic peak area of glycerol for 6 consecutive injections .The RSD should not exceed 5.0% ,based on chromatographic peak area of each substance adding with bracketing standard solution, Inject the test solution and record the chromatogram. According to the external standard method, the content of glycerol was calculated by peak area,the content of glycerol in the test sample shall not exceed 0.50%

Calculation formula:

$$\text{Glycerol}(\%) = \frac{m_{对} \times \text{purity of reference substance} \times A_{供} \times \text{dilution ratio of test solution}}{V_{对} \times A_{对} \times m \times 1000} \times 100$$

Where,

$m_{对}$: the weight of glycerol reference substance, mg;

$A_{供}$, the peak area of glycerol in the test solution;

$V_{对}$, diluted volume of glycerol reference substance, ml;

$A_{对}$, peak area of glycerol reference substance;

m. weight of the test sample, g.

2.7 Related substances

Solution A: Acetonitrile and methanol (3:1)

Solution B: Transfer 1.98 g of ammonium acetate to a 500-mL volumetric flask. Dissolve in about 470mL of water. Adjust with acetic acid to a pH of 4.5 and dilute with water to volume.

Solution C: Transfer 100.0mL of *Solution B* to a 1000mL volumetric flask and dilute with water to

volume. Check the pH of the solution. If it is not 4.5, adjust with diluted ammonia solution or diluted acetic acid to a pH of 4.5.

Solution D: Mix 300mL of *Solution B* and 1700mL of *Solution A*.

Solution E: Mix 700mL of *Solution C* and 1300mL of *Solution A*.

Mobile phase: See *Table 1*

Table 1

Time (min)	Solution D (%)	Solution E (%)
0	98	2
5	98	2
18	44	56
30	32	68
34	10	90
42	10	90
43	98	2
55	98	2

Diluent: Methanol and water (80:20)

Internal standard solution: Transfer 100 mg of L-Serine RS to a 100-mL volumetric flask. Dissolve in and dilute with *Diluent* to volume. Transfer 5.0mL of the

resultant solution to a 250mL volumetric flask and dilute with *Diluent* to volume.

Take 2.5mg of L- alpha-Glycerophosphorylethanolamine RS and beta- Glycerylphosphorylcholine RS into the same 10ml Volumetric flask, add the serine internal standard solution to dissolve and dilute to the volume, used as a mixed stock solution. Take 200mg of L- alpha- Glycerylphosphorylcholine RS into a 10ml volumetric flask and accurately measure 0.8ml of mentioned above mixed stock solution into the same 10ml volumetric flask, add serine internal standard solution to dissolve, and dilute to the volume.used as the system suitability solution.

Sample solution: Transfer 0.2g of L- alpha- Glycerylphosphorylcholine to a 10-mL volumetric flask. Dissolve in and dilute with the *Internal standard solution* to volume.

Chromatographic system

(See *Chromatography* 〈621〉, *System Suitability*.)

Mode: LC

Detector: Evaporative light-scattering detector (ELSD)

Detector temperature: 90°

Column: 4.6-mm × 25-cm; 5-µm packing L111

Carrier gas: Nitrogen

Flow rate: 0.65 mL/min

Injection volume: 40 µL

System suitability

Sample: *System suitability solution*

[NOTE—Adjust the low rate and/or isocratic portion of the gradient program to obtain the retention time of serine at 28 ± 2 min. See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.2 between the serine and L- alpha-glycerophosphorylethanolamine peaks; NLT 0.4 between the beta- glycerylphosphorylcholine and L- alpha- glycerylphosphorylcholine peaks

Relative standard deviation: NMT 10% for the serine peak

Analysis

Samples: *Diluent*, *Internal standard solution*, and *Sample solution*

[NOTE—The response factor of serine equals that of L- alpha- glycerylphosphorylcholine. Disregard peaks that are observed in both *Diluent* and *Sample solution* chromatograms. Disregard peaks below 0.05% observed in the chromatogram of the *Sample solution*.]

Calculate the percentage of each impurity in the portion of L- alpha- Glycerylphosphorylcholine or L- alpha- Glycerylphosphorylcholine solution taken:

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Result = $(r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$

r_U= peak response of each impurity from the *Sample solution*

r_S= peak response of serine from the *Internal standard solution*

C_S= concentration of L-Serine RS in the *Internal standard solution* (mg/mL)

C_U= concentration of L- alpha- Glycerylphosphorylcholine or L- alpha- Glycerylphosphorylcholine solution in the *Sample solution* (mg/mL)

F= relative response factor (see *Table 2*)

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Beta- Glycerylphosphorylcholine	0.96	1.0	0.10
L- alpha- Glycerylphosphorylcholine	1.0	—	—
Serine	1.75	1.0	—
L- alpha- Glycerophosphorylethanolamine	1.83	1.0	—
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	2.0

2.8.Residual solvents

Take 50mg of the test sample, put it into a 20ml head-space bottle, add 5ml of water and seal it as the test solution. In addition, take appropriate amount of ethanol and N-butanol, accurately weigh them, dilute them with water, and make a mixed solution containing 0.05mg ethanol and N-butanol per1ml as the control solution.Accurately measure 5ml of test solution and 5ml of control solution, put them into 20ml head-space bottle respectively, and seal . According to the method, use DB-WAX capillary column (60m × 0.32mm × 0.5μ m) as the chromatographic column.Column temperature : 120 ℃. Flow rate :1ml / min; Inlet temperature : 200 ℃; Split ratio: 10:1; Hydrogen

flame ionization detector （ FID; Detector temperature :200 ℃; Equilibrium temperature of head-space bottle: 85 ℃. Equilibrium time: 15min.

Take the control solution as the system suitability solution, inject the sample by head-space, and record the chromatogram. Starting from the last injection of system suitability solution, the bracketing standard solution (that is, System suitability solution) is respectively injected once after every 12 times injection and ending the sequence. and record the chromatogram.

The RSD should meet the requirements, base on the chromatographic peak area of each substance for 6 consecutive injections.The RSD still meets the above requirements, based on chromatographic peak area of each substance adding with bracketing standard solution and the resolution of ethanol and N-butanol should meet the requirements.and the number of theoretical plates calculated by ethanol is not less than 5000; Then take the test solution ,inject the sample by head-space and record the chromatogram. According to the external standard method, the content of ethanol and N-butanol was calculated by peak area. The content of Ethanol should not exceed 0.50%. The content of N-butanol should not exceed 0.50%.

$$\text{Residual solvent（%）} = \frac{m_{对} \times \text{purity of reference substance} \times A_{作} \times \text{dilution ratio of test solution}}{V_{对} \times A_{对} \times m \times 1000} \times 100$$

Where,

$m_{对}$: the weight of ethanol or n-butanol reference substance, mg;

$A_{作}$, the peak area of ethanol or n-butanol in the test solution;

$V_{对}$, diluted volume of ethanol or n-butanol reference substance, ml;

$A_{对}$, Average peak area of ethanol or n-butanol in the control solution;

m. weight of the test sample, g.

2.9. Microbial limits

2.9.1 Total bacterial count

Preparation of test solution :weigh 10g of test sample and add pH7 0 sterile Sodium Chloride-Peptone buffer to 100ml , dissolve and mix well.Use as 1:10 test solution. Take 1ml of 1:10 test solution and add 9ml pH 7 0 sterile Sodium Chloride -Peptone buffer, mix well . Use as 1:100 test solution.

Preparation of 1: 10 test solution :take 1ml of 1:10 test solution, put it in a plate and prepare 2 samples in parallel.

Preparation of 1: 100 test solution :take 1ml of 1:100 test solution, put it in a plate and prepare 2 samples in parallel.

Preparation of negative control solution: Take 1ml of pH 7.0 sterile Sodium Chloride -Peptone buffer, prepare 2 samples in parallel.

Pour about 20ml of Trypsin casein soy peptone agar medium(TSA) into the above plates. After all of them are solidified, place them upside down and incubate at 30 ~ 35 ℃ for 5 days and count.

For the total aerobic microbial count (TAMC) choose a dilution less than 300cfu. The levels of dilution is the basis of microbial counts of reporting. Calculate the number of microorganisms in 1g of test sample, based on the highest mean colony count. Declare microbial counts of reporting to 2 significant figures. The total bacterial count in each 1g of test sample shall not exceed 1000cfu.

2.9.2 Yeasts and molds

Preparation of 1: 10 test solution: take 1ml of 1:10 test solution in "2.9.1 total bacterial count" inspection, put it in a plate and prepare 2 samples in parallel.

Preparation of negative control solution:Take 1ml of pH 7.0 sterile Sodium Chloride -Peptone buffer, prepare 2 samples in parallel.

Pour about 20ml of Sabouraud's glucose agar medium into the above plates. After all of them are solidified, place them upside down and incubate at 20 ~ 25℃ for 5 days and count. For the total aerobic microbial count (TAMC) choose a dilution less than 100cfu . The levels of dilution is the

basis of microbial counts of reporting . Calculate the number of microorganisms in 1g of test sample,based on the highest mean colony count. Declare microbial counts of reporting to 2 significant figures .The total number of molds and yeasts in each 1g of test sample shall not exceed 100cfu.

2.9.3 Escherichia coli

Sample preparation and pre-incubation:Take 10g of the test sample, inoculate it into 100ml of soya bean casein digent broth .and inoculate it at 30 ~ 35 ℃ for 18 ~ 48 hours.

Transfer 1ml of pre-incubation broth to 100ml macconkey broth and incubate at 42~44℃ for 24-48 hours.Subculture a small amount of macconkey broth onto macconkey agar and incubate at 30~35℃ for 18-72 hours.

Growth of colonies on macconkey agarindicates the possible presence of E. coli. This is confirmed by isolation, purification and appropriate identification tests.The product is qualified if no colonies are present or if the identification tests are negative.

2.9.4 Salmonella

Sample preparation and pre-incubation: Inoculate 10g of sample to a suitable amount of soya beancasein digest broth , mix and incubate at 30-35℃for 18 - 24 hours.

Transfer 0.1ml pre-incubation culture to 10 ml rappaport vassiliadis salmonella enrichment broth and incubate at 30~35℃ for 18-24 hours. Subculture asmall amount of the rappaport vassiliadis salmonella enrichment broth on xylose-lysine-deoxycholate agar and incubate at 30~35℃ for 18-48 hours.

The Salmonella is indicated by the growth of well-developed, erythroic , colourless , transparent or semitransparent colonies, with or without black centres. Select suspected colonies with aninoculating needle and puncture into the triple sugar iron agar, then incubate at 30-35℃ for 18-24 hours.

If there are suspected colonies grow on xylose lysine deoxycholate agar, and the triple sugar iron agar with red in the slant, yellow in the bottom, or yellow in the slant, black in the bottom,

appropriate identification should be performed to confirm if they are Salmonella. The product is qualified if no colonies grow on the plates, or the identification tests are negative, or the triple sugar iron agar shows no red/yellow in the slant, no yellow/black in the bottom.

2.9.5 Staphylococcus. aureus

Preparation of test solution and pre-incubation: Inoculate 10g of the sample into 100 ml of Trypticase Soy Broth (TSB) to obtain the sample solution; inoculate 10g of the sample and 1ml of Staphylococcus aureus (microbial suspension containing microorganisms less than 100cfu/ml) into 100 ml of TSB to obtain the positive control solution; inoculate 10ml of pH 7.0 sterile sodium chloride-peptone buffer solution into 100ml of TSB to obtain the negative control solution. Incubate at 30-35°C for 18-24 hours.

Procedure: Subculture the pre-incubation culture described above on Mannitol Salt Agar and incubate at 30-35°C for 18-72 hours. Growth of colonies on Mannitol Salt Agar with yellow/white colonies surrounded by a yellow zone indicates the possible presence of S. aureus. This is confirmed by isolation, purification and appropriate identification tests. The sample is qualified (absence per 10g) if no colony is similar with the feature described above, or if the identification tests of colonies are negative.

2.10 Coliforms

Sample preparation: weigh 25g of sample and put it into a volumetric flask containing 225ml physiological saline to prepare a 1:10 sample homogenate. Take 1ml of 1:10 sample homogenate and add it to 9ml of physiological saline to prepare 1:100 sample homogenate; take 1ml of 1:100 sample homogenate and add it to 9ml physiological saline to prepare 1:1000 sample homogenate. Stay for use

Operation: take 1ml of the above 1:10, 1:100 and 1:1000 sample homogenates respectively, add them to 10ml of lauryl sulfate tryptone (LST) broth, inoculate 3 tubes at each dilution, and incubate them at 36°C±1°C for 24h ± 2h. Observe whether there are bubbles in the inverted tube. Conduct the refermentation test (confirmation test) for samples which produced gas for 24h ± 2h. If no gas is produced, continue to incubate them for 48h ± 2h. Conduct the refermentation test for sample which

produced gas. Those without gas production were negative for coliform bacteria.

Refermentation test (confirmation test)

Take 1 ring of culture from the gas producing LST broth tube with inoculation ring, transfer it into bright green lactose bile salt broth (BGLB) tube, and incubate it at 36℃±1℃ for 48h±2h ,observe whether gas is produced. Gas producing samples are counted as coliform positive tubes.

2.11. Assay

Take about 0.2g of this product, weigh it accurately, add 20ml of glacial acetic acid and 40ml of acetic anhydride to dissolve, titrate with perchloric acid titrant (0.1mol/l) according to potentiometric titration (general rule 0701), and correct the titration result with blank solution. Each 1ml perchloric acid titrant (0.1mol/l) is equivalent to 25.722 mg of $C_8H_{20}NO_6P$. The content of choline alfoscerate (C8H20NO6P) should be 98.0% to 102.0%.calculated on the anhydrous basis.

Calculation formula: $Assay\ (\%) = \frac{25.722 \times F \times (V - V_0)}{m \times 1000 \times (1 - w)} \times 100$

Where:

25.722, each 1ml perchloric acid titrant (0. 1mol / L) is equivalent to the weight of choline alfoscerate (C8H20NO6P), mg / ml;

F, The calibration value of perchloric acid titrant (0.1mol/l);

V,The volume of perchloric acid titrant (0.1mol/l) consumed by the test sample, ml;

V_0, volume of perchloric acid titrant (0.1mol/l) consumed by blank solution, ml;

m, weight of test sample, g;

w, water content of the test sample.

2.12 Particle size

Place 100g of the substance being examined, in the sieve with 80 Mesh (the sieve is equipped with

a close receiving container), cover the sieve, horizontally rotate and vibrate the sieve at least 3 minutes, and gently pat the sieve from time to time in the vertical direction, take particles and powder under the sieve, weigh, calculate the passing rate (%).

Calculation formula:

$$\text{Passing rate (\%)} = \frac{\text{Weight of particle and powder under the sieve}}{\text{Weight of sample}}$$

Acceptance criterion: the passing rate through the sieve with 80 mesh should be not less than 85%.

2.13 Bulk density

Accurately weigh 100g of the substance being examined (if necessary, the sample should be through the sieve with the pore size of 1.0mm, fully disperse the clumps formed in storage. The sieving operation should be gentle to avoid changing the properties of the powder), slowly pour into the 250ml glass measuring cylinder, carefully scrape the top of the cup, avoid pressing the powder, record the apparent volume with the nearest scale line, and calculate the bulk density as following formula:

$\rho_B = M/V_0$

Wherein: ρ_B, is the density of the fixed mass method,g/ml; M is the mass of sample to be examined, g; V0 is the apparent volume of sample to be examined, ml.

Note: Three samples of the same batch were determined in parallel, and the readings were recorded. The average value was used as the test result.

Acceptance criterion: the bulk density should be 0.4g/ml to 0.7g/mL

2.14 Tapped density

Place the loose sample into a 250ml measuring cylinder on a table with rubber pad and vibrate by hand until the volume no longer changes. Calculate the tapped density (g/ml) according to the formula: m/V_F, where V_F is the tapped volume of sample, ml, and m is the mass of sample, g.

Note: Three samples of the same batch were determined in parallel, and the readings were recorded. The average value was used as the test result.

Acceptance criterion: the bulk density should be 0.5g/ml to 0.8g/mL.

2.15 Arsenic, Lead, Mercury and Cadmium

The Arsenic, Lead, Mercury and Cadmium is tested by a qualified third party, according to the National Food safety standard GB 5009.268-2016 for Determination of Multiple Elements, Method I.

Acceptance criterion: the Cadmium should be not more than 0.5μg/g; the Arsenic should be not more than 1.0μg/g; the lead should be not more than 0.5 μg/g; the mercury should be not more than 0.1μg/g.

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EXHIBIT E
Shelf-Life Data for alpha-GPC

Summery of stability tests

1.1. Accelerated stability test

Table 1-1 Accelerated stability test protocol

Packaging	Simulated commercial packaging(the primary packaging is one layer of medical low density polyethylene bag, and the secondary packaging is Aluminum foil bag)	
Conditions	Temperature:: 40°C±2°C; Humidity:: 75% RH±5%RH	
Sampling time and monitoring items.	0、1st、2nd、3rd and 6thmonth	test all items

Table 1-2 test results of accelerated stability test

monitoring items		Limits	Batch No	0 h	1st month	2nd month	3rd month	6th month
Test	Appearance	White crystal or crystalline powder	D01-GH-190 301	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder
			D01-GH-190 302	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder
			D01-GH-190 303	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder
	Specific rotation	-2.4°~-2.8°	D01-GH-190 301	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°
			D01-GH-190 302	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°
			D01-GH-190 303	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°
Identification		IR method, the infrared spectrum of this product should be consistent with that of the reference substance	D01-GH-190 301	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190 302	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190 303	Conforms	Conforms	Conforms	Conforms	Conforms

2

Test	pH value	5.0~7.0	D01-GH-190 301	6.0	6.1	6.0	6.1	6.0
			D01-GH-190 302	6.1	6.0	6.2	6.1	6.1
			D01-GH-190 303	6.2	6.2	6.2	6.2	6.3
	Water	≤1.0%	D01-GH-190 301	0.20%	0.21%	0.23%	0.30%	0.40%
			D01-GH-190 302	0.25%	0.28%	0.30%	0.35%	0.42%
			D01-GH-190 303	0.30%	0.35%	0.35%	0.40%	0.46%
	Chloride	≤0.02%	D01-GH-190 301	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190 302	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190 303	Conforms	Conforms	Conforms	Conforms	Conforms
	Sulfate	≤0.02%	D01-GH-190 301	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190 302	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190 303	Conforms	Conforms	Conforms	Conforms	Conforms
	Phosphate	≤0.005%	D01-GH-190 301	Conforms	Conforms	Conforms	Conforms	Conforms

			D01-GH-190 302	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190 303	Conforms	Conforms	Conforms	Conforms	Conforms
	Glycerol	≤0.50%	D01-GH-190 301	Not detected	Not detected	Not detected	Not detected	Not detected
			D01-GH-190 302	Not detected	Not detected	Not detected	Not detected	Not detected
			D01-GH-190 303	Not detected	Not detected	Not detected	Not detected	Not detected
	Related substances	Beta-GPC: ≤0.10%; Any individual unspecified impurity: ≤0.10%; Total impurities: ≤2.0%	D01-GH-190 301	Beta-GPC : 0.064%; Any individual unspecified impurity : 0.080%; Total impurities:0.14 %	Beta-GPC : 0.068%; Any individual unspecified impurity: 0.081%; Total impurities:0.15 %	Beta-GPC: 0.067%; Any individual unspecified impurity: 0.082%; Total impurities:0.15%	Beta-GPC: 0.060%; Any individual unspecified impurity : 0.083%; Total impurities:0.14%	Beta-GPC: 0.060%; Any individual unspecified impurity: 0.078%; Total impurities:0.14%
			D01-GH-190 302	Beta-GPC: 0.079%; Any individual unspecified impurity: 0.080%; Total impurities:0.16 %	Beta-GPC: 0.074%; Any individual unspecified impurity: 0.080%; Total impurities:0.15 %	Beta-GPC: 0.072%; Any individual unspecified impurity: 0.082%; Total impurities:0.15%	Beta-GPC: 0.075%; Any individual unspecified impurity: 0.085%; Total impurities:0.16%	Beta-GPC: 0.074%; Any individual unspecified impurity: 0.089%; Total impurities:0.16%

			D01-GH-190303	Beta-GPC0.057%; Any individual unspecified impurity: 0.079%; Total impurities:0.14%	Beta-GPC0.056%; Any individual unspecified impurity: 0.082%; Total impurities:0.14%	Beta-GPC0.058%; Any individual unspecified impurity: 0.086%; Total impurities:0.14%	Beta-GPC0.057%; Any individual unspecified impurity: 0.089%; Total impurities:0.15%	Beta-GPC0.061%; Any individual unspecified impurity: 0.083%; Total impurities:0.14%
	Residual Solvents	Ethanol、N-butanol≤0.50%	D01-GH-190301	Ethanol : 0.20%, N-butanol :not detected	Ethanol : 0.19%, N-butanol :not detected	Ethanol : 0.17%, N-butanol :not detected	Ethanol: 0.18%, N-butanol :not detected	Ethanol: 0.16%, N-butanol :not detected
			D01-GH-190302	Ethanol: 0.15%, N-butanol :not detected	Ethanol: 0.14%, N-butanol :not detected	Ethanol: 0.14%, N-butanol :not detected	Ethanol: 0.12%, N-butanol :not detected	Ethanol: 0.11%, N-butanol :not detected
			D01-GH-190303	Ethanol: 0.16%, N-butanol :not detected	Ethanol: 0.17%, N-butanol :not detected	Ethanol: 0.14%, N-butanol :not detected	Ethanol: 0.14%, N-butanol :not detected	Ethanol: 0.13%, N-butanol :not detected
	microbial limits	The total number of aerobic bacteria shall not exceed 1000cfu/1 g, and the total number of molds and	D01-GH-190301	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190302	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190	Conforms	Conforms	Conforms	Conforms	Conforms

5

		yeasts shall not exceed 100cfu/1 g. Salmonella, Escherichia coli ,Staphylococcus and coliforms should be absent.	303					
Assay		calculated on the anhydrous basis, 98.0%~102.0%	D01-GH-190 301	99.9%	100.0%	100.1%	100.0%	100.2%
			D01-GH-190 302	100.0%	100.0%	100.2%	100.1%	100.3%
			D01-GH-190 303	99.8%	100.0%	99.9%	99.8%	100.0%

Conclusion :In accelerated stability test (6 months) of three batches, the results showed that monitoring items have almost no change compared with that in 0 h, and test results of all items meet the specification.

Drafted by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

6

2.2 Long term stability test

Table 2-1 long term stability test protocol

Packaging	Simulated commercial packaging(the primary packaging is one layer of medical low density polyethylene bag, and the secondary packaging is Aluminum foil bag)	
Conditions	Temperature:25°C±2°C; Humidity:60% RH±5%RH	
Sampling time and monitoring items.	0h, 3rd,6th,9th, 12th,18th, 24th,36th and 48th month	test all items

Table 2-2 results of long term stability test

monitoring items		Limits	Batch No	0 h	3rd month	6th month	9th month	12th month	18th month	24th month	36th month
test	Appearance	White crystal or crystalline powder	D01-GH-190301	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder
			D01-GH-190302	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder
			D01-GH-190303	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder	white crystal powder
	Specific rotation	-2.4°~-2.8°	D01-GH-190301	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°
			D01-GH-190302	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°
			D01-GH-190303	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°	-2.8°
Identification		IR method, the infrared spectrum of this product should be consistent with that of the reference substance	D01-GH-190301	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190302	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190303	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms

8

test	pH value	5.0~7.0	D01-GH-190301	6.0	6.1	6.2	6.1	6.0	6.1	6.0	6.1
			D01-GH-190302	6.1	6.2	6.0	6.1	6.1	6.1	6.1	6.2
			D01-GH-190303	6.2	6.2	6.1	6.1	6.2	6.2	6.1	6.2
	Water	≤1.0%	D01-GH-190301	0.20%	0.20%	0.26%	0.25%	0.31%	0.37%	0.40%	0.52%
			D01-GH-190302	0.25%	0.26%	0.28%	0.30%	0.36%	0.40%	0.45%	0.57%
			D01-GH-190303	0.30%	0.29%	0.32%	0.37%	0.42%	0.41%	0.50%	0.61%
	Chloride	≤0.02%	D01-GH-190301	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190302	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190303	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
	Sulfate	≤0.02%	D01-GH-190301	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190302	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190303	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
	Phosphate	≤0.005%	D01-GH-190301	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms

9

			D01-GH-190302	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190303	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
	Glycerol	≤0.50%	D01-GH-190301	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
			D01-GH-190302	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
			D01-GH-190303	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected	Not detected
	Related substances	Beta-GPC: ≤0.10%; Any individual unspecified impurity: ≤0.10%; Total impurities: ≤2.0%	D01-GH-190301	Beta-GPC: 0.064% ; Any individual unspecified impurity0.080%; Total impurities:0.14%	Beta-GPC: 0.062% ; Any individual unspecified impurity0.088%; Total impurities:0.15%	Beta-GPC : 0.060%; Any individual unspecified impurity0.090% ; Total impurities: 0.15%	Beta-GPC: 0.068% ; Any individual unspecified impurity0.080%; Total impurities: 0.15%	Beta-GPC : 0.058%; Any individual unspecified impurity0.090% ; Total impurities:0.15%	Beta-GPC : 0.062%; Any individual unspecified impurity0.090% ; Total impurities:0.15%	Beta-GPC: 0.060% ; Any individual unspecified impurity0.089%; Total impurities: 0.15%	Beta-GPC : 0.065%; Any individual unspecified impurity0.088% ; Total impurities:0.15%
			D01-GH-190302	Beta-GPC: 0.079%; Any individual unspecified	Beta-GPC: 0.070%; Any individual unspecified	Beta-GPC : 0.072%; Any individual unspecifie	Beta-GPC: 0.077%; Any individual unspecified	Beta-GPC: 0.070%; Any individual unspecified impurity0.08	Beta-GPC: 0.071%; Any individual unspecified impurity0.08	Beta-GPC: 0.082%; Any individual unspecified	Beta-GPC: 0.074%; Any individual unspecified impurity0.08

10

				impurity0.080%; Total impurities:0.16%	impurity0.082%; Total impurities:0.15%	d impurity0.084%; Total impurities: 0.16%	impurity0.084%; Total impurities: 0.16%	6%; Total impurities:0.16%	6%; Total impurities:0.16%	impurity0.088%; Total impurities: 0.17%	6%; Total impurities:0.16%
			D01-GH-190303	Beta-GPC: 0.057%; Any individual unspecified impurity: 0.079%; Total impurities:0.14%	Beta-GPC: 0.052%; Any individual unspecified impurity: 0.077%; Total impurities:0.13%	Beta-GPC: 0.060%; Any individual unspecified impurity: 0.071%; Total impurities: 0.13%	Beta-GPC: 0.059%; Any individual unspecified impurity: 0.071%; Total impurities: 0.13%	Beta-GPC: 0.056%; Any individual unspecified impurity: 0.077%; Total impurities:0.13%	Beta-GPC: 0.058%; Any individual unspecified impurity: 0.078%; Total impurities:0.14%	Beta-GPC: 0.051%; Any individual unspecified impurity: 0.083%; Total impurities: 0.13%	Beta-GPC: 0.054%; Any individual unspecified impurity: 0.078%; Total impurities:0.13%
	Residual Solvents	Ethanol、N-butanol≤0.50%	D01-GH-190301	Ethanol: 0.20%, N-butanol : not detected	Ethanol: 0.20%, N-butanol : not detected	Ethanol: 0.19%, N-butanol :not detected	Ethanol: 0.20%, N-butanol : not detected	Ethanol: 0.18%, N-butanol :not detected	Ethanol: 0.16%, N-butanol :not detected	Ethanol: 0.14%, N-butanol : not detected	Ethanol: 0.12%, N-butanol :not detected
			D01-GH-190302	Ethanol: 0.15%, N-butanol : not	Ethanol: 0.14%, N-butanol : not detected	Ethanol: 0.15%, N-butanol :not	Ethanol: 0.15%, N-butanol : not	Ethanol: 0.14%, N-butanol :not detected	Ethanol: 0.12%, N-butanol :not detected	Ethanol: 0.14%, N-butanol : not	Ethanol: 0.09%, N-butanol :not detected

11

				detected		detected	detected			detected	
			D01-GH-190303	Ethanol: 0.16%, N-butanol not detected	Ethanol: 0.17%, N-butanol : not detected	Ethanol: 0.16%, N-butanol :not detected	Ethanol: 0.15%, N-butanol : not detected	Ethanol: 0.13%, N-butanol :not detected	Ethanol: 0.13%, N-butanol :not detected	Ethanol: 0.12%, N-butanol : not detected	Ethanol: 0.10%, N-butanol :not detected
	microbial limits	The total number of aerobic bacteria shall not exceed 1000cfu/1 g, and the total number of molds and yeasts shall not exceed 100cfu/1 g. Salmonella, Escherichia coli ,Staphylococcus and coliforms should be absent.	D01-GH-190301	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190302	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
			D01-GH-190303	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
Assay		calculated on the anhydrous	D01-GH-190301	99.9%	99.9%	100.0%	100.1%	100.2%	100.1%	100.1%	100.0%

	basis,98.0%~102.0%	D01-GH-190302	100.0%	100.1%	100.2%	100.2%	100.2%	100.3%	100.2%	100.1%
		D01-GH-190303	99.8%	99.9%	100.0%	100.0%	100.1%	100.0%	100.1%	100.1%

Conclusion :In long term stability test (36months) of three batches，the results showed that monitoring items have almost no change compared with that in 0 h, and test results of all items meet the specification.It has proved that the GPC is stable within 36 months. It is reasonable to set the shelf life of GPC at 24 months.

Drafted by: [redacted] Reviewed by: [redacted] Approved by: [redacted]

13

EXHIBIT F

WWEIA Food Codes for Exposure Assessment

NHANES Group Code	NHANES Group Name	NHANES Food Codes	NHANES Food Code Names	Additional Description
5404	**Nutrition bars**			
5404	Nutrition bars	53710800	Cereal or granola bar (Kashi Chewy)	chocolate coated; all flavors; GOLEAN; TLC
5404	Nutrition bars	53710802	Cereal or granola bar (Kashi Crunchy)	all flavors; GOLEAN; TLC
5404	Nutrition bars	53720100	Nutrition bar (Balance Original Bar)	all flavors
5404	Nutrition bars	53720200	Nutrition bar (Clif Bar)	all flavors; Clif Minis
5404	Nutrition bars	53720210	Nutrition bar (Clif Kids Organic Zbar)	all flavors
5404	Nutrition bars	53720300	Nutrition bar (PowerBar)	all flavors; PowerBar energy bar
5404	Nutrition bars	53720400	Nutrition bar (Slim Fast Original Meal Bar)	Slim Fast meal-on-the-go and granola meal bars, all flavors
5404	Nutrition bars	53720500	Nutrition bar (Snickers Marathon Protein Bar)	
5404	Nutrition bars	53720600	Nutrition bar (South Beach Living Meal Bar)	all flavors
5404	Nutrition bars	53720610	Nutrition bar (South Beach Living High Protein Bar)	all flavors
5404	Nutrition bars	53720700	Nutrition bar (Tiger's Milk)	
5404	Nutrition bars	53720800	Nutrition bar (Zone Perfect Classic Crunch)	all flavors
5404	Nutrition bars	53729000	Nutrition bar or meal replacement bar, NFS	
7202	**Soft drinks**			
7202	Soft drinks	92400000	Soft drink, NFS	
7202	Soft drinks	92410310	Soft drink, cola	Coca Cola; Coke; Pepsi; RC Cola; NS as to caffeine; Pepsi Throwback
7202	Soft drinks	92410315	Soft drink, cola, reduced sugar	Coca Cola C2; Pepsi Next
7202	Soft drinks	92410340	Soft drink, cola, decaffeinated	caffeine free Coke; caffeine free Pepsi
7202	Soft drinks	92410360	Soft drink, pepper type	Dr. Pepper; Mr. Pibb; Pibb Xtra
7202	Soft drinks	92410390	Soft drink, pepper type, decaffeinated	caffeine free Dr. Pepper
7202	Soft drinks	92410410	Soft drink, cream soda	
7202	Soft drinks	92410510	Soft drink, fruit flavored, caffeine free	cherry, grape, lemon, lime, orange, strawberry; Tom Collins mixer; 7-Up; Sprite; Slice; caffeine free Mountain Dew; 7-Up, NS as to caffeine; Squirt; Orange Crush; Citra; Sierra Mist; fruit flavored soda, all types; Fanta; Tropicana Twister Soda
7202	Soft drinks	92410550	Soft drink, fruit flavored, caffeine containing	Mellow Yellow; Mountain Dew; Big Red; Sunkist Orange; Mountain Dew, NS as to caffeine; Ruby Red Squirt; Moon Mist; Ale 8; Mountain Dew Code Red; Inca Kola; Cheerwine
7202	Soft drinks	92410610	Soft drink, ginger ale	
7202	Soft drinks	92410710	Soft drink, root beer	
7202	Soft drinks	92410810	Soft drink, chocolate flavored	
7202	Soft drinks	92411510	Soft drink, cola, fruit or vanilla flavored	cherry cola; Cherry Coke; Pepsi Wild Cherry; Vanilla Coke
7202	Soft drinks	92411520	Soft drink, cola, chocolate flavored	
7206	**Sport and energy drinks**			
7206	Sport and energy drinks	95310200	Energy drink (Full Throttle)	
7206	Sport and energy drinks	95310400	Energy drink (Monster)	
7206	Sport and energy drinks	95310500	Energy drink (Mountain Dew AMP)	
7206	Sport and energy drinks	95310550	Energy drink (No Fear)	
7206	Sport and energy drinks	95310555	Energy drink (No Fear Motherload)	
7206	Sport and energy drinks	95310560	Energy drink (NOS)	

7206	Sport and energy drinks	95310600	Energy drink (Red Bull)	
7206	Sport and energy drinks	95310700	Energy drink (Rockstar)	
7206	Sport and energy drinks	95310750	Energy drink (SoBe Energize Energy Juice Drink)	all flavors
7206	Sport and energy drinks	95310800	Energy drink (Vault)	all flavors
7206	Sport and energy drinks	95311000	Energy Drink	NS as to brand
7206	Sport and energy drinks	95312560	Energy drink (Ocean Spray Cran-Energy Juice Drink)	all flavors
7206	Sport and energy drinks	95312900	Energy drink (XS)	all flavors
7206	Sport and energy drinks	95312905	Energy drink (XS Gold Plus)	all flavors
7206	Sport and energy drinks	95320200	Sports drink (Gatorade G)	all flavors; Gatorade, NFS
7206	Sport and energy drinks	95320500	Sports drink (Powerade)	all flavors
7206	Sport and energy drinks	95321000	Sports drink, NFS	All Sport; fruit flavored thirst quencher beverage; NS as to brand
7206	Sport and energy drinks	95330100	Fluid replacement, electrolyte solution	Pedialyte
7206	Sport and energy drinks	95330500	Fluid replacement, 5% glucose in water	
7208	**Nutritional beverages**			
7208	Nutritional beverages	95101000	Nutritional drink or shake, ready-to-drink (Boost)	Boost Nutritional Energy Drink
7208	Nutritional beverages	95101010	Nutritional drink or shake, ready-to-drink (Boost Plus)	
7208	Nutritional beverages	95102000	Nutritional drink or shake, ready-to-drink (Carnation Instant Breakfast)	instant breakfast, ready-to-drink, NFS
7208	Nutritional beverages	95103000	Nutritional drink or shake, ready-to-drink (Ensure)	Ensure, NFS; all flavors; Bone Health; Immune Health; Muscle Health; high calcium; high protein
7208	Nutritional beverages	95103010	Nutritional drink or shake, ready-to-drink (Ensure Plus)	all flavors; Clinical Strength
7208	Nutritional beverages	95104000	Nutritional drink or shake, ready-to-drink, sugar free (Glucerna)	Glucerna shakes, all flavors
7208	Nutritional beverages	95105000	Nutritional drink or shake, ready-to-drink (Kellogg's Special K Protein)	all flavors
7208	Nutritional beverages	95106000	Nutritional drink or shake, ready-to-drink (Muscle Milk)	
7208	Nutritional beverages	95106010	Nutritional drink or shake, ready-to-drink, light (Muscle Milk)	
7208	Nutritional beverages	95110000	Nutritional drink or shake, ready-to-drink (Slim Fast)	all flavors; 3-2-1 Plan; Optima; meal replacement
7208	Nutritional beverages	95110010	Nutritional drink or shake, ready-to-drink, sugar free (Slim Fast)	all flavors; 3-2-1 Plan; lower carb; meal replacement
7208	Nutritional beverages	95110020	Nutritional drink or shake, high protein, ready-to-drink (Slim Fast)	all flavors; 3-2-1 Plan; meal replacement
7208	Nutritional beverages	95120000	Nutritional drink or shake, ready-to-drink, NFS	brands such as Nutrament and Equate meal replacement shake; meal replacement
7208	Nutritional beverages	95120010	Nutritional drink or shake, high protein, ready-to-drink, NFS	brands such as Monster Milk and EAS Myoplex; meal replacement, NFS
7208	Nutritional beverages	95120020	Nutritional drink or shake, high protein, light, ready-to-drink, NFS	brands such as Myoplex Lite; meal replacement
7208	Nutritional beverages	95120050	Nutritional drink or shake, liquid, soy-based	Isocal liquid nutrition; Osmolite liquid nutrition; meal replacement
7302	**Coffee**			
7302	Coffee	92100000	Coffee, NS as to type	
7302	Coffee	92100500	Coffee, NS as to brewed or instant	coffee singles, bags, pods, or K-cups
7302	Coffee	92101000	Coffee, brewed	coffee, brewed, NS as to regular or decaffeinated; coffee singles, bags, pods, or K-cups
7302	Coffee	92101500	Coffee, brewed, blend of regular and decaffeinated	half-caf; reduced caffeine; coffee singles, bags, pods or K-cups
7302	Coffee	92101600	Coffee, Turkish	

7302	Coffee	92101610	Coffee, espresso	demi-tasse
7302	Coffee	92101630	Coffee, espresso, decaffeinated	demi-tasse
7302	Coffee	92101700	Coffee, brewed, flavored	coffee singles, bags, pods, or K-cups
7302	Coffee	92101800	Coffee, Cuban	
7302	Coffee	92101810	Coffee, macchiato	
7302	Coffee	92101820	Coffee, macchiato, sweetened	caramel macchiato
7302	Coffee	92101850	Coffee, cafe con leche	beverage made with equal amounts of coffee and milk, sugar added
7302	Coffee	92101851	Coffee, cafe con leche, decaffeinated	beverage made with equal amounts of decaffeinated coffee and milk, sugar added
7302	Coffee	92101900	Coffee, Latte	NS as to regular or decaffeinated; 2% or whole milk; plain or unflavored
7302	Coffee	92101901	Coffee, Latte, nonfat	low fat, fat free, skim or 1% milk; sugar free; plain or unflavored; NS as to regular or decaffeinated
7302	Coffee	92101903	Coffee, Latte, with non-dairy milk	almond, coconut, rice, or soy milk; plain or unflavored; NS as to regular or decaffeinated
7302	Coffee	92101904	Coffee, Latte, flavored	2% or whole milk; flavors other than chocolate; NS as to regular or decaffeinated
7302	Coffee	92101905	Coffee, Latte, nonfat, flavored	low fat, fat free, skim or 1% milk; flavors other than chocolate; NS as to regular or decaffeinated
7302	Coffee	92101906	Coffee, Latte, with non-dairy milk, flavored	almond, coconut, rice, or soy milk; flavors other than chocolate; NS as to regular or decaffeinated
7302	Coffee	92101910	Coffee, Latte, decaffeinated	2% or whole milk; plain or unflavored
7302	Coffee	92101911	Coffee, Latte, decaffeinated, nonfat	low fat, fat free, skim or 1% milk; sugar free; plain or unflavored
7302	Coffee	92101913	Coffee, Latte, decaffeinated, with non-dairy milk	almond, coconut, rice, or soy milk; plain or unflavored
7302	Coffee	92101917	Coffee, Latte, decaffeinated, flavored	2% or whole milk; flavors other than chocolate
7302	Coffee	92101918	Coffee, Latte, decaffeinated, nonfat, flavored	low fat, fat free, skim or 1% milk; flavors other than chocolate
7302	Coffee	92101919	Coffee, Latte, decaffeinated, with non-dairy milk, flavored	almond, coconut, rice, or soy milk; flavors other than chocolate
7302	Coffee	92101920	Frozen coffee drink	NS as to regular or decaffeinated; 2% or whole milk; plain, unflavored, or flavors other than chocolate; McDonald's McCafe Frappe; Starbuck's Frappuccino; Dunkin Donut's Coffee Coolatta
7302	Coffee	92101921	Frozen coffee drink, nonfat	low fat, fat free, skim or 1% milk; sugar free; plain, unflavored, or flavors other than chocolate; Starbuck's Skinny Frappuccino; Dunkin Donut's Coffee Coolatta; NS as to regular or decaffeinated
7302	Coffee	92101923	Frozen coffee drink, with non-dairy milk	almond, coconut, rice, or soy milk; plain, unflavored or flavors other than chocolate; NS as to regular or decaffeinated
7302	Coffee	92101925	Frozen coffee drink, with whipped cream	NS as to regular or decaffeinated; NS as to with or without whipped cream; McDonald's McCafe Frappe; Starbuck's Coffee Frappuccino; 2% or whole milk; plain, unflavored, or flavors other than chocolate
7302	Coffee	92101926	Frozen coffee drink, nonfat, with whipped cream	low fat, fat free, skim or 1% milk; sugar free; plain, unflavored, or flavors other than chocolate; NS as to with or without whipped cream; Starbuck's Skinny Frappuccino; NS as to regular or decaffeinated
7302	Coffee	92101928	Frozen coffee drink, with non-dairy milk and whipped cream	almond, coconut, rice, or soy milk; plain, unflavored, or flavors other than chocolate; NS as to with or without whipped cream; NS as to regular or decaffeinated
7302	Coffee	92101930	Frozen coffee drink, decaffeinated	2% or whole milk; plain, unflavored, or flavors other than chocolate; Starbuck's Frappuccino
7302	Coffee	92101931	Frozen coffee drink, decaffeinated, nonfat	low fat, fat free, skim or 1% milk; sugar free; plain, unflavored, or flavors other than chocolate; Starbuck's Skinny Frappuccino
7302	Coffee	92101933	Frozen coffee drink, decaffeinated, with non-dairy milk	almond, coconut, rice, or soy milk; plain, unflavored, or flavors other than chocolate
7302	Coffee	92101935	Frozen coffee drink, decaffeinated, with whipped cream	NS as to with or without whipped cream; 2% or whole milk; plain, unflavored, or flavors other than chocolate; Starbuck's Coffee Frappuccino
7302	Coffee	92101936	Frozen coffee drink, decaffeinated, nonfat, with whipped cream	low fat, fat free, skim or 1% milk; sugar free; plain, unflavored, or flavors other than chocolate; NS as to with or without whipped cream; Starbuck's Skinny Frappuccino
7302	Coffee	92101938	Frozen coffee drink, decaffeinated, with non-dairy milk and whipped cream	almond, coconut, rice, or soy milk; plain, unflavored, or flavors other than chocolate; NS as to with or without whipped cream

7302	Coffee	92101950	Coffee, Cafe Mocha	mocha latte; 2% or whole milk; chocolate flavored; NS as to regular or decaffeinated
7302	Coffee	92101955	Coffee, Cafe Mocha, nonfat	mocha latte; low fat, fat, free, skim or 1% milk; chocolate flavored; NS as to regular or decaffeinated
7302	Coffee	92101960	Coffee, Cafe Mocha, with non-dairy milk	mocha latte; chocolate flavored; NS as to regular or decaffeinated
7302	Coffee	92101965	Coffee, Cafe Mocha, decaffeinated	mocha latte; 2% or whole milk; chocolate flavored
7302	Coffee	92101970	Coffee, Cafe Mocha, decaffeinated, nonfat	mocha latte; low fat, fat free, skim or 1% milk; chocolate flavored
7302	Coffee	92101975	Coffee, Cafe Mocha, decaffeinated, with non-dairy milk	almond, coconut, rice, or soy milk; mocha latte; chocolate flavored
7302	Coffee	92102000	Frozen mocha coffee drink	2% or whole milk; chocolate or cocoa flavored; McDonald's McCafe Frappe Mocha; Starbuck's Mocha Frappuccino; NS as to regular or decaffeinated
7302	Coffee	92102010	Frozen mocha coffee drink, nonfat	low fat, fat free, skim or 1% milk; sugar free; chocolate or cocoa flavored; Starbuck's Skinny Mocha Frappuccino; NS as to regular or decaffeinated
7302	Coffee	92102020	Frozen mocha coffee drink, with non-dairy milk	almond, coconut, rice, or soy milk; chocolate or cocoa flavored; NS as to regular or decaffeinated
7302	Coffee	92102030	Frozen mocha coffee drink, with whipped cream	2% or whole milk; NS as to with or without whipped cream; chocolate or cocoa flavored; McDonald's McCafe Frappe Mocha; Starbuck's Mocha Frappuccino; NS as to regular or decaffeinated
7302	Coffee	92102040	Frozen mocha coffee drink, nonfat, with whipped cream	low fat, fat free, skim or 1% milk; sugar free; NS as to with or without whipped cream; chocolate or cocoa flavored; Starbuck's Skinny Mocha Frappuccino; NS as to regular or decaffeinated
7302	Coffee	92102050	Frozen mocha coffee drink, with non-dairy milk and whipped cream	almond, coconut, rice, or soy milk; chocolate or cocoa flavored; NS as to with or without whipped cream; NS as to regular or decaffeinated
7302	Coffee	92102060	Frozen mocha coffee drink, decaffeinated	2% or whole milk; chocolate or cocoa flavored; Starbuck's Mocha Frappuccino
7302	Coffee	92102070	Frozen mocha coffee drink, decaffeinated, nonfat	low fat, fat free, skim, or 1% milk; sugar free; chocolate or cocoa flavored; Starbuck's Skinny Mocha Frappuccino
7302	Coffee	92102080	Frozen mocha coffee drink, decaffeinated, with non-dairy milk	almond, coconut, rice, or soy milk; chocolate or cocoa flavored
7302	Coffee	92102090	Frozen mocha coffee drink, decaffeinated, with whipped cream	2% or whole milk; NS as to with or without whipped cream; chocolate or cocoa flavored; Starbuck's Mocha Frappuccino
7302	Coffee	92102100	Frozen mocha coffee drink, decaffeinated, nonfat, with whipped cream	low fat, fat free, skim or 1% milk; sugar free; NS as to with or without whipped cream; chocolate or cocoa flavored; Starbuck's Skinny Mocha Frappuccino
7302	Coffee	92102110	Frozen mocha coffee drink, decaffeinated, with non-dairy milk and whipped cream	almond, coconut, rice, or soy milk; chocolate or cocoa flavored; NS as to with or without whipped cream
7302	Coffee	92102400	Iced Coffee, brewed	unsweetened; coffee singles, bags, pods, or K-cups; NS as to regular or decaffeinated
7302	Coffee	92102401	Iced Coffee, brewed, decaffeinated	unsweetened; coffee singles, bags, pods, or K-cups
7302	Coffee	92102450	Iced Coffee, pre-lightened and pre-sweetened	from vending; McDonald's Iced Coffee; beverage dispensers; NS as to regular or decaffeinated
7302	Coffee	92102500	Coffee, Iced Latte	2% or whole milk; plain or unflavored; NS as to regular or decaffeinated
7302	Coffee	92102501	Coffee, Iced Latte, nonfat	low fat, fat free, skim or 1% milk; sugar free; plain or unflavored; NS as to regular or decaffeinated
7302	Coffee	92102502	Coffee, Iced Latte, with non-dairy milk	almond, coconut, rice, or soy milk; plain or unflavored; NS as to regular or decaffeinated
7302	Coffee	92102503	Coffee, Iced Latte, flavored	2% or whole milk; flavors other than chocolate; NS as to regular or decaffeinated
7302	Coffee	92102504	Coffee, Iced Latte, nonfat, flavored	low fat, fat free, skim or 1% milk; flavors other than chocolate; NS as to regular or decaffeinated
7302	Coffee	92102505	Coffee, Iced Latte, with non-dairy milk, flavored	almond, coconut, rice, or soy milk; flavors other than chocolate; NS as to regular or decaffeinated
7302	Coffee	92102510	Coffee, Iced Latte, decaffeinated	2% or whole milk; plain or unflavored
7302	Coffee	92102511	Coffee, Iced Latte, decaffeinated, nonfat	low fat, fat free, skim or 1% milk; sugar free; plain or unflavored
7302	Coffee	92102512	Coffee, Iced Latte, decaffeinated, with non-dairy milk	almond, coconut, rice, or soy milk; plain or unflavored
7302	Coffee	92102513	Coffee, Iced Latte, decaffeinated, flavored	2% or whole milk; flavors other than chocolate
7302	Coffee	92102514	Coffee, Iced Latte, decaffeinated, nonfat, flavored	low fat, fat free, skim or 1% milk; flavors other than chocolate
7302	Coffee	92102515	Coffee, Iced Latte, decaffeinated, with non-dairy milk, flavored	almond, coconut, rice, or soy milk; flavors other than chocolate

7302	Coffee	92102600	Coffee, Iced Cafe Mocha	iced mocha latte; 2% or whole milk; chocolate flavored; NS as to regular or decaffeinated
7302	Coffee	92102601	Coffee, Iced Cafe Mocha, nonfat	iced mocha latte; low fat, fat free, skim or 1% milk; chocolate flavored; NS as to regular or decaffeinated
7302	Coffee	92102602	Coffee, Iced Cafe Mocha, with non-dairy milk	almond, coconut, rice, or soy milk; mocha latte; chocolate flavored; NS as to regular or decaffeinated
7302	Coffee	92102610	Coffee, Iced Cafe Mocha, decaffeinated	iced mocha latte; 2% or whole milk; chocolate flavored
7302	Coffee	92102611	Coffee, Iced Cafe Mocha, decaffeinated, nonfat	iced mocha latte; low fat, fat free, skim or 1% milk; chocolate flavored
7302	Coffee	92102612	Coffee, Iced Cafe Mocha, decaffeinated, with non-dairy milk	almond, coconut, rice, or soy milk; mocha latte; chocolate flavored
7302	Coffee	92103000	Coffee, instant, reconstituted	powdered mix; NS as to regular or decaffeinated; made from liquid concentrate
7302	Coffee	92104000	Coffee, instant, 50% less caffeine, reconstituted	powdered mix; blend of regular and decaf; half-caf; reduced caffeine
7302	Coffee	92111000	Coffee, NS as to brewed or instant, decaffeinated	coffee singles, bags, pods, or K-cups
7302	Coffee	92111010	Coffee, brewed, decaffeinated	coffee singles, bags, pods, or K-cups
7302	Coffee	92114000	Coffee, instant, decaffeinated, reconstituted	powdered mix
7302	Coffee	92121000	Coffee, instant, pre-lightened and pre-sweetened with sugar, reconstituted	powdered mix; NS as to sweetener; Maxwell House International, flavors other than chocolate, cocoa, or mocha
7302	Coffee	92121001	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, reconsitituted	powdered mix; Maxwell House International, flavors other than chocolate, cocoa, or mocha
7302	Coffee	92121010	Coffee, instant, pre-sweetened with sugar, reconstituted	powdered mix; NS as to sweetener
7302	Coffee	92121020	Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, reconstituted	NS as to sweetener; powdered mix; coffee and cocoa mix; Maxwell House International Coffee flavors, Chocolate, Cocoa, or Mocha
7302	Coffee	92121030	Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	powdered mix; sugar free; Maxwell House International Coffee flavors, Chocolate, Cocoa, or Mocha
7302	Coffee	92121040	Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	powdered mix; sugar free; Maxwell House International Sugar Free Coffee; flavors other than chocolate, cocoa, or mocha
7302	Coffee	92121041	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	powdered mix; sugar free; Maxwell House International Sugar Free Coffee; flavors other than chocolate, cocoa, or mocha
7302	Coffee	92121050	Coffee, mocha, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	powdered mix; sugar free; Maxwell House International Coffee flavors, Chocolate, Cocoa, or Mocha
7302	Coffee	92130000	Coffee, pre-lightened and pre-sweetened with sugar	from vending machine; NS as to regular or decaffeinated; NS as to type of sweetener
7302	Coffee	92130001	Coffee, decaffeinated, pre-lightened and pre-sweetened with sugar	from vending machine; NS as to type of sweetener
7302	Coffee	92130005	Coffee, pre-lightened and pre-sweetened with low calorie sweetener	from vending machine; NS as to regular or decaffeinated
7302	Coffee	92130006	Coffee, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener	from vending machine
7302	Coffee	92130010	Coffee, pre-lightened	from vending machine; NS as to regular or decaffeinated; unsweetened or sugar-free
7302	Coffee	92130011	Coffee, decaffeinated, pre-lightened	from vending machine; unsweetened or sugar-free
7302	Coffee	92130020	Coffee, pre-sweetened with sugar	from vending machine; NS as to regular or decaffeinated; NS as to type of sweetener
7302	Coffee	92130021	Coffee, decaffeinated, pre-sweetened with sugar	from vending machine; NS as to type of sweetener
7302	Coffee	92130030	Coffee, pre-sweetened with low calorie sweetener	from vending machine; NS as to regular or decaffeinated
7302	Coffee	92130031	Coffee, decaffeinated, pre-sweetened with low calorie sweetener	from vending machine

7302	Coffee	92152000	Coffee and chicory, brewed	
7302	Coffee	92152010	Coffee and chicory, brewed, decaffeinated	
7302	Coffee	92161000	Coffee, Cappuccino	2% or whole milk; NS as to regular or decaffeinated
7302	Coffee	92161001	Coffee, Cappuccino, nonfat	low fat, fat free, skim or 1% milk; NS as to regular or decaffeinated
7302	Coffee	92161002	Coffee, Cappuccino, with non-dairy milk	NS as to regular or decaffeinated; almond, coconut, rice, or soy milk
7302	Coffee	92162000	Coffee, Cappuccino, decaffeinated	2% or whole milk
7302	Coffee	92162001	Coffee, Cappuccino, decaffeinated, nonfat	low fat, fat free, skim or 1% milk
7302	Coffee	92162002	Coffee, Cappuccino, decaffeinated, with non-dairy milk	almond, coconut, rice, or soy milk
7302	Coffee	92171000	Coffee, bottled/canned	NS as to brand or variety; from carton; all flavors; all brands; all varieties
7302	Coffee	92171010	Coffee, bottled/canned, light	NS as to brand or variety; from carton; all flavors; all brands; all varieties
7302	Coffee	92201010	Coffee substitute	
7302	Coffee	92202010	Chicory beverage	
7302	Coffee	92203000	Cereal beverage	Pero
7302	Coffee	92203110	Cereal beverage with beet roots, from powdered instant	Cafix
7304	**Tea**			
7304	Tea	92302000	Tea, hot, leaf, black	tea bags; spiced, lemon- or other fruit-flavored tea; unsweetened; brewed; chai tea; black tea blends; tea, NS as to type
7304	Tea	92302500	Tea, hot, leaf, black, decaffeinated	spiced, lemon- or other fruit-flavored tea; unsweetened; tea bags; brewed; chai tea; black tea blends
7304	Tea	92303010	Tea, hot, leaf, green	unsweetened; tea bags; brewed; Japanese green tea; green tea blends
7304	Tea	92303100	Tea, hot, leaf, green, decaffeinated	unsweetened; tea bags; brewed; white tea; Japanese green tea; green tea blends; rice tea
7304	Tea	92304100	Tea, hot, leaf, oolong	unsweetened; tea bags; brewed
7304	Tea	92305010	Tea, iced, instant, black, unsweetened	powdered mix; liquid concentrate; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92305040	Tea, iced, instant, black, pre-sweetened with sugar	powdered mix; liquid concentrate; NS as to sweetener; sweet tea; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92305050	Tea, iced, instant, black, decaffeinated, pre-sweetened with sugar	powdered mix; liquid concentrate; NS as to sweetener; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92305090	Tea, iced, instant, black, pre-sweetened with low calorie sweetener	powdered mix; liquid concentrate; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea; light, reduced calorie, diet, sugar free
7304	Tea	92305110	Tea, iced, instant, black, decaffeinated, pre-sweetened with low calorie sweetener	powdered mix; liquid concentrate; light; reduced calorie; diet; sugar free; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92305180	Tea, iced, instant, black, decaffeinated, unsweetened	powdered mix; liquid concentrate; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92305900	Tea, iced, instant, green, unsweetened	powdered mix; liquid concentrate; white tea; herbal tea; green and fruit, herbal, or white tea blends; decaffeinated
7304	Tea	92305910	Tea, iced, instant, green, pre-sweetened with sugar	powdered mix; liquid concentrate; white tea; herbal tea; NS as to sweetener; green and fruit, herbal, or white tea blends; decaffeinated
7304	Tea	92305920	Tea, iced, instant, green, pre-sweetened with low calorie sweetener	powdered mix; liquid concentrate; light, reduced calorie, diet, sugar free; white tea; herbal tea; green and fruit, herbal, or white tea blends; decaffeinated
7304	Tea	92306000	Tea, hot, herbal	herbal tea, NFS; unsweetened; leaf; tea bags; brewed; rooibos tea; mate tea; caraway seed tea
7304	Tea	92306090	Tea, hot, hibiscus	Agua de Jamaica; unsweetened; leaf; tea bags; brewed
7304	Tea	92306700	Tea, hot, chamomile	unsweetened; leaf; tea bags; brewed
7304	Tea	92306800	Tea, hot, chai, with milk	Indian Masala chai; spiced milk tea; chai tea latte; tea latte; NS as to type
7304	Tea	92307500	Iced Tea / Lemonade juice drink	half and half beverage, all flavors; Arizona Half & Half; Arnold Palmer Half & Half
7304	Tea	92307510	Iced Tea / Lemonade juice drink, light	half and half beverage, all flavors, light; Arizona Lite Half & Half; Arnold Palmer Lite Half & Half

7304	Tea	92307520	Iced Tea / Lemonade juice drink, diet	diet half and half beverage, all flavors; Diet Snapple Half n' Half; Arnold Palmer Lite Half & Half, made from powdered mix
7304	Tea	92308000	Tea, iced, brewed, black, pre-sweetened with sugar	sweet tea; leaf, bag, or vending; McDonald's Iced Sweet Tea; black and fruit, green, herbal, white, or other tea blends; NS as to regular or decaffeinated; iced tea, NS as to type; NS as to sweetener
7304	Tea	92308010	Tea, iced, brewed, black, pre-sweetened with low calorie sweetener	leaf, baf, or vending; black and fruit, green, herbal, white, or other tea blends; NS as to regular or decaffeinated; NS as to type of tea
7304	Tea	92308020	Tea, iced, brewed, black, unsweetened	leaf, bag, or vending; McDonald's Iced Tea; black and fruit, green, herbal, white, or other tea blends; NS as to regular or decaffeinated; NS as to type of tea
7304	Tea	92308030	Tea, iced, brewed, black, decaffeinated, pre-sweetened with sugar	sweet tea; leaf, bag, or vending; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea; NS as to sweetener
7304	Tea	92308040	Tea, iced, brewed, black, decaffeinated, pre-sweetened with low calorie sweetener	leaf, bag, or vending; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92308050	Tea, iced, brewed, black, decaffeinated, unsweetened	leaf, bag, or vending; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92308500	Tea, iced, brewed, green, pre-sweetened with sugar	leaf, bag, or vending; white tea; herbal tea; green and fruit, herbal, or white tea blends; NS as to regular or decaffeinated; NS as to sweetener
7304	Tea	92308510	Tea, iced, brewed, green, pre-sweetened with low calorie sweetener	leaf, bag, or vending; white tea; herbal tea; green and fruit, herbal, or white tea blends; NS as to regular or decaffeinated
7304	Tea	92308520	Tea, iced, brewed, green, unsweetened	leaf, bag, or vending; white tea; herbal tea; green and fruit, herbal, or white tea blends; NS as to regular or decaffeinated
7304	Tea	92308530	Tea, iced, brewed, green, decaffeinated, pre-sweetened with sugar	leaf, bag, or vending; white tea; herbal tea; green and fruit, herbal, or white tea bleads; NS as to sweetener
7304	Tea	92308540	Tea, iced, brewed, green, decaffeinated, pre-sweetened with low calorie sweetener	leaf, bag, or vending; white tea; herbal tea; green and fruit, herbal, or white tea blends
7304	Tea	92308550	Tea, iced, brewed, green, decaffeinated, unsweetened	leaf, bag, or vending; white tea; herbal tea; green and fruit, herbal, or white tea blends
7304	Tea	92309000	Tea, iced, bottled, black	can, carton, or fountain; sweet tea; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea; Snapple, all flavors
7304	Tea	92309010	Tea, iced, bottled, black, decaffeinated	can, carton, or fountain; sweet tea; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea; caffeine free Snapple Tea, all flavors
7304	Tea	92309020	Tea, iced, bottled, black, diet	light, reduced calorie, or sugar free; can, carton, or fountain; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea; Diet Snapple Tea, all flavors
7304	Tea	92309030	Tea, iced, bottled, black, decaffeinated, diet	light, reduced calorie, or sugar free; can, carton, or fountain; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea; caffeine free Diet Snapple Tea, all flavors
7304	Tea	92309040	Tea, iced, bottled, black, unsweetened	can, carton, or fountain; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92309050	Tea, iced, bottled, black, decaffeinated, unsweetened	can, carton, or fountain; black and fruit, green, herbal, white, or other tea blends; NS as to type of tea
7304	Tea	92309500	Tea, iced, bottled, green	can, carton, or fountain; white tea; herbal tea; green and fruit, herbal, or white tea blends; decaffeinated; Snapple
7304	Tea	92309510	Tea, iced, bottled, green, diet	light, reduced calorie, or sugar free; can, carton, or fountain; white tea; herbal tea; green and fruit, herbal, or white tea blends; decaffeinated; Diet Snapple
7304	Tea	92309520	Tea, iced, bottled, green, unsweetened	can, carton, or fountain; white tea; herbal tea; green and fruit, herbal, or white tea blends; decaffeinated
9802	**Protein and nutritional powders**			
9802	Protein and nutritional powders	95201000	Nutritional powder mix (Carnation Instant Breakfast)	instant breakfast, powdered, NFS
9802	Protein and nutritional powders	95201010	Nutritional powder mix, sugar free (Carnation Instant Breakfast)	
9802	Protein and nutritional powders	95201200	Nutritional powder mix (EAS Whey Protein Powder)	all flavors

9802	Protein and nutritional powders	95201300	Nutritional powder mix (EAS Soy Protein Powder)	all flavors
9802	Protein and nutritional powders	95201500	Nutritional powder mix, high protein (Herbalife)	all flavors; Healthy Meal nutritional shake mix
9802	Protein and nutritional powders	95201600	Nutritional powder mix (Isopure)	all flavors
9802	Protein and nutritional powders	95201700	Nutritional powder mix (Kellogg's Special K20 Protein Water)	all flavors
9802	Protein and nutritional powders	95202000	Nutritional powder mix (Muscle Milk)	all flavors
9802	Protein and nutritional powders	95202010	Nutritional powder mix, light (Muscle Milk)	all flavors
9802	Protein and nutritional powders	95210000	Nutritional powder mix (Slim Fast)	all flavors; 3-2-1 Plan; Optima
9802	Protein and nutritional powders	95210010	Nutritional powder mix, sugar free (Slim Fast)	all flavors; 3-2-1 Plan; lower carb
9802	Protein and nutritional powders	95210020	Nutritional powder mix, high protein (Slim Fast)	all flavors; 3-2-1 Plan
9802	Protein and nutritional powders	95220000	Nutritional powder mix, NFS	meal replacement, NFS
9802	Protein and nutritional powders	95220010	Nutritional powder mix, high protein, NFS	brands such as D.E.L.T.A. Enhance Formula and Joe Weider's Dynamic Protein Shake; Monster Milk; meal replacement
9802	Protein and nutritional powders	95230000	Nutritional powder mix, whey based, NFS	protein shake mix; brands such as Gold Standard, NOW Foods
9802	Protein and nutritional powders	95230010	Nutritional powder mix, protein, soy based, NFS	protein shake mix; brands such as Gold Standard, NOW Foods
9802	Protein and nutritional powders	95230020	Nutritional powder mix, protein, light, NFS	protein shake mix; brands such as Reliv Now, Beneprotein
9802	Protein and nutritional powders	95230030	Nutritional powder mix, protein, NFS	protein shake mix, NFS; brands such as NOW Foods, NFS and Gold Standard, NFS
5704	**Candy not containing chocolate**			
5704	Candy not containing chocolate	91745010	Gumdrops	gummy bears; gummy worms; gummy fish; gummy dinosaurs; Hot tamales; Jelly beans; Jujubes; Jujy Fruits; Mike and Ike; Mint Leaves; Chuckles; Dots; Fruit slices, jellied; Good and Fruity; Brach's Rocks; spice sticks and drops; Life Savers Gummi Savers; Gummy animals/shapes
9999	**Other unreconstituted powders (fruit, tea, sports drinks)**			
9999	Not included in a food category	92900300	Sports drink, dry concentrate, not reconstituted	Gatorade; fruit flavored thirst quencher beverage; NS as to brand

EXHIBIT G
alpha-GPC USP Monograph

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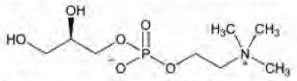
L- alpha -Glycerylphosphorylcholine



$C_8H_{20}NO_6P$ 257.22

Choline hydroxide, (*R*)-2,3-dihydroxypropyl hydrogen phosphate, inner salt;
(*R*)-2,3-Dihydroxypropyl 2-(trimethylammonio)ethyl phosphate;
L-α-Glycerylphosphorylcholine [28319-77-9].

DEFINITION

L- alpha -Glycerylphosphorylcholine (L- alpha - GPC) is obtained by base-catalyzed transesterification of enriched phosphatidylcholine soy lecithin extract and subsequent physicochemical purification processes. L- alpha -Glycerylphosphorylcholine is anhydrous or an aqueous solution containing NLT 14.0% and NMT 16.0% of water. It contains NLT 98.0% and NMT 102.0% of L- alpha - glycerylphosphorylcholine ($C_8H_{20}NO_6P$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A

▲**Standard**

For L- alpha - GPC : Use USP L- alpha -Glycerylphosphorylcholine RS.

For L- alpha - GPC solution: Accurately transfer 50 mg of USP L- alpha -Glycerylphosphorylcholine RS into a 2-mL, v-bottom vial and add 20 µL of water. Heat in a water bath at 35° for 30 min, and vortex to dissolve.

Sample: L- alpha - GPC or L- alpha - GPC solution▲ (USP 1-May-2021)

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *System suitability solution*, as obtained in the test for *Organic Impurities*.

ASSAY

• **Procedure**

Sample: 350 mg of L- alpha - GPC or L- alpha - GPC solution

Titrimetric system

(See *Titrimetry* ⟨541⟩.)

Mode: Direct titration

Titrant: 0.1 N perchloric acid in glacial acetic acid VS

Electrode system: A glass–calomel with lithium chloride salt bridge in acetic acid

Endpoint detection: Potentiometric

Analysis: Dissolve the *Sample* in 100 mL of glacial acetic acid and add 5 mL of acetic anhydride. Titrate with the *Titrant*. Perform a blank determination and make any necessary correction.

Calculate the percentage of L- alpha -glycerylphosphorylcholine ($C_8H_{20}NO_6P$) in the portion of *Sample* taken:

$$\text{Result} = [(V_S - V_B) \times N_A \times F \times 100]/W$$

V_S = *Titrant* volume consumed by the *Sample* (mL)

V_B = *Titrant* volume consumed by the blank (mL)

N_A = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 257.2 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• Limit of Chloride, Sulfate, Phosphate, and Acetate

Mobile phase: Potassium hydroxide solution, concentration gradient with the use of eluent generator cartridge.[1] See *Table 1*.

Table 1

Time (min)	Potassium Hydroxide (KOH) Concentration (mM)
0	5
3	5
4	10
5	20
8	40
10	5
15	5

Acetate standard stock solution: Transfer 230 mg of sodium acetate trihydrate to a 100-mL volumetric flask. Dissolve in and dilute with water to volume. Transfer 1.0 mL of the resultant solution to a 10-mL volumetric flask and dilute with water to volume. The acetate concentration is 0.1 mg/mL.

Chloride and sulfate standard stock solution: Transfer 210 mg of potassium chloride and 148 mg of sodium sulfate to a 100-mL volumetric flask. Dissolve in and dilute with water to volume. Transfer 1.0 mL of the resultant solution to a 10-mL volumetric flask and dilute with water to volume. The concentration for chloride and sulfate is 0.1 mg/mL each.

Phosphate standard stock solution: Transfer 143 mg of potassium dihydrogen phosphate to a 100-mL volumetric flask. Dissolve in and dilute with water to volume. Transfer 1.0 mL of the resultant solution to a 100-mL volumetric flask and dilute with water to volume. The phosphate concentration is 0.01 mg/mL.

Standard solution: Transfer 1.0 mL of *Acetate standard stock solution*, 0.2 mL of *Chloride and sulfate standard stock solution*, and 0.5 mL of *Phosphate standard stock solution* to a 10-mL volumetric flask. Dilute with water to volume.

Sample solution: Transfer 100 mg of L-alpha-GPC or 120 mg of L-alpha-GPC solution to a 10-mL volumetric flask. Dissolve in and dilute with water to volume.

Chromatographic system

(See *Chromatography (621), System Suitability*.)

Mode: HPIC

Detector: Conductivity

Columns

Precolumn: 4.0-mm × 5-cm; 10.5-µm packing L83

Analytical: 4.0-mm × 25-cm; 10.5-µm packing L83

Flow rate: 1.0 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times of the analytes are listed in *Table 2*.]

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Acetate	1.0	0.1
Chloride	1.7	0.02
Sulfate	4.4	0.02
Phosphate	5.0	0.005

Suitability requirements

Resolution: NLT 5 between the acetate and chloride peaks

Relative standard deviation: NMT 10% each for acetate, chloride, sulfate, and phosphate

Analysis

Samples: *Standard solution* and *Sample solution*

Separately calculate the percentage of acetate, chloride, sulfate, and phosphate in the portion of L-alpha-GPC or L-alpha-GPC solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of acetate, chloride, sulfate, or phosphate from the appropriate *Sample solution*

r_S = peak response of acetate, chloride, sulfate, or phosphate from the *Standard solution*

C_S = concentration of acetate, chloride, sulfate, or phosphate in the *Standard solution* (mg/mL)

C_U = concentration of L-alpha-GPC or L-alpha-GPC solution in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*.

• **Limit of Glycerol**

Mobile phase: Acetonitrile and water (55:45)

System suitability solution: 2 mg/mL of USP Glycerin RS and 400 mg/mL of L-alpha-GPC or 470 mg/mL of L-alpha-GPC solution in water

Standard solution: 2 mg/mL of USP Glycerin RS in water

Sample solution: 400 mg/mL of L-alpha-GPC or 470 mg/mL of L-alpha-GPC solution in water

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 25-cm; 5-µm packing L14

Column temperature: 40°

Flow rate: 0.5 mL/min

Injection volume: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

[Note—The relative retention times for glycerol and L-alpha-GPC are about 0.6 and 1.0, respectively.]

Resolution: NLT 2.0 between the glycerol and L-alpha-GPC peaks, *System suitability solution*

Relative standard deviation: NMT 5.0% for the glycerol peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of glycerol in the portion of *Sample solution* taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of glycerol from the appropriate *Sample solution*

r_S = peak response of glycerin from the *Standard solution*

C_S = concentration of USP Glycerin RS in the *Standard solution* (mg/mL)

C_U = concentration of L-alpha-GPC or L-alpha-GPC solution in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 0.5%

Change to read:

• **Organic Impurities**

Solution A: Mixture of acetonitrile and methanol (3:1)

Solution B: Transfer 1.98 g of ammonium acetate to a 500-mL volumetric flask. Dissolve in about 470 mL of water. Adjust with acetic acid to a pH of 4.5 and dilute with water to volume.

Solution C: Transfer 100.0 mL of *Solution B* to a 1000-mL volumetric flask and dilute with water to volume. Check the pH of the solution. If it is not 4.5, adjust with diluted ammonia solution or diluted acetic acid to a pH of 4.5.

Solution D: Mix 300 mL of *Solution B* and 1700 mL of *Solution A*.

Solution E: Mix 700 mL of *Solution C* and 1300 mL of *Solution A*.

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution D (%)	Solution E (%)
0	98	2
5	98	2
18	44	56
30	32	68
34	10	90
42	10	90
43	98	2
55	98	2

Diluent: Methanol and water (80:20)

Internal standard solution: Transfer 100 mg of USP L-Serine RS to a 100-mL volumetric flask. Dissolve in and dilute with *Diluent* to volume. Transfer 5.0 mL of the resultant solution to a 250-mL volumetric flask and dilute with *Diluent* to volume.

L-alpha-GPE, beta-GPC, and serine solution: Transfer 2.5 mg each of USP L-alpha-Glycerophosphorylethanolamine RS and USP beta-Glycerylphosphorylcholine RS to a 10-mL volumetric flask. Dissolve in and dilute with the *Internal standard solution* to volume. Transfer 0.8 mL of the resultant solution to a 10-mL volumetric flask and dilute with the *Internal standard solution* to volume.

System suitability solution: Transfer 100 mg of USP L-alpha-Glycerylphosphorylcholine RS▲ (USP 1-May-2021) to a 5-mL volumetric flask. Dissolve in and dilute with the *L-alpha-GPE, beta-GPC*, and *serine solution* to volume.

Sample solution: Transfer 200 mg of L-alpha-GPC or L-alpha-GPC solution to a 10-mL volumetric flask. Dissolve in and dilute with the *Internal standard solution* to volume.

Chromatographic system

(See *Chromatography (621), System Suitability*.)

Mode: LC

Detector: Evaporative light-scattering detector (ELSD)

Detector temperature: 90°

Column: 4.6-mm × 25-cm; 5-µm packing L111

Carrier gas: Nitrogen

Flow rate: 0.7 mL/min

Injection volume: 40 µL

System suitability

Sample: *System suitability solution*

[NOTE—Adjust the flow rate and/or isocratic portion of the gradient program to obtain the retention time of serine at 28 ± 2 min. The relative retention times of the analytes are listed in *Table 4*.]

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Pinitol[a]	0.76	0.48	0.1
beta- GPC[b]	0.96	1.0	0.1
L- alpha - GPC[c]	1.0	—	—
Sucrose[d]	1.38	1.0	0.1
Serine[e]	1.88	1.0	—
L- alpha -GPE[f]	1.93	1.0	0.1
Any individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	2.0

[a] 3-*O*-Methyl-*chiro*-inositol.

[b] 1,3-Dihydroxypropan-2-yl 2-(trimethylammonio)ethyl phosphate.

[c] (*R*)-2,3-Dihydroxypropyl 2-(trimethylammonio)ethyl phosphate.

[d] β-D-Fructofuranosyl α-D-glucopyranoside.

[e] L-2-Amino-3-hydroxypropanoic acid.

[f] 2-Aminoethyl [(*R*)-2,3-dihydroxypropyl] hydrogen phosphate.

Suitability requirements

Resolution: NLT 1.2 between the serine and L- alpha -GPE peaks; NLT 0.4 between the beta- GPC and L- alpha - GPC peaks

Relative standard deviation: NMT 10% for the serine peak

Analysis

Samples: *Diluent*, *Internal standard solution*, and *Sample solution*

[NOTE—The response factor of serine equals that of L- alpha - GPC . Disregard peaks that are observed in both *Diluent* and *Sample solution* chromatograms. Disregard peaks below 0.05% observed in the chromatogram of the *Sample solution*.]

Calculate the percentage of each impurity in the portion of L- alpha - GPC or L- alpha - GPC solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of serine from the *Internal standard solution*

C_S = concentration of USP L-Serine RS in the *Internal standard solution* (mg/mL)

C_U = concentration of L- alpha - GPC or L- alpha - GPC solution in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 4*)

Acceptance criteria: See *Table 4*

SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*
Sample solution: 100 mg/mL of L-alpha-GPC or L-alpha-GPC solution in water
Acceptance criteria: −2.4° to −2.8°, determined at 20°, on the anhydrous basis

• **Microbial Enumeration Tests** ⟨2021⟩**:** The total bacterial count does not exceed 1000 cfu/g, and the total combined molds and yeasts count does not exceed 100 cfu/g.

• **Absence of Specified Microorganisms** ⟨2022⟩, *Test Procedures, Test for Absence of Salmonella Species*, *Test for Absence of Escherichia coli*, and *Test for Absence of Staphylococcus aureus:* It meets the requirements.

• **pH** ⟨791⟩
Sample solution: 8.5 g/100 mL of L-alpha-GPC or 10 g/100 mL of L-alpha-GPC solution in water
Acceptance criteria: 5.0–7.0

• **Water Determination** ⟨921⟩, *Method I, Method Ia*
L-alpha-GPC: NMT 1.0%
L-alpha-GPC solution: 14%–16%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **Labeling:** Label it to indicate whether the material is the L-alpha-Glycerylphosphorylcholine or L-alpha-Glycerylphosphorylcholine solution.

Change to read:

• **USP Reference Standards** ⟨11⟩
USP Glycerin RS
USP L-alpha-Glycerophosphorylethanolamine RS
USP L-alpha-Glycerylphosphorylcholine RS
▲▲ (USP 1-May-2021)
USP beta-Glycerylphosphorylcholine RS
USP L-Serine RS

[1] Dionex EGC III KOH or equivalent.

Auxiliary Information Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
L-ALPHA-GLYCERYLPHOSPHORYLCHOLINE	Fatkhulla K Tadjimukhamedov Associate Scientific Liaison	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

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EXHIBIT H

GRAS Panel Consensus Statement Use of L-alpha-Glycerylphosphorylcholine (alpha-GPC) Under Specified Conditions of Intended Use

GRAS Panel Consensus Statement on the Generally Recognized as Safe Determination for the Use of L-alpha-Glycerylphosphorylcholine (alpha-GPC) Under Specified Conditions of Intended Use

July 26, 2022

Introduction

Summit Life Science, Inc. (hereafter "Summit") convened a panel of scientists (GRAS Panel), qualified by their scientific training and relevant national and international experience in the safety evaluation of food ingredients, to conduct a critical and comprehensive assessment pertinent to the safety of Shenyang Gold Jyouki Technology Co.,Ltd (hereafter "Jyouki) L-alpha-Glycerylphosphorylcholine (a-GPC) and to determine whether its intended use in in beverage, beverage bases and powders, coffee and tea, gummies, protein and nutrition bars and powders as a nutrient ingredient would be Generally Recognized as Safe (GRAS) based on scientific procedures. The GRAS Panel consisted of the below-signed qualified scientific experts: Jimmy Wang, Ph.D. (Chief Scientific Officer, Summit Life Science, Inc.); Qinge Wei, M.P.H (Regulatory Affairs Associate, Summit Life Science, Inc.); and Nancy A. Higley, Ph.D. (Managing Member, Regulatory Connections, LLC).

The GRAS Panel independently critically evaluated a summary of publicly available scientific data and information compiled from the literature in the dossier titled **"***Safety Evaluation Dossier Supporting a Generally Recognized as Safe (GRAS) Conclusion for the Intended Use of alpha-GPC,"* which included an evaluation of scientific data, both favorable and unfavorable, relevant to the safety of the intended food uses of alpha-GPC. This information was prepared based on a comprehensive search of the scientific literature performed by Summit and included information characterizing the identity and purity of the ingredient, the manufacture of the ingredient, product specifications, supporting analytical data, intended conditions of use, estimated exposure under the intended uses, and the safety of alpha-GPC.

Following its independent critical evaluation, the GRAS Panel unanimously concluded that the proposed uses of alpha-GPC in the indicated conditions of use as a nutrient ingredient, meeting food-grade specifications and manufactured in accordance with current Good Manufacturing Practice (cGMP), is safe and suitable and GRAS based on scientific procedures.

Summary and Basis for GRAS

PhoslipGPC^{TM} is a trademark for Jyouki's L-alpha-glycerylphosphorylcholine (alpha-GPC). alpha-GPC is a choline-containing phospholipid. alpha-GPC can be produced chemically or using enzymatic methods. The chemical methods typically involve hydrolysis of phosphatidyl choline or condensation of glycerol derivatives with phosphocholine donors using basic catalysts. The GRAS Panel evaluated details of the manufacturing process summarized below, using food grade raw materials and processing aids and cGMP conditions.

Step 1: Phosphorylcholine is prepared by esterifying polyphosphoric acid and choline chloride using basic conditions.

Step 2: The phosphorylcholine, from step 1, is added to the glycidol formed by the condensation reaction of 3-chloro-1,2-propanediol under basic conditions.

Step 3: Crude L-alpha-glycerylphosphorylcholine, prepared in step 2, is purified via crystallization with anhydrous ethanol.

The GRAS Panel noted that residues of starting materials, by-products, intermediates, and reagents potentially present in the final material are listed and limited by the product specifications. The GRAS Panel specifically reviewed the manufacturing process use of R-3-chloro-1,2-propanediol and the production of the intermediate glycidol.

R-3-Chloro-1,2-propanediol is a suspect carcinogen and reproductive toxicant. Jyouki confirmed that R-3-chloro-1,2-propanediol may be surplus. As part of the in -process control, the manufacturer tested the residue of R-3-chloro-1,2-propanediol and indicates that the R-3-chloro-1,2-propanediol will be removed in the purification process. In addition, Jyouki has studied the residue of R-3-chloro-1,2-propanediol in the finished product of L-α-glycerylphosphorylcholine according to ICH M7[1]. According to ICH M7, Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, the daily intake of an individual impurity should be controlled at 1.5μg/day. Jyouki has sent the limit of R-3-chloro-1,2-to no more than 1.25ppm. The impurity control strategy indicates, in analysis of 3 non-consecutive batches, that the levels of R-3-Chloro-1,2-propanediol is non-detected. Jyouki indicates that they will comply with ICH M7 impurity guidelines indicating periodic verification testing is justified when it can be shown that levels of the impurity in the substance is less than 30% of the acceptable limit for at least six consecutive pilot scale or three consecutive production scale batches. Therefore, the control strategy for the R-3-Chloro-1,2-propanediol is to perform verification testing in three consecutive production batches of samples per year.

Glycidol is an intermediate formed in the manufacturing process and is a probable human carcinogen. Jyouki confirmed that the glycidol is not totally reacted with the phosphorylcholine. During the reaction, because glycidol is unstable, the glycidol will break down to glycerol. The specifications control the amount of glycerol in the alpha-GPC to 0.5%. In addition, Jyouki has studied the residue of glycidol in the finished product according to ICH M7. Jyouki has set the limit of glycidol in alpha-GPC to no more than 1.25ppm, based on the TD50 of glycidol is, 4.28 mg/kg bw/day (rats) and 34.7 mg/kg bw/day (mice) (Carcinogenic Potency Database, CPDB)[2]. The impurity control strategy indicates, in analysis of 3 non-consecutive batches, that the levels of glycidol is non-detected. Jyouki indicates that they will comply with ICH M7 impurity guidelines indicating periodic verification testing is justified when it can be shown that levels of the impurity in the substance is less than 30% of the acceptable limit for at least six consecutive pilot scale or three consecutive production scale batches. Therefore, the control strategy for the glycidol is to perform verification testing in three consecutive production batches of samples per year.

The synthesis is performed in aqueous solution and the water-soluble process chemicals are removed in the final steps of the manufacturing process and non-water-soluble process materials, e.g. activated charcoal, are removed by filtration. The final product is vacuum dried and packaged in low density polyethylene as a primary packaging and aluminum foil as a secondary packaging.

[1] FDA Center for Drug Evaluation and Research (2018) M7(R1)Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk. Guidance for Industry https://www.fda.gov/media/85885/download
[2] Fitzpatrick RB. 2008 CPDB: Carcinogenic Potency Database. *Med Ref Serv Q* 27(3):303-11

The molecular weight of alpha-GPC, 28319-77-9, is 257.22. By weight, alpha-GPC contains 40.8% of choline.

The ingredient is a white crystalline powder, soluble in water.

All methods of analysis are internationally recognized standard procedures or internal methods that have been validated. The GRAS Panel reviewed the results of 3 non-consecutive batches of alpha-GPC and concluded that the manufacturing process produces a consistent product that conforms to the established product specifications.

The purity of alpha-GPC is not less than 98.0% and not more than 102.0% of L-alpha-glycerylphosphorylcholine, calculated on an anhydrous basis. The assay is within the acceptance criteria in the alpha-GPC monograph. The consistency of the purity standards were demonstrated in the accelerated stability studies.

Limits for the elemental impurities arsenic (inorganic), cadmium, lead, and mercury are within the USP Chapter 2232 acceptance criteria for individual components used to prepare a finished dietary supplement[3].

Organic impurities may be present as residues of solvents used in the manufacture and purification of alpha-GPC. Food grade n-butanol is used is the preparation of crude alpha-GPC and is subsequently removed after solution separation. Food grade anhydrous ethanol is used in washing and crystallization steps in the manufacture of alpha-GPC. Residues of both n-butanol and ethanol are reported to be ≤0.5%. This agrees with ICH[4] Guidelines for residual solvents[5] which lists both n-butanol and ethanol as class 3 solvents that should be limited by cGMP or other quality-based requirements. Solvents in this class may be regarded as less toxic and of lower risk to human health and is considered that amounts of these residual solvents of 50 mg/day corresponding to 0.5% would be acceptable without justification. The manufacturer analyzed batches of alpha-GPC to confirm that residues of n-butanol and ethanol are below the limit of ≤0.5%.

Impurities limits for acetate, chloride, sulfate, phosphate, and glycerol are indicated in the alpha-GPC USP monograph. The process does not use acetic acid and the manufacturer confirmed that no acetic acid is present in the raw materials or processing aids. Therefore, acetate is not tested. The specifications and batch analyses indicate that chloride, sulfate, phosphate, and glycerol are within the acceptance criteria in the alpha-GPC USP monograph. Certificates of analysis for three non-consecutive batches of alpha-GPC confirm that the impurities limits are within limits.

The manufacturer tests every batch of alpha-GPC for total bacterial counts and total combined molds and yeasts and specifies ≤1000 and ≤100 cfu/g, respectively. In addition, absence of the specified microorganisms *Salmonella* species, *Escherichia coli*, and *Staphylococcus aureus* was confirmed. Certificates of analysis of three batches of alpha-GPC confirm that microbial counts meet the manufacturer's specified limit as well as the limits published in the alpha-GPC USP monograph.

The GRAS Panel noted that the manufacturer of alpha-GPC specifies a shelf-life of 24 months from the date of manufacture when stored in the unopened original container at room temperature.

The GRAS Panel reviewed the information on the intended use and function of alpha-GPC in conventional

[3] 1_GUID-10BD0BE0-5ACE-4E28-8E25-734F99315F3E_1_en-US
[4] The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human use (ICH).
[5] https://database.ich.org/sites/default/files/ICH_Q3C-R8_Guideline_Step4_2021_0422_1.pdf.

food and found the intended uses applicable within 21 CFR 170.3(n) and 21 CFR 170.3(o), respectively. The uses indicated include beverage, beverage bases and powders, coffee and tea, gummies, protein and nutrition bars and powders at maximum intended use levels of 10 – 600 mg/serving.

Food Category	Serving Size *	Maximum IntendedUse Level (mg/serving)
Carbonated Soft Drinks	360 mL	20
Sports and Energy Drinks	360 mL	20
Un-reconstituted Powders	amount to make 240 – 360 mL	20
Coffee	360 mL	10
Tea	360 mL	10
Gummies (Candy not Chocolate)	15-30 g	20
Nutritional Beverages	240 mL	600
Nutritional Bars	40 g	100
Protein and Nutritional Powders	amount to make 240 – 360 mL	600

*Based on Reference Amounts Customarily Consumed (RACC) per Eating Occasion established in 21 CFR 101.12(b)[6]

The dietary exposure under the proposed conditions of intended use was estimated for the for the U.S. population using food consumption data from the What We Eat in America (WWEIA) component of the National Health and Nutrition Examination Surveys (NHANES). The most recent data available at the time of this writing (2017–2018) were analyzed using Creme Food Safety software 3.6[7]. These data were obtained from 6639 individuals who underwent two non-consecutive 24-hour dietary recall interviews (the first was collected in-person, the second by phone 3–10 days later). The estimated daily intake from the proposed conditions of intended use of alpha-GPC was determined on a “per capita” and “per user” basis at the mean and 90th percentile of intake and reported as both absolute exposure (mg/day) and exposure relative to body weight (mg/kg bw/day).

The GRAS Panel noted that the relative standard error (RSE) calculation indicated that the values were considered reasonably reliable, using a RSE 25% cut-off. Approximately 85% of the U.S. population, ages 2 and above, was identified as potential users of alpha-GPC under the proposed conditions of intended use. The mean intake for “users” of foods with consumption data available is estimated to be 80.1 mg/day (1.1 mg/kg bw/day). The user 90th percentile is 113.3 mg/day (1.6 mg/kg bw/day). The GRAS Panel noted that these estimates are considered extremely conservative, as they assume that 100% of the numerous intended use food products in the market will contain the maximum intended use levels of the ingredient.

[6] FDA Center for Food Safety and Applied Nutrition (2018) Guidance for Industry: Estimating Dietary Intake of Substances in Food https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-estimating-dietary-intake-substances-food
[7] www.cremeglobal.com

Based on the radiolabeled alpha-GPC studies[8,9], after oral administration of alpha-GPC, the main circulating metabolite was choline and intact alpha-GPC was not present. It is assumed that alpha-GPC is hydrolyzed in the rat intestinal mucosa by a specific enzyme system degrading alpha-GPC to choline and glycerol-3-phosphate. This enzyme system has been shown not only in the gut mucosa but also in liver, brain, and kidney. Based on the studies, the amount of available choline can be estimated on a molecular weight basis and, therefore, alpha-GPC contains 40.8% choline.

The main dietary sources of choline in the United States consist primarily of animal-based products that are particularly rich in choline, including meat, poultry, fish, dairy products, and eggs. Choline is an essential nutrient and dietary reference intakes for choline have been developed by the Food Nutrition Board (FNB) at the Institute of Medicine (IOM). The Adequate Intake (AI)[10] of choline was established based on the prevention of liver damage, as measured by serum alanine aminotransferase levels. The current AIs for choline are 550 mg/day for adult males, 425 mg/day for adult females, approximately 7-9 mg/kg bw/day. Analysis of the NHANES[11] survey data indicates that most people in the U.S. consume less than the AI for choline. Therefore, these is support for the addition of alpha-GPC to conventional food as a nutrient ingredient.

Tolerable Upper Intake Levels (ULs)[12] for choline from food and supplements were established by the FNB based on the amounts of choline that are associated with hypotension and fishy body odor. The UL for choline for adults is 3500 mg/day.

The total choline consumption from foods and from the proposed uses of alpha-GPC was calculated and compared with the UL. The pseudo 90th percentile consumption of choline from food was estimated as twice the mean consumption reported in the NHANES 2017-2018. The 90th percentile choline consumption from the diet and proposed "user" uses of alpha-GPC is 669 mg/day. This indicates that the additional choline consumed from proposed uses of alpha-GPC do not result in a 90th percentile intake that exceeds the tolerable upper level.

Age (Years)	Gender	90th Percentile Choline Consumption from Foods (mg/day)	90th Percentile Choline Consumption from Proposed alpha-GPC Uses (mg/day)*		90th Percentile Total Choline Consumption (mg/day)		UL Choline (mg/day)
			Per Capita	**Users**	**Per Capita**	**Users**	
2-19	Both	492	35	50	527	542	1000-3500
19+	Both	664	45	48	709	712	3500
2+	Both	624	37	45	661	669	1000-3500
	Female	534	33	39	567	573	1000-3500
	Male	718	41	50	759	768	1000-3500

[8] Abbati, C., Rondi, G., Rosloa, R. & Vavassori, F. (1991) Nootropic therapy of cerebral aging. *Adv Therapy* 8: 268-276

[9] Abbiati, G., Fossati, T., Lachmann, G., Bergamaschi, M. & Castiglioni, C. (1993) Absorption, tissue distribution and excretion of radiolabeled compounds in rats after administration of [14C]-L-a-glycerylphosphorylcholine. *Eur J Drug Metab Pharmacokinet* 18: 173-180

[10] Adequate Intake (AI): a recommended daily intake value based on observed or experimentally determined approximations of nutrient intake by a group (or groups) of healthy people that are assumed to be adequate used when an RDA cannot be determined.

[11] National Health and Examination Survey

[12] Tolerable Upper Intake Level (UL): the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the risk of adverse effects increases.

The GRAS Panel reviewed the absorption, distribution, metabolism, and excretion studies on alpha-GPC. Following oral administration, alpha-GPC is converted to phosphorylcholine, a metabolically active form of choline able to reach cholinergic synaptic endings where it increases acetylcholine synthesis and release.[6] The phosphorylcholine crosses the blood brain barrier and then may be utilized for acetylcholine and phosphatidyl choline biosynthesis in the brain. Normal, human volunteers given an i.m. dose of alpha-GPC demonstrated a rapid rise in plasma choline, peaking between 0.25 and 0.5 hours. Thereafter, the concentration of choline declined gradually and returned to near baseline values at the end of the 6-hour observation period.[13]

The first step in the GPC breakdown pathway is the hydrolysis of phosphatidylcholine by the enzyme cytosolic phospholipase A2 (cPLA2), which removes one fatty acid to produce 1-acyl-GPC. This is followed by a second hydrolysis step by the enzyme lysophospholipase A1 (lyso-PLA1), which removes the second fatty acid to produce GPC[14,15]. GPC is then converted to free choline and glycerol-3-phosphate by the enzyme glycerophosphocholine phosphodiesterase (GPC-PDE, EC 3.1.4.2). These three key enzymes directly regulate GPC levels in mammalian cells.

Rats have been extensively used in neurochemical studies with alpha-GPC. In a study on the absorption, distribution, and excretion of alpha-GPC [6]. alpha-GPC was labeled in the glycerol part ([14C]-glycerol-GPC) and in the choline part ([14C]-choline-GPC) of the molecule. Sprague Dawley rats received the labeled compound either by iv into the tail vein at 10 mg/kg or orally by gastric intubation at 100 mg/kg. The study demonstrated that the different labelled metabolites have different kinetic properties of absorption, distribution, and clearance, leading to different blood concentration-time curves of total radioactivity. Both labelled compounds gave a wide distribution of radioactivity, particularly concentrated in the liver, kidney, lung, and spleen compared to blood. Tissue distribution studies showed that alpha-GPC and its metabolites do not accumulate in particular organs and tissues after oral administration. Choline was incorporated into brain phospholipids in increasing amounts within 24 h of dosing. In all cases renal and fecal excretion of radioactivity was low and comparable for [14C]-glycerol-GPC and [14C]-choline -GPC. Mostly the administered radioactivity was exhaled as 14CO2, this degradation being faster and more pronounced for the glycerol-labelled metabolites than for the choline-labelled metabolites. Based on the radiolabeled alpha-GPC studies, after oral administration, the main circulating metabolite was choline and intact alpha-GPC was not present after either labelled compound.

A reasonable amount of toxicological data is available for alpha-GPC of equivalent quality, i.e. 90% active alpha-GPC. The GRAS Panel relied heavily on the peer-reviewed publication data that includes *in vitro* studies, acute oral toxicity studies in rats, mice and dogs, sub-chronic oral toxicity studies in rats, and chronic oral toxicity studies in rats and dogs has been published in a peer-reviewed journal.[16].

[13] Gatti G, Barzaghi N, Acuto G, Abbiati G, Fossati T, Perucca E. (1992) A comparative study of free plasma choline levels following intramuscular administration of L-alpha-glycerylphosphorylcholine and citicoline in normal volunteers. *Int J Clin Pharmacol Ther Toxicol* 30(9): 331-5

[14] Strauss H, Leibovitz-Ben Gershon Z, Heller M. (1976) Enzymatic hydrolysis of 1-monoacyl-SN-glycerol-3-phosphorylcholine (1-lysolecithin) by phospholipases from peanut seeds. *Lipids* 11(6):442–448

[15] Loo RW, Conde-Frieboes K, Reynolds LJ, Dennis EA. (1997) Activation, inhibition, and regiospecificity of the lysophospholipase activity of the 85-KDa group IV cytosolic phospholipase A2. *Journal of Biological Chemistry* 272(31): 19214–19219

[16] Brownawell, A. M., Carmines, E. L., Chemi SpA. (2011) Safety assessment of AGPC as a food ingredient. *Food Chem Toxicol* 49: 1303-1315

Study Type	Test System/Species	Concentrations/Dosages	Results
***In vitro* studies**			
Bacterial reverse mutation, direct plate incorporation	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	100, 300, 1000, 3000, or 10,000 ug/plate +/- S9	Non-mutagenic
Yeast forward mutation, standard plate method	Schizosacchoromyces Pombe (strain P1)	30, 100, 300, 1000, or 3000 ug/ml +/- S9	Non-mutagenic
Gene conversion, standard plate method	Saccharomyces cerevisiae (strain D4)	100, 300, 1000, or 3000 ug/ml +/- S9	Non-mitotic gene conversion
Gene conversion, host-mediated technique	S. cerevisiae (strain D4)		Non-mitotic gene conversion
***In vivo* studies**			
Mammalian erythrocyte micronucleus test	Male and female Swiss mice	30, 100, or 300 mg/kg was administered twice, via subcutaneous injection, at a 24 h intervals	Non-genotoxic
Acute toxicity	Male and female Swiss mice	521, 729, 1,020, 1,429, or 2,000 mg/kg, intravenous via tail vein	LD50 Males: 1267 mg/kg LD50 Females: 1027 mg/kg
		781, 1,093, 1,531, 2,143, or 3,000 mg/kg, intraperitoneal	LD50 Males: 2053mg/kg LD50 Females: 1809 mg/kg
		2500, 5000, or 10000 mg/kg by oral gavage	LD50 Males: >10,000 mg/kg LD50 Females: 10,000 mg/kg
	Male and female Sprague-Dawley rats	781, 1,093, 1,531, 2,143, and 3,000, intravenous via tail vein	LD50 Males: 1621 mg/kg LD50 Females: 1531 mg/kg
		781, 1,093, 1,531, 2,143, or 3,000 mg/kg intraperitoneal	LD50 Males: 2215 mg/kg LD50 Females: 2017 mg/kg
		2,500, 5,000 or 10,000 mg/kg by oral gavage	LD50 Males: >10,000 mg/kg LD50 Females: >10,000 mg/kg
	Male and female Beagle dogs	200 or 500 mg/kg, intramuscular	LD50 >500 mg/kg
		1000 or 3000 mg/kg by oral gavage	LD50 >3000
13-Week sub-chronic oral toxicity test with 4-week recovery period	Male and female Sprague-Dawley rats	100, 300, or 1000 mg/kg/day by oral gavage	No treatment-related adverse effects. NOAEL at highest level tested, 1000 mg/kg
26-Week chronic oral toxicity test with 4-week recovery period	Male and female Sprague-Dawley rats	100, 300, or 1000 mg/kg/day by oral gavage	Reversible reduced activity and body weight gain at highest dose, no histopathological correlates. NOAEL 300 mg/kg
	Male and female Beagle dogs	75, 150 mg, or 300 mg/kg/day by oral gavage	Reduced activity and body weight gain at highest dose, suggested reduced liver function. NOAEL 150 mg/kg

The *in vitro* studies showed no evidence of mutagenicity of alpha-GPC. The bacterial reverse mutation test showed no significant increase in the number of revertant colonies after treatment with up to 10,000 ug/plate. alpha-GPC was not mutagenic, with or without S9 activation, in *Salmonella typhimurium* strains TA90, TA100, TA1535, and TA1537. In the yeast mutation study, alpha-GPC did not change the frequency of spontaneous forward mutations of *Schizosacchoromyces pombe* P1 up to 3,000 ug/mL, with or without S9 activation. alpha-GPC was not found to be mutagenic in the yeast conversion test or the host-mediated yeast conversion test with *Saccharomyces cerevisiae* up to 3000 ug/mL, with and without S9 activation. In the mammalian erythrocyte micronucleus test, alpha-GPC was shown to be non-genotoxic at doses up to 300 mg/kg.

alpha-GPC demonstrates a low order of acute toxicity, both by oral and parenteral routs. The oral LD_{50} in rodents was equal to or greater than 10 g/kg. The oral LD_{50} in dogs was estimated to be greater than 3 g/kg. Toxic symptoms at lethal doses after parenteral and oral administration consisted of motor and respiratory depression. Depressed animal activity was also observed in the high dose groups after sub-chronic and chronic oral dosing in both rats and dogs. The severity of symptoms was usually limited, and stabilization tended to occur within a few weeks of continuous treatment. In some cases the reduced activity was associated with reduced food consumption and failure to gain weight.
In the rat oral sub-chronic (4 weeks) toxicity study, hematology, clinical chemistry, and urinalysis as well as gross autopsy and histological examinations consistently failed to reveal any evidence of a specific toxic effect of alpha-GPC on the principal organs or their function.
In chronic toxicity studies (26 weeks), high dose rats and dogs displayed reduced activity after dosing and reduced body weight gain. In the rat study, the reduced activity abated during a 4-week recovery period and the body weights caught up to the controls. Some clinical chemistry parameters did show significant reductions versus control values in the high dose dogs and rats, including plasma triglycerides, plasma bilirubin, and alkaline phosphatase. The reduced triglycerides may have been due to reduced food consumption. There were no histopathological correlates to the clinical chemistry changes.

alpha-GPC has been investigated in a number of human trials. An open multicenter trial on 2044 patients suffering from recent stroke or transient ischemic attacks investigated the clinical efficacy and tolerability of alpha-GPC administered at the daily dose of 1000 mg i.m. for 28 days and orally at the dose of 400 mg three times a day during the following 5 months. Forty-four patients (2.14%) complained of adverse effects. The most frequent complaints were heartburn (0.7%), nausea–vomiting (0.5%), insomnia–excitation (0.4%), and headache (0.2%).[17] The weight of evidence review of at least 20 clinical trials with at least 5000 patients evaluated the efficacy of alpha-GPC for various forms of dementia, cerebrovascular disease, and physical and psychomotor performance indicates that at doses as high as 1200 mg/day for 6 months no serious side effects or toxicities were observed, and alpha-GPC is well-tolerated.

The mean “user” intake of alpha-GPC under the proposed conditions of intended use is 80.5 mg/day (1.1 mg/kg bw/day). The estimated daily intake of alpha-GPC if used in the specified food and beverages at the specified level for a consumer in the 90th percentile is 113 mg/day (1.6 mg/kg bw/day). This estimated intake is lower than the dose,1200mg/day, found to be well-tolerated, with no serious side effects in clinical studies. The No Adverse Effect Level (NOAEL) of 150 mg/kg bw/day is established based on the dog chronic study. The margin of safety of the 90th percentile “users” consumption under the proposed conditions of intended use is 95. The GRAS Panel considers the safety margin adequate demonstration of safety of use of alpha-GPC under the proposed conditions of intended use.

[17] Barbagallo Sangiorgi, G., Barbagallo, M., Giordano, M., Meli, M., Panzarasa, R. (1994) Alpha-Glycerophosphocholine in the mental recovery of cerebral ischemic attacks. An Italian multicenter clinical trial. *Ann. N. Y. Acad. Sci*. 717: 253–269

Conclusion

We, the undersigned independent qualified members of the Generally Recognized as Safe (GRAS) Panel, have, independently and collectively, critically evaluated published and unpublished data and information pertinent to the safety of the intended uses of Shenyang Gold Jyouki Technology Co.,Ltd's alpha-glycerylphosphorylcholine (alpha-GPC) as a nutrient ingredient in beverages (soft drinks, sports and energy drinks), beverage bases and powders, coffee and tea, soft candy (gummies), nutritional beverages and bars, and protein and nutrition bars and powders at levels not to exceed 600 mg/serving. We unanimously conclude that the intended uses of alpha-GPC, produced in a manner that is consistent with current Good Manufacturing Practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier "*Safety Evaluation Dossier Supporting a Generally Recognized as Safe (GRAS) Conclusion for the Intended Use of alpha-GPC"* is safe.

We further conclude that the intended uses of Shenyang Gold Jyouki Technology Co., Ltd's alpha-GPC as described above, produced in a manner that is consistent with current Good Manufacturing Practice (cGMP) and meeting appropriate food-grade specifications as presented in the supporting dossier is Generally Recognized as Safe (GRAS) based on scientific procedures.

It is our professional opinion that other qualified experts would concur with this conclusion.

[redacted]

Jimmy Wang, Ph.D.
Chief Scientific Officer
Summit Life Science, Inc.

4/6/2023
Date

[redacted]

Qinge Wei, M.P.H.
Regulatory Affairs Associate
Summit Life Science, Inc.

4/6/2023
Date

[redacted]

Nancy A. Higley, Ph.D.
Managing Member
Regulatory Connections, LLC

April 6 ,2023
Date

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

GENERALLY RECOGNIZED AS SAFE *(GRAS)* NOTICE

Form Approved: OMB No. ; Expiration Date:
(See last page for OMB Statement)

FDA USE ONLY

GRN NUMBER	DATE OF RECEIPT
001141	Apr 6, 2023
ESTIMATED DAILY INTAKE	INTENDED USE FOR INTERNET
NAME FOR INTERNET	
KEYWORDS	

Transmit completed form and attachments electronically via the Electronic Submission Gateway *(see Instructions)*; OR Transmit completed form and attachments in paper format or on physical media to: Office of Food Additive Safety *(HFS-200)*, Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740-3835.

PART I – INTRODUCTORY INFORMATION ABOUT THE SUBMISSION

1. Type of Submission *(Check one)*

☒ New ☐ Amendment to GRN No. _____ ☐ Supplement to GRN No. _____

2. ☒ All electronic files included in this submission have been checked and found to be virus free. *(Check box to verify)*

3a. For New Submissions Only: Most recent presubmission meeting *(if any)* with FDA on the subject substance *(yyyy/mm/dd):* _____

3b. For Amendments or Supplements: Is your amendment or supplement submitted in response to a communication from FDA? *(Check one)* ☐ Yes ☐ No If yes, enter the date of communication *(yyyy/mm/dd):* _____

PART II – INFORMATION ABOUT THE NOTIFIER

1a. Notifier

Name of Contact Person	Position
Shao Dongmei	Vice General Manager of Quality

Company *(if applicable)*
Shenyang Gold Jyouki Technology Co., Ltd

Mailing Address *(number and street)*
Room 401, Building F8, No.860-1 Shenben Avenue, Hunnan District

City	State or Province	Zip Code/Postal Code	Country
Shenyang	Liaoning	110167	China

Telephone Number	Fax Number	E-Mail Address
+86 13840535809		shaodm@jyouki.com

1b. Agent or Attorney *(if applicable)*

Name of Contact Person	Position
Jimmy Wang, Ph.D	Chief Scientific Officer

Company *(if applicable)*
Summit Life Science, Inc.

Mailing Address *(number and street)*
45 Adams Ave

City	State or Province	Zip Code/Postal Code	Country
Hauppauge	New York	11788	United States of America

Telephone Number	Fax Number	E-Mail Address
(631) 670 3646	631-274-4819	Jimmy@summit-life-science.com

PART III – GENERAL ADMINISTRATIVE INFORMATION

1. Name of Substance

alpha-GPC

2. Submission Format: *(Check appropriate box(es))*

☒ Electronic Submission Gateway

☐ Paper

☐ Electronic files on physical media with paper signature page

If applicable give number and type of physical media

3. For paper submissions only:

Number of volumes _____

Total number of pages _____

4. Does this submission incorporate any information in FDA's files by reference? *(Check one)*

☒ Yes *(Proceed to Item 5)* ☐ No *(Proceed to Item 6)*

5. The submission incorporates by reference information from a previous submission to FDA as indicated below *(Check all that apply)*

☒ a) GRAS Notice No. GRN 419

☐ b) GRAS Affirmation Petition No. GRP _____

☐ c) Food Additive Petition No. FAP _____

☐ d) Food Master File No. FMF _____

☐ e) Other or Additional *(describe or enter information as above)* _____

6. Statutory basis for determination of GRAS status *(Check one)*

☒ Scientific Procedures *(21 CFR 170.30(b))* ☐ Experience based on common use in food *(21 CFR 170.30(c))*

7. Does the submission (including information that you are incorporating by reference) contain information that you view as trade secret or as confidential commercial or financial information?

☐ Yes *(Proceed to Item 8)*

☒ No *(Proceed to Part IV)*

8. Have you designated information in your submission that you view as trade secret or as confidential commercial or financial information *(Check all that apply)*

☐ Yes, see attached Designation of Confidential Information

☐ Yes, information is designated at the place where it occurs in the submission

☐ No

9. Have you attached a redacted copy of some or all of the submission? *(Check one)*

☐ Yes, a redacted copy of the complete submission

☐ Yes, a redacted copy of part(s) of the submission

☐ No

PART IV – INTENDED USE

1. Describe the intended use of the notified substance including the foods in which the substance will be used, the levels of use in such foods, the purpose for which the substance will be used, and any special population that will consume the substance *(e.g., when a substance would be an ingredient in infant formula, identify infants as a special population).*

The intended use of alpha-GPC is as a nutrient (21 CFR 170.3(o)(20)) in beverage, beverage bases and powders, coffee and tea, gummies, protein and nutrition bars and powders, (21 CFR 170.3(n)). Levels per serving range from 10 mg to 600 mg/serving.

2. Does the intended use of the notified substance include any use in meat, meat food product, poultry product, or egg product? *(Check one)*

☐ Yes ☒ No

DRAFT

PART V – IDENTITY

1. Information about the Identity of the Substance

	Name of Substance[1]	Registry Used (*CAS, EC*)	Registry No.[2]	Biological Source *(if applicable)*	Substance Category *(FOR FDA USE ONLY)*
1	alpha-GPC	CAS	28319-77-9		
2					
3					

[1] Include chemical name or common name. Put synonyms *(whether chemical name, other scientific name, or common name)* for each respective item (1 - 3) in Item 3 of Part V *(synonyms)*

[2] Registry used e.g., CAS *(Chemical Abstracts Service)* and EC *(Refers to Enzyme Commission of the International Union of Biochemistry (IUB), now carried out by the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (IUBMB))*

2. Description

Provide additional information to identify the notified substance*(s)*, which may include chemical formula*(s)*, empirical formula*(s)*, structural formula*(s)*, quantitative composition, characteristic properties *(such as molecular weight(s)),* and general composition of the substance. For substances from biological sources, you should include scientific information sufficient to identify the source *(e.g., genus, species, variety, strain, part of a plant source (such as roots or leaves), and organ or tissue of an animal source)*, and include any known toxicants that could be in the source.

Molecular weight: 257.22

Molecular formula: $C_8H_{20}NO_6P$

Chemical formula: [(2R)-2,3-dihydroxypropyl] 2-(trimethylazaniumyl)ethyl phosphate

alpha-GPC is a white crystal or crystalline powder. Slightly sweet and odorless.

Impurities:

Beta-GPC	$\leq 0.10\%$
Chloride	$\leq 0.02\%$
Phosphate	$\leq 0.005\%$
Sulfate	$\leq 0.02\%$
Glycerol	$\leq 0.50\%$

3. Synonyms

Provide as available or relevant:

1	PhoslipGPC™ L-alpha-Glycerylphosphorylcholine Choline Alfoscerate
2	
3	

DRAFT

PART VI – OTHER ELEMENTS IN YOUR GRAS NOTICE

(check list to help ensure your submission is complete – check all that apply)

- ☒ Any additional information about identity not covered in Part V of this form
- ☒ Method of Manufacture
- ☒ Specifications for food-grade material
- ☒ Information about dietary exposure
- ☒ Information about any self-limiting levels of use *(which may include a statement that the intended use of the notified substance is not-self-limiting)*
- ☒ Use in food before 1958 *(which may include a statement that there is no information about use of the notified substance in food prior to 1958)*
- ☒ Comprehensive discussion of the basis for the determination of GRAS status
- ☒ Bibliography

Other Information

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

☐ Yes ☒ No

Did you include this other information in the list of attachments?

☐ Yes ☐ No

PART VII – SIGNATURE

1. The undersigned is informing FDA that Jimmy Wang, Ph.D
(name of notifier)

has concluded that the intended use*(s)* of alpha-GPC
(name of notified substance)

described on this form, as discussed in the attached notice, is (are) exempt from the premarket approval requirements of section 409 of the Federal Food, Drug, and Cosmetic Act because the intended use(s) is (are) generally recognized as safe.

2. ☒ Jimmy Wang, Ph.D *(name of notifier)* agrees to make the data and information that are the basis for the determination of GRAS status available to FDA if FDA asks to see them.

Jimmy Wang, Ph.D *(name of notifier)* agrees to allow FDA to review and copy these data and information during customary business hours at the following location if FDA asks to do so.

45 Adams Ave, Hauppauge, NY 11788
(address of notifier or other location)

Jimmy Wang, Ph.D *(name of notifier)* agrees to send these data and information to FDA if FDA asks to do so.

OR

☐ The complete record that supports the determination of GRAS status is available to FDA in the submitted notice and in GRP No. ----------
(GRAS Affirmation Petition No.)

3. Signature of Responsible Official, Agent, or Attorney	Printed Name and Title	Date (mm/dd/yyyy)
Jimmy Wang (Digitally signed by Jimmy Wang DN: cn=Jimmy Wang, o=Summit Life Science, Inc. (SLS), ou=Summit Life Science, Inc. (SLS), email=jimmy@summit-life-science.com, c=US Date: 2023.04.06 11:23:24 -04'00')	Jimmy Wang, Ph.D, Chief Scientific Officer	04/06/2023

PART VIII – LIST OF ATTACHMENTS

List your attached files or documents containing your submission, forms, amendments or supplements, and other pertinent information. Clearly identify the attachment with appropriate descriptive file names (or titles for paper documents), preferably as suggested in the guidance associated with this form. Number your attachments consecutively. When submitting paper documents, enter the inclusive page numbers of each portion of the document below.

Attachment Number	Attachment Name	Folder Location (select from menu) (Page Number(s) for paper Copy Only)
	CoverLetter_alpha-GPC_2023-04-06.pdf	Administrative
	Form3667_alpha-GPC_2023-04-06.pdf	Administrative
	GRASNotice_alpha-GPC_2023-04-06.pdf	Submission

DRAFT

OMB Statement: Public reporting burden for this collection of information is estimated to average XX hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Department of Health and Human Services,Food and Drug Administration, Office of Chief Information Officer, 1350 Piccard Drive, Room 400, Rockville, MD 20850. (Please do NOT return the form to this address.). An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

October 26, 2023

Marissa Santos, M.S.
Regulatory Review Scientist
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
5001 Campus Drive
College Park, MD 20740-3835

Re: GRAS Notice No. GRN 1141

Dear Marissa,

Thank you for your letter dated October 12, 2023 outlining a number of questions/comments for GRN 1141 on behalf of Shenyang Gold Jyouki Technology Co., Ltd, regarding uses of "L-alpha-Glyceryl phosphorylcholine" (alpha-GPC). Please find below the responses to those questions – numbered specifically as per your original letter.

Question/Comment 1. In Tables 13, 14, 15, and 16 (pages 20-22), you provide the specifications for L-alpha- glycerylphosphorylcholine (L-alpha-GPC) and the results from the batch analyses.

a) We note that the results some of the impurities in Table 13 and the heavy metals in Table 15 are reported as "Conforms" or "< [a value]". Please provide the actual measured values or state that the levels are below the limit of quantitation (LOQ) or the limit of detection (LOD), and provide either the LOQ or the LOD, as appropriate, of the analytical method(s) used to analyze the batches for these specification parameters.

Response:

In response to the Agency's inquiry regarding Tables 13, 14, 15, and 16 in GRN 1141 submission, we have provided detailed updates on the specifications for L-alpha-glycerylphosphorylcholine (L-alpha-GPC) and batch analysis results. We have also addressed the Agency's request for measured values and associated analytical methods, please see the updated GRN 1141 Table 13 and the updated GRN 1141 Table 15 below:

Updated GRN 1141 Table 13: Batch Analysis Results for alpha-GPC

Test	Method	Specification	D01-GH- 211101	D01-GH- 211201	D01-GH- 220101
Appearance	Visual	White crystal or crystalline powder	White crystalline powder	White crystalline powder	White crystalline powder
Specific Rotation	USP43-NF38 (100mg/ml, 20°, anhydrous）	-2.4° - -2.8°	-2.8°	-2.7°	-2.8°

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Identification	USP43-NF38 (IR method)	Consistent with the reference standard	Consistent	Consistent	Consistent
Particle Size	ChP2020 Vol.4, Chap. 0982	≥85% passing 80 mesh	87%	87%	88%
Bulk density	ChP2020 Vol.4, Chap.0993	0.4 - 0.7g/mL	0.6g/ml	0.6g/ml	0.6g/ml
Tap density	ChP2020 Vol.4, Chap.0993	0.5 - 0.8g/mL	0.7g/ml	0.7g/ml	0.7g/ml
pH	USP43-NF38 (85mg/mL solution)	5.0 - 7.0	5.8	6.1	6.2
Water	USP43-NF38 (KF method)	≤ 1.0%	0.33%	0.32%	0.09%
Assay	In-house method (anhydrous basis)	98.0% - 102.0%	99.9%	99.6%	100.4%
Impurities					
Organic Impurities	USP43-NF38 (HPLC)				
Beta-GPC		≤ 0.10%	0.056%	0.053%	0.056%
Any individual unspecified impurity		≤ 0.10%	0.069%	0.069%	0.083%
Total impurities		≤ 2.0%	0.12%	0.12%	0.14%
Other Impurities					
Chloride	ChP2020 Vol.4, Chap.0801	≤ 0.02%	＜ 0.02%（LOD: 0.02μg/mg）	＜ 0.02%（LOD: 0.02μg/mg）	＜ 0.02%（LOD: 0.02μg/m）
Phosphate`	In-house method (# SOP-QC1-318-01)	≤ 0.005%	＜0.005% (LOD: 0.002μg/mg)	＜ 0.005% (LOD: 0.002μg/mg)	＜ 0.005% (LOD: 0.002μg/mg)
Sulfate	ChP2020 Vol.4, Chap.0802	≤ 0.02%	＜ 0.02% (LOD: 0.07μg/mg)	＜ 0.02% (LOD: 0.07μg/mg)	＜ 0.02% (LOD: 0.07μg/mg)
Glycerol	USP43-NF38 (HPLC)	≤ 0.50%	Not Detected（LOD: 0.104ug/mg）	Not Detected（LOD: 0.104ug/mg）	Not Detected（LOD: 0.104ug/mg）
Residual Solvents	In-house method (GC, # SOP-QC1-318-01)				
Ethanol		≤ 0.50%	0.11%	0.24%	0.12%
N-Butanol		≤ 0.50%	Not Detected (LOD:0.05ug/mg）	Not Detected (LOD:0.05ug/mg）	Not Detected (LOD:0.05ug/mg）

ChP: Chinese Pharmacopoeia

A summary of updates for GRN 1141 Table 13:

(1) Appearance: the result is updated and expressed as “White crystal or crystalline powder”.
(2) Identification: the result is updated and expressed as “consistent”.
(3) Particle Size: the result is updated and expressed as actual measured values, 87%, 87% and 88%, respectively.
(4) Chloride: the result is updated and expressed as less than the limit, and added the LOD of 0.02 μg/mg in table. Please see **Question/Comment Attachment 1** for method and validation report of ChP2020 Vol.4, Chap.0801 for chloride.
(5) Phosphate: the result is updated and expressed as less than the limit, and added the LOD of 0.002 μg/mg in table. Please see **Question/Comment Attachment 2** for method and validation report of in-house method (SOP-QC1-318-01) for phosphate.
(6) Sulfate: the result is updated and expressed as less than the limit, and added the LOD

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of 0.07 µg/mg in table. Please see **Question/Comment Attachment 3** for method and validation report of ChP2020 Vol.4, Chap.0802 for sulfate.

(7) Glycerol: the result is added with the LOD of 0.104 µg/mg in the table. Please see **Question/Comment Attachment 4** for method and validation report of USP43-NF38 (HPLC) for glycerol.

(8) N-butanol: the result is added with the LOD of 0.05 µg/mg in the table. Please see **Question/Comment Attachment 5** for method and validation report of in-house method (GC, SOP-QC1-318-01) for residual solvents.

Updated GRN 1141 Table 15: Batch Heavy Metal Analysis Results for alpha-GPC

Analyte	Method	Specification	LOQ	D01-GH-211101	D01-GH-211201	D01-GH-220101
Arsenic (Inorganic)	In-house method	≤ 1.0µg/g	0.01630µg/g	< 0.0163µg/g	< 0.0163µg/g	< 0.0163µg/g
Lead	In-house method	≤ 0.5µg/g	0.00725µg/g	< 0.00725µg/g	< 0.00725µg/g	< 0.00725µg/g
Mercury	In-house method	≤ 0.1µg/g	0.06515µg/g	< 0.06515µg/g	< 0.06515µg/g	< 0.06515µg/g
Cadmium	In-house method	≤ 0.5µg/g	0.002875µg/g	< 0.002875µg/g	< 0.002875µg/g	< 0.002875µg/g

GB: China National Standard (Mandatory)

A summary of updates for GRN 1141 Table 15:

(1) Arsenic, Lead, Mercury, and Cadmium: the results are updated and expressed as less than LOQ, and added the LOQ respectively, in table. Please see **Question/Comment Attachment 6** for method and validation report of in-house method for heavy metals (As, Pb, Hg and Cs).

b) In line with FDA's "Closer to Zero" initiative that focuses on reducing dietary exposure to heavy metals, we recommend that you establish the specification limits for arsenic, lead, and cadmium that reflect the actual measured levels of these metals in the analyzed batches and that are as low as possible.

Response:

We appreciate the Agency's guidance and commitment to the "Closer to Zero" initiative aimed at reducing dietary exposure to heavy metals, including arsenic, lead, and cadmium. In response to this important initiative, we align the heavy metal specifications (Arsenic, Lead, Mercury, and Cadmium) to the California Proposition 65 and update the specification limits for Arsenic, Lead, and Cadmium, please see **Question/Comment Attachment 6**.

c) Please provide the LOD of the analytical methods used to test batches for n-butanol and glycerol (Table 13, page 20). We also recommend that you establish the specification limits for residual solvents (i.e., n-butanol and ethanol) and glycerol that reflect the results of the batch analyses and that are as low as possible.

Response:

For glycerol, the LOD is 0.104 ug/mg; please see **Question/Comment Attachment 4** for the analytical method. For n-butanol, the LOD is 0.05 ug/mg, please see

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Question/Comment Attachment 5 for the analytical method. In line with the Agency's recommendation, we have reviewed our specification limits for residual solvents, including n-butanol and glycerol, with the intention of aligning them as closely as possible with the results of the batch analyses. Our commitment is to establish limits that are not only compliant but also reflect our dedication to consumer safety and quality standards.

d) The results for glycidol and chlorinated impurities in Table 16 (page 22) demonstrate that the levels of these impurities are consistently below the LOD. We recommend that you lower the specification limits for these impurities to better reflect the batch analyses and to be as low as possible. We also note that the ICH M7 guideline (Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals To Limit Potential Carcinogenic Risk) pertains to pharmaceuticals, not ingredients intended for use in foods.

Response:

We appreciate the Agency's recommendation to lower the specification limits for glycidol and chlorinated impurities in Table 16 to better align with batch analyses and minimize these impurities. In response to this recommendation, the LOD and LOQ for glycidol and chlorinated impurities are added in the updated GRN 1141 Table 16 below. Please see **Question/Comment Attachment 7** for analytical method and validation report for glycidol and chlorinated impurities. It is worth noting that while the ICH M7 guideline primarily pertains to pharmaceuticals, our focus remains on adhering to the highest safety standards for ingredients intended for use in foods.

Updated GRN 1141 Table 16: Batch Analysis Results for alpha-GPC Impurities of Concern

Analyte	Method	Specification	LOD&LOQ	D01-GH-210301	D01-GH-210302	D01-GH-210303
Glycidol	ICAS "prior art" for test research or reference	1.25 ppm	LOD: 0.313 ppm LOQ: 0.625 ppm	ND	ND	ND
R-3-chloro- 1,2-propanediol	ICAS "prior art" for test research or reference	1.25 ppm	LOD: 0.313 ppm LOQ: 0.625 ppm	ND	ND	ND
Epichlorohydrin	PVA-R-2020-078.01	1.25 ppm	LOD:0.188 ppm LOQ: 0.375 ppm	ND	ND	ND
1,3-Chloro-2-propanol	PVA-R-2020-078.01	1.25 ppm	LOD:0.188 ppm LOQ: 0.375 ppm	ND	ND	ND
2,3-Chloro- 1-propanol	PVA-R-2020-078.01	1.25 ppm	LOD:0.188 ppm LOQ: 0.375 ppm	ND	ND	ND
2-Chloroethanol	PVA-R-2020- 101.01	1.25 ppm	LOD: 0.313 ppm LOQ: 0.625 ppm	ND	ND	ND

ND: Not detected

e) We note that the specifications include a limit for sulfate (≤0.02%). Please specify the source of the sulfate in L-alpha-GPC.

Response:

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We would like to clarify that there are no inherent sources of sulfate in L-alpha-GPC product during our manufacturing process at Jyouki. The inclusion of sulfate specifications in our product is in alignment with USP monograph for L-alpha-GPC. Our commitment is to ensure that our L-alpha-GPC meets the standards set by USP, and, as such, we maintain control over the sulfate content to ensure consistency with these established guidelines.

Question/Comment 2. ***Please clarify whether all analytical methods listed in Tables 13, 14, 15, and 16 (pages 20-22) and used to analyze the batches of L-alpha-GPC are validated for their intended use. In addition, please clarify whether the analytical methods used to test for glycidol and chlorinated impurities listed in Table 16 (page 22) are internally- developed or published. If they are published, please provide full citations for these methods.***

Response:

All analytical methods presented in Tables 13, 14, 15, and 16 (pages 20-22) and used to analyze the batches of L-alpha-GPC have been thoroughly validated to ensure their suitability for their intended use. In the case of the analytical methods used for glycidol and chlorinated impurities listed in Table 16 (page 22), we would like to clarify that these analytical method were internally developed by ourselves, and we have carried out the method validation for these methods, affirming their suitability for their intended use. For the details, please see **Question/Comment Attachment 7**.

Question/Comment 3. ***For the record, please confirm that L-alpha-GPC is not intended for use in foods where standards of identity preclude its use or in alcoholic beverages.***

Response:

We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity. We confirm that L-alpha-GPC is not intended for use in foods where the standards of identity preclude its use or in alcoholic beverages.

Question/Comment 4. ***In Table 17 (page 24), you provide the intended food uses and the corresponding use levels of L-alpha-GPC. In addition, in Exhibit E, you provide the food codes considered in the dietary exposure assessment. Please provide clarification regarding the following food uses:***

Response:

The below responses pertain to the information included in the dossier with regard to dietary exposure the specific food codes represented in Exhibit F of the GRAS Notification submitted to the FDA with the modified date of March 30, 2030. The dietary exposure assessment was completed by Crème, which is proprietary software.

a) Please clarify whether the use levels for unreconstituted powders (20 mg/serving) and protein and nutritional powders (600 mg/serving) are for the powders before reconstitution or for the beverages as consumed. If it the use level is for the beverage

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as consumed, please provide the reconstitution factor and the use level in the unreconstituted powder.

Response:

The use levels that the Agency stated above are for a serving of beverage as consumed. The concentrations and reconstitution factors for the powders that were utilized for the exposure estimate are as follows:

- Unreconstituted nutritional powders: 25 mg ingredient per gram. Assuming 24 g as a typical serving size of powder; 25 mg/g x 24 g/serving = 600 mg/final serving.
- Other unreconstituted powders: 0.83 mg ingredient per gram. Assuming 24 g as a typical serving size of powder; 0.83 mg/g x 24 g/serving = 20 mg/final serving.

b) Please confirm that the "Un-reconstituted powders" food category includes instant tea and instant coffee. In addition, please clarify if the intended uses within the "Un-reconstituted powders" food category include unreconstituted powdered fruit drinks. We note that unreconstitituted powdered fruit drinks are indicated in Exhibit E (page 133) under the food category "Other unreconstituted powders (fruit, tea, sports drinks)"; however, no food codes for powdered fruit flavored drinks were included in the dietary exposure assessment.

Response:

The "Un-reconstituted powders" food category, for the purpose of the exposure estimate in GRN1141, encompasses only the following two NHANES food codes:

- 92900200 (Fruit flavored drink, powdered, not reconstituted, diet)
- 92900300 (Sports drink, dry concentrate, not reconstituted)

Tea and coffee powders are not included within this specific food category.

c) Please clarify whether diet, sugar-free, and low-calorie carbonated soft drinks and sports and energy drinks are excluded from the intended uses of L-alpha-GPC. We note that food codes representing these types of carbonated soft drinks and sports and energy drinks were not listed in Exhibit E.

Response:

Diet, sugar-free, and low-calorie carbonated soft drinks and sports and energy drinks were not indicated as intended uses, and were not included in the exposure assessments. Therefore, it is appropriate that food codes representing these types of carbonated soft drinks and sports and energy drinks are not listed in Exhibit F.

d) Please clarify if cereal bars, granola bars, and breakfast bars within the "Nutritional bars" food category are excluded from the intended uses. We note that many food codes representing cereal, granola, or breakfast bars were not listed in Exhibit E.

Response:

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The conditions of intended use do not include cereal bars, granola bars and breakfast bars within the "Nutritional bars" food category, classified as Code 5402 by Crème. The list below is used by Crème in the "Nutritional Bars" category selected for the conditions of intended use and these food codes are represented in Exhibit F.

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

Question/Comment 5. ***In Tables 18, 19, 20, and 21 (pages 25-26), you provide the estimates of dietary exposure to L-alpha-GPC from the intended uses only. We note that a conclusion of a GRAS status should also consider cumulative dietary exposure to L-alpha-GPC including all sources of the ingredient. Please provide the mean and 90th percentile estimates of cumulative dietary exposure to L-alpha-GPC that includes the intended uses described in GRN 001141 as well as uses previously notified in GRN 000419. Providing the food codes that you consider in your cumulative dietary exposure assessment would also be helpful.***

Response:

In addition to the tables noted in the above Comment/Question 5, the GRAS Notification also includes a discussion of the cumulative dietary exposure to L-alpha-GPC in section 3.3 Dietary Exposure to Choline, pages 27 to 29. Comment/Question 5 suggests that this analysis should also include the cumulative exposure to L-alpha-GPC under the conditions of intended use in notified GRN419. GRN419 does not include an exhibit of the food codes used for that dossier's estimate of cumulative dietary exposure, resulting in this respondent making conclusions of food codes based on their experiences with L-alpha-GPC in GRN1141 rather than the availability of any report specifically for GRN419.

The table below compares the conditions of intended use for GRN419 and GRN1141. GRN419, receiving a letter of "no questions" on November 20, 2012, includes several categories of intended use that are not included in the list of intended uses for GRN1141, in particular dairy and cereal products. The L-alpha-GPC in GRN1141 is intended as an alternate source for the categories listed in the table below as partial substitute or replacement of GRN419. Two (2) proposed food uses appear to be unique to GRN1141, sports & energy drinks and protein & nutritional powders. These

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differences are reflective in the higher 90th percentile user estimated daily intake of GRN419 vs. GRN1141, 3.53 mg/kg bw/d and 1.6 mg/kg bw/d respectively.

Comments Table 1: Conditions of Intended Use for GRN419 vs GRN1141

Proposed Food or Beverage	GRN419			GRN1141			GRN1141 vs GRN419
	mg/serving	Serving size		mg/serving	Serving size		
Carbonated beverages	20	240 ml		20	360 mL		Partial substitute of GRN419
Sports and energy drinks				20	360 mL		Additional to GRN419
Meal replacement liquid	100	240 ml					Replacement of GRN419, at higher max use
Nutritional beverages				600	240 mL		
Powdered beverage	100	1 packet / 1 or 2 tablespoon(s)		20	240-360 mL		Replacement of GRN419
Coffee	10	240 ml		10	360 mL		Replacement of GRN419
Tea	10	240 ml		10	360 mL		Replacement of GRN419
Milk fluid	20	240 ml					Additional consumption from GRN419
Flavored milk/milk drink	20	240 ml					Additional consumption from GRN419
Yogurt	40	225 g					Additional consumption from GRN419
Powdered milk	10	1/3 cup					Additional consumption from GRN419
Ready-to-eat breakfast cereals weighing < 20 g per cup	20	15 g					Additional consumption from GRN419
Ready-to-eat breakfast cereals weighing ≥20g and <43 g per cup or high fiber cereals containing 28g or more fiber per 100g	20	30 g					Additional consumption from GRN419
Ready-to-eat breakfast cereal weighing ≥43 g per cup or biscuit types	20	55 g					Additional consumption from GRN419
Grain-based bars	100	40 g					Additional consumption from GRN419
Protein bars	100	40 g					Replacement of GRN419
Nutritional bars				100	40 g		
Chocolate	20	40 g					Additional consumption from GRN419
Candies	20	40 g					Partial substitute of GRN419
Gummies (Candy not chocolate)				20	15-30 g		
Chewing gum	20	3 g					Additional consumption from GRN419
Protein and nutritional powders				600	240-360 mL		Additional to GRN419

GRN419 and GRN1141 estimations of dietary exposure were conducted with two different National Health and Nutrition Examination Surveys (NHANES) and with different Reference Amounts Customarily Consumed (RACC) which was updated in 2016. Therefore, to respond to the Agency's request for cumulative dietary exposure to L-alpha-GPC, a new dietary exposure estimate was conducted using the combined conditions of intended use (in the table above), the dietary survey data

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from the NHANES 2017-2022 pre-pandemic, and with DaDiet Software.[1] As mentioned above, the submitter for GRN1141 does not have access to the Food Codes used for GRN419 which resulted in conservative assumptions of the food codes to be applied for the cumulative estimation. To estimate the intake of L-alpha-GPC from its proposed uses, the following steps were performed:

- Step 1: Identify WWEIA foods to which L-alpha-GPC may be applied, including both GRN419 and GRN1141
- Step 2: Identify and eliminate Food Codes which are not applicable to L-alpha-GPC intended use
- Step 3: Identify, if applicable, Food Codes which include only a proportion of L-alpha-GPC intended use
- Step 4: Search, if applicable, FNDDS database recipes for determination of ingredient fraction
- Step 5: Analyze intake of L-alpha-GPC for individual NHANES respondents, using DaDiet Software
- Step 6: Generate an estimated daily intake (EDI) report for per capita and "users", stratified by age and gender, and on both an absolute and body weight basis.

The number of food codes for the cumulative dietary exposure was 780, an additional 542 food codes specific to the intended uses in GRN419 but not GRN1141. The result of the analysis using NHANES 2017-2020 Prepandemic Survey is presented in the table below.

Comments Table 2: Total Population "User" Cumulated Estimated Daily Intake of L-alpha-GPC

Age (Years)	Gender	Per User Consumption (mg/day)		Per User Consumption (mg/kg bw/d)	
		Mean	90th Percentile	Mean	90th Percentile
2+	Both	80.9	142	1.42	2.82

The total choline consumption was calculated using the same procedures and assumptions presented on pages 27-29 of the submitted notification, GRN1141. The choline content of alpha-GPC is approximately 40% choline by weight. Therefore, a factor of 40% was applied to the mean and 90th percentile user consumption from the cumulative alpha-GPC assessment for total population (2+) to determine the contribution of alpha-GPC to choline consumption. The table below confirms that the additional choline consumption from the cumulative proposed uses of alpha-GPC does not result in total choline consumption in excess of the upper levels of choline proposed by the Institute of Medicine. The 90th percentile total choline consumption of users/eaters, age 2+, from all sources, diet, and alpha-GPC (GRN419 and GRN1141), was estimated to be 681 mg/day. This is well below

[1] DaDiet Software is a web-based software tool that allows accurate estimation 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.

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the upper limit of 1000 mg/day (1-8 years), 2000 mg/day (9-13 years), 3000 mg/day (14-18 years) and 3500 mg/day (19+ years) (IOM, 1998).

Comments Table 3: 90th Percentile Choline Consumption, mg/day, from Foods and Cumulative Proposed Use of alpha-GPC

Age (Years)	Gender	90th Percentile Choline Consumption from Foods (mg/day)	90th Percentile Choline Consumption from Cumulative Proposed alpha-GPC Uses (mg/day) *		90th Percentile Total Choline Consumption (mg/day)		UL Choline (mg/day)
			Per Capita	Users	Per Capita	Users	
2+	Both	624	54	57	678	681	1000 - 3500
	Female	534	48	50	582	584	1000 - 3500
	Male	718	60	65	778	783	1000 - 3500

*Choline consumption adjusted as 40% of alpha-GPC

As per the notation in Question/Comment %, the food codes used for the cumulative dietary exposure assessment is provided in the attached **Question/Comment Exhibit A**.

Question/Comment 6. ***As each GRAS notice stands on its own, for the administrative record, please provide a brief paragraph summarizing the information in GRN 000419 pertaining to safety.***

Response:

The following summary is an excerpt of GRN419 Expert Panel evaluation of the safety of alpha-GPC.

> "In evaluating the safety of A-GPC, the Expert Panel placed emphasis on chronic toxicity studies of A-GPC conducted on Sprague Dawley R rats and beagle dogs, especially two studies done by the oral route. These studies were described in Brownawell et al. (2011) and De Caro (1986) unpublished report… The NOAEL for A-GPC is greater than 150 mg/kg in dogs and 300 mg/kg in rats… AGPC has low toxicity to pregnancy outcomes, physical neurological and sensory development of F1 animals, fertility of F1 rats, and findings at Caesarian sections for F1 rats and F2 fetuses…
>
> A number of clinical studies have been conducted on A-GPC, some of which have not been published or are published in Italian and have been summarized based on other publications. Clinical studies have tested up to 1,200 mg/person/d A-GPC for up to 6 months. A number of studies have reported no adverse health effects of A-GPC (Canal et al., 1991; Frattola et al., 1991; Muratorio et al., 1992; Ziegenfuss et al., 2008) or mild effects (Ban et al., 1991; De Jesus Moreno Moreno, 2003; Parnetti et al., 1993) or overall tolerability was said to be good (Abbati et al., 1991; Barbagallo Sangiorgi et al., 1994). The large number of clinical trials where no or mild adverse health effects were observed have led to a conclusion of safety at the dose of 1,200 mg/person/day.

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No effect levels in the chronic animal toxicology studies ranged from 150 mg/kg bw/day (dogs) and 300 mg/kg bw/day (rats). The only effects observed in the chronic studies were mild (sedation). Although a 100-fold margin of safety gives increased confidence in safety of a substance, the estimated intake of AGPC places exposure in the range of a 50-fold margin of safety. The Panel considers use of A-GPC at the proposed levels in the specified foods and beverages, resulting in an estimated daily intake of 196.2 mg/person/day for a consumer in the 90th percentile, to be GRAS."

Question/Comment 7. Please search the literature for mutagenicity or genotoxicity studies on the effects of alpha-GPC exposure and discuss them. Please indicate whether the test substance administered in these studies was L-alpha-GPC or not.

Response:

A PubMed literature search was conducted. The Literature search strategy included

(1) The following MESH terms did not return any literature hits
MESH "Glycerylphosphorylcholine"
MESH "Mutagenicity Tests"

MESH Glycerylphosphorylcholine includes:

- Glycerol 3-Phosphocholine
- 3-Phosphocholine, Glycerol
- Glycerol 3 Phosphocholine
- Choline Alphoscerate
- Alphoscerate, Choline
- Choline Alfoscerate
- Alfoscerate, Choline
- L-alpha-Glycerylphosphorylcholine
- L alpha Glycerylphosphorylcholine
- Choline Glycerophosphate
- Glycerophosphate, Choline
- Glycerophosphorylcholine

MESH: Mutagenicity Tests includes:

- Mutagenicity Test
- Toxicity Tests, Genetic
- Mutagen Screening
- Mutagen Screenings
- Screening, Mutagen
- Screenings, Mutagen
- Tests, Genetic Toxicity
- Genetic Toxicity Test
- Toxicity Test, Genetic

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- Genetic Toxicity Tests
- Genotoxicity Tests
- Genotoxicity Test
- Test, Genotoxicity
- Tests, Genotoxicity

(2) Brownawell et al. (2011) is the primary reference summarizing the safety of alpha-Glycerylphosphorylcholine as a food ingredient. The referenced studies were summarized in Table 26 of the notification. All the studies conclude that L-alpha-GPC is not mutagenic or genotoxic.

Bacterial Reverse Mutation

Brownawell et al. (2011) reported that alpha-GPC was evaluated for mutagenic activity in the bacterial reverse mutation test using standard *Salmonella typhimurium* direct plate incorporation method. The vehicle (DMSO) was used as the negative control and 2-acetylaminofluorene and N-methyl-N'-nitro-N-nitrosoguanidine mutagens were used as positive controls. The potential for mutagenicity was assessed in *S. typhimurium* tester strains TA98, TA100, TA1535, TA1537, TA1538. The tester strains were incubated with alpha-GPC (dissolved in DMSO) at concentrations of 100, 300, 1000, 3000, and 10,000 lg/plate in the presence and absence of the post-mitochondrial fraction of liver homogenates (S9) from rats pretreated with Aroclor 1254.

There were no significant increases in the number of revertant colonies or cytotoxicity in any *S. typhimurium* strain exposed to alpha-GPC, with or without metabolic activation, up to 10,000 lg/plate. Under the conditions of this study, alpha-GPC was nonmutagenic in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 or TA1538.

Yeast Forward Mutation

Brownawell et al. (2011) reported that alpha-GPC was evaluated for mutagenic activity in the gene mutation assay using a standard plate method. The vehicle (phosphate buffer) was used as the negative control and dimethylnitrosoamine and methyl methanesulfonate were used as positive controls. The potential for mutagenicity was assessed in *Schizosaccharomyces pombe* (strain P1). Mutant colonies turn white, while the non-mutated ones are red. The yeast were incubated with alpha-GPC (diluted in phosphate buffer) at concentrations of 30, 100, 300, 1000, and 3000 lg/ml in the presence and absence of the post-mitochondrial fraction of liver homogenates (S9) from rats pre-treated with Aroclor 1254. The gene conversion frequency was determined based on the number of colonies present.

alpha-GPC did not alter the frequency of spontaneous forward mutations of *S. pombe* P1 at concentrations up to 3000 lg/mL with or without microsomal activation.

Yeast Gene Conversion

Brownawell et al. (2011) reported that alpha-GPC was evaluated for mutagenic activity in the gene conversion assay using a standard plate method. The vehicle (phosphate buffer) was used as the

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negative control and cyclophosphamide and N-methyl-N'-nitro-N-nitrosoguanidine were used as positive controls. The potential for mutagenicity was assessed in *Saccharomyces cerevisiae* (strain D4) with selective media for the gene TRP 5 (tryptophan) or for the gene ADE 3 (adenine). The yeast was incubated with alpha-GPC (diluted in phosphate buffer) at concentrations of 100, 300, 1000, and 3000 lg/ml in the presence and absence of the post-mitochondrial fraction of liver homogenates (S9) from rats pre-treated with Aroclor 1254. The gene conversion frequency was determined based on the number of colonies present.

alpha-GPC did not alter the mitotic gene conversion frequency of *S. cerevisiae* at concentrations up to 10,000 lg/mL. No concentration of alpha-GPC with or without microsomal activation increased the frequency of Ade2 or Trp5 gene conversion above controls.

Host mediated Gene Conversion in Yeast

Brownawell et al. (2011) reported that alpha-GPC was evaluated for mutagenic activity in the yeast gene conversion assay using a host-mediated technique exposing the yeast to the test material in the peritoneum of rats. Rats were pretreated (s.c.) with alpha-GPC for 2 days. Immediately after the second alpha-GPC dose, the rats were injected with *S. cerevisiae* (strain D4). After 4 h the yeast were removed and plated on selective media. Cyclophosamide was the positive control being administered just before the yeast. The gene conversion frequency was determined based on the number of colonies present.

alpha-GPC administered s.c. at doses up to 300 mg/kg to rats did not alter the mitotic gene conversion of *S. cerevisiae* at the Ade2 or Trp5 genes.

Micronucleus Assay

Brownawell et al. (2011) reported that alpha-GPC was assessed in mammalian cells by investigating the effect of alpha-GPC on the normal variation range of micronucleated polychromatic erythrocytes in the bone marrow of male and female Swiss mice. alpha-GPC at 30, 100, and 300 mg/kg was administered twice, via subcutaneous injection, at a 24 h intervals. Mitomycin C (7 mg/kg) was the positive control. Six hours after the last alpha-GPC injection, the animals were killed, and the femur removed. The number of micronucleated and polychromatic erythrocytes was counted.

There was no mortality. AGPC did not induce any significant increases in the incidence of micronucleated immature erythrocytes and was not cytotoxic in Swiss mice administered AGPC at doses of 3, 30 or 300 mg/kg bw, compared to the vehicle control. Under the conditions of this study, AGPC is not genotoxic in the micronucleus assay.

Question/Comment 8. ***In Part 6, Narrative and Safety Information on page 34, you state based on 2013- 2014 NHANES data that "Most people in the United States consume less than the AI for choline" and that the average daily dietary choline intake "among children and teens is 256 mg for ages 2-19." These statements conflict with the fact that the IOM AI for those 1 to 8 years old***

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is 200-250 mg/day and the 256 mg exposure is greater than the AI for this age group. With respect to your reasoning, please address the following:

a) further explain your statements and justify keeping them as is, or
b) provide a correction to these statements.

Response:
An analysis of data from the 2017–2018 NHANES (USDA, 2020) reported that the average daily choline intake from foods and beverages among children and teens is 246 ± 4.5 mg for ages 2–19. The survey data indicates that the consumption of choline in the 1-3 age group is approximately at the AI. With increasing age, the consumption of choline becomes less than the AI, as indicated by the reporting of 256 and 229 mg choline (males and females, respectively) in age group 6-11 and 303 and 224 mg choline (males and females, respectively) in age group 12-19. In adults, the average daily choline intake from foods and beverages is 388 mg in men and 281 mg in women. The groups most at risk for choline inadequacy include pregnant women, people with genetic alterations, and patients requiring total parenteral nutrition. Approximately 90-95% of pregnant women consume less than the choline AI (Brunst et al., 2014) and evidence suggests an association with increased neural tube defects in offspring (Wu et al., 2012; Shaw et al., 2009).

Question/Comment 9. ***In Parts 6.5.1.2, 6.5.1.3, and 6.5.1.4 starting on page 38, you describe the findings of animal studies that administered alpha-GPC. No journal citation(s) for the described studies are provided in the text. Please clearly indicate whether each described study is published in full in a reputed, peer-reviewed journal and cite the article(s), or whether it is unpublished information. Also please indicate whether the test substance administered in these studies was L-alpha-GPC or not.***

Response:
We apologize for confusion or lack of clarity. The description of the studies, starting on page 38, relate to the Table 26 which precedes the summary. Table 26 "Summary of Pre-Clinical Studies with a-GPC*" accurately describes the studies as those relevant to alpha-GPC and the table footnote (represented by *) indicates the publication as Brownawell et al. (2011). Brownawell al. (2011) is the "Safety assessment of AGPC as a food ingredient" and is published in a peer-reviewed journal. The studies represented in this safety assessment were described as studies conducted under OECD Guidelines for Testing Chemicals and GLP regulations. This section represents peer-reviewed preclinical data for the test substance alpha-GPC.

Question/Comment 10. ***In Parts 6.5.1.3 and 6.5.1.4 on page 40-41, you describe the protocols and findings of rat studies that administered alpha-GPC. Information on study treatment durations and recovery periods are noted in the text and/or in Table 26. However, as written or presented in the table, it is often not clear at which time point during the study were experimental measurements taken or analytical samples collected with respect to these two study phases (i.e., treatment vs. recovery with no treatment). Please clearly indicate what samples or measurements were collected***

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at each time point for each study described in these two sections. Also please indicate whether the test substance administered in these studies was L-alpha-GPC or not.

Response:

The below is a direct copy of the protocols conducted in accordance with OECD protocol as presented in the peer-reviewed journal article authored by Brownawell, et al. (2011) for studies in which the test substance administered was alpha-GPC:

2.5. Acute toxicity studies

2.5.1. Rats and mice

The acute toxicity of AGPC was investigated in mice and rats of both sexes (6 male/6 female in each dosing group) receiving single administrations by intravenous, intraperitoneal, and oral routes. The appearance and behavior of the animals were observed for 6 h after dosing and then daily for 2 weeks. Deaths were recorded daily, and post mortem examinations were performed on all dead animals, as well as on the survivors at the end of the observation period.

2.5.2. Dogs

The acute toxicity was investigated as a Maximum Tolerated Dose (MTD) in young Beagle dogs of both sexes after intramuscular or oral dosing. The animals were observed for 6 h following dosing and then daily for 2 weeks.

2.6. Sub-chronic toxicity study

2.6.1. 4-Week oral rat

Eighty Sprague–Dawley rats were randomly divided into 4 groups of 10 males and 10 females each and orally administered (by gavage) the following treatments: controls, NaCl 0.9%; low-dose, 100 mg AGPC/kg/day; mid-dose, 300 mg AGPC/kg/day; high-dose, AGPC 1000 mg/kg/day. The volume of all treatments was 5 mL/kg. Daily clinical observation and weekly body weight measurements were conducted during the pre-treatment and active phases of the study. Following 4 weeks of AGPC treatment, urine samples were collected, and blood drawn from the abdominal aorta under fasting conditions and general anesthesia. Hematology and limited clinical chemistry analyses were performed on all animals. A post-mortem examination
including organ weights and histopathology was conducted on all animals at termination.

2.7. Chronic toxicity studies

2.7.1. 26-Week oral rat

One-hundred forty-four Sprague–Dawley rats were randomly divided into 4 groups of 18 males and 18 females each and dosed by gavage (5 mL/kg): controls, distilled water; low-dose, 100 mg AGPC/kg; mid-dose, 300 mg AGPC/kg; high-dose, 1000 mg AGPC/kg. Individual daily clinical observations were performed during both the pre-test and dosing phases of the study. Body weights were measured weekly during the first 3 months of treatment, and every 2 weeks thereafter. Food consumption was measured every 2 weeks during the first 3 months, and every 4 weeks thereafter. During the 13th week of treatment, blood samples were drawn
from the retro-orbital plexus under fasting conditions for limited hematology and

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clinical chemistry evaluations. Blood and urine was collected from 10/sex/group after 26 week of treatment. Recovery animals (controls and high dose) were observed for 4 additional weeks. A full necropsy was performed following sacrifice under general anesthesia. The parameters evaluated included: body weight, organ weight, hematology (hematocrit, hemoglobin, erythrocyte count, platelet count (13th and 26th week), total and differential leukocytes, prothrombin time (26th week), clinical chemistry (glucose, BUN, creatinine, AST, ALT, alkaline phosphatase, total serum proteins, bilirubin, cholesterol, triglycerides, sodium, and potassium), and urinalysis (specific weight, pH, protein, bilirubin, blood). Histopathologic examinations were performed on all high dose and control animals and those showing gross lesions in the mid- and low-dose groups.

2.7.2. 26-Week oral dog
Twenty-four beagle dogs were randomly divided into 4 groups of 3 males and 3 females each and administered one of the following daily treatments by gavage (1 mL/kg): controls, distilled water; low-dose, 75 mg AGPC/kg; mid-dose, 150 mg AGPC/kg; high-dose, 300 mg AGPC/kg for 26 consecutive weeks. The dogs were dosed in the morning and fed in the afternoon. The animals were observed daily, and body weights were measured at monthly intervals during the first 3 months of treatment, and then at the end of the study. Venous blood samples were collected under fasting conditions before study initiation and at the end of the 13th and 26th
week for hematology and clinical chemistry evaluations. Urine samples were also collected at the same time points. A full necropsy was performed on all animals at study termination. The parameters examined included: body weight, organ weight, hematology (hematocrit, hemoglobin, erythrocyte count, platelet count, total and differential leukocytes, and prothrombin time), clinical chemistry (glucose, BUN, creatinine, AST, ALT, alkaline phosphatase, total serum proteins, bilirubin, cholesterol, triglycerides, sodium, and potassium), and urinalysis (specific weight, pH, protein, bilirubin, and blood). Necropsy and select histopathological examination of certain tissues were also performed on all animals.

Question/Comment 11. ***The European Food Safety Authority (EFSA) conducted a 2016 review and reevaluation of data on the effects of dietary choline to determine updated dietary reference values such as adequate intake levels for choline. For completeness in your review of available published literature in the Narrative section, please briefly discuss the published literature EFSA relied on and its findings. Also consider the EFSA dietary references values in your safety evaluation.***

Response:

IOM (1998) set the Adequate Intakes (AI) for choline based on data on the prevention of liver damage, as assessed by measuring serum ALT concentrations. The estimate was considered by the IOM as being uncertain because it was based on a single depletion/repletion study RCT by Zeisel et al. (1991). This study examined serum ALT activity in 16 healthy male hospitalized volunteers. They were supplemented with 500 mg choline/day for 1 week, then randomized to receive for three additional weeks either the choline-supplemented diet (control group, n = 7) or the same diet without choline but with cellulose as placebo (n = 8), then all subjects consumed the choline-supplemented diet

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during the fifth week of the study. A choline intake of 500 mg/day, which is approximately 7 mg/kg bw per day using the mean body weight for the control group, i.e. 74.4 kg, prevented ALT abnormalities in these healthy men. Thus, the AI was set at 550 mg/day after rounding, considering the US reference weight of 76 kg for men.

The EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) published a Scientific Opinion on Dietary Reference Values (DRVs) for the European population, including choline (EFSA, 2016). EFSA reviewed possible biomarkers of choline intake and/or status and determined that the available data do not allow conclusions to be drawn on a dose–response relationship between choline intake or status, and that plasma choline concentrations cannot be used to set DRVs for dietary choline.

The EFSA Panel noted that choline depletion/repletion studies indicate large variability in dietary choline requirement. The table summarizing the available 11 studies is copied from the EFSA opinion into **Question/Comment Exhibit B**. EFSA did not use 10 depletion/repletion studies, including Zeisel et al. (1991) which was used by IOM, as these did not provide information on the amount needed/sufficient to reverse the signs of deficiency. EFSA noted that only one depletion/repletion study was informative on the choline amount needed/ sufficient to reverse signs of choline deficiency. Fischer et al. (2007) defined choline deficiency by biochemical or clinical changes between the baseline diet (550 mg choline per 70 kg per day) and the low-choline diet (<50 mg choline per 70 kg per day over ≤42 days). Six subjects (all male) showed signs of choline deficiency after the baseline diet. After 42 days with <50 mg choline per 70 kg per day, 33 subjects had become depleted, but 18 had not. Fisher et al. determined that the amount of choline needed to replete the depleted subjects, using a protocol of 10-day periods with increasing choline intake levels. In 25 depleted subjects, the amount of choline needed to replete them was available. About 70% needed up to 400 mg choline per 70 kg body weight for repletion. Some subjects required more than IOM's AIs for choline for repletion; some subjects became depleted quickly, whereas others took almost 7 weeks on a low-choline diet to develop organ dysfunction. Fischer et al. concluded that "the requirement for choline in the diet is quite variable". For all adults, the EFSA Panel set an AI of 400 mg/day, based on the midpoint of the range of observed mean intakes in healthy EU populations (about 370 mg/day), and in consideration of the results of the depletion/ repletion study in which about 70% of the depleted subjects who had developed signs of organ dysfunction were repleted with an intake of about 400 mg/70 kg body weight per day.

EFSA's AI applies to men and women, whereas IOM set a higher AI for men than for women. Although premenopausal women may have a lower requirement for dietary choline than postmenopausal women or men, and ranges of estimated mean total choline intake in Europe are slightly lower in women than men, the EFSA Panel considered it unnecessary to give sex-specific AIs for adults. The Panel is unaware of any data in infants aged 7–11 months and children on indicators of choline requirement. In order to estimate the AI of infants aged 7–11 months by upwards extrapolation from the calculated choline intake for exclusively breast-fed infants from birth to 6 months, allometric scaling was applied, yielding a value of 155, which gives an AI of 160 mg/day after rounding. The Panel chose to derive AIs for all children by downwards extrapolation from the AI for adults (400 mg/day). Calculated AIs were rounded to the nearest 10. Although the calculations

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yielded an AI for children aged 15–17 years that was higher (i.e. 410 mg/day) than the value set for adults (i.e. 400 mg/day), the Panel considered that there was no reason for such a difference, thus decided to set the same AI for children aged 15–17 years and adults. The Panel concluded that calculation of choline transfer from the mother to the fetus and choline accretion in the fetus and placenta during the duration of pregnancy is not feasible to set DRVs for dietary choline during pregnancy due to a lack of data. The Panel calculated the additional choline intake needed by pregnant woman, by isometric scaling from the AI of non-pregnant women.

Comments Table 4: Comparison of EFSA and IOM Dietary Reference Values for Choline

Age	Adequate Intakes (mg/day)
7–11 months	160
1–3 years	140
4–6 years	170
7–10 years	250
11–14 years	340
15–17 years	400
Adults	400
Pregnancy	480
Lactation	520

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	125 mg/day	125 mg/day		
7–12 months	150 mg/day	150 mg/day		
1–3 years	200 mg/day	200 mg/day		
4–8 years	250 mg/day	250 mg/day		
9–13 years	375 mg/day	375 mg/day		
14–18 years	550 mg/day	400 mg/day	450 mg/day	550 mg/day
19+ years	550 mg/day	425 mg/day	450 mg/day	550 mg/day

The cumulative, 90th percentile "user" total choline exposure, presented in Comment/Question 5, above, is 681 mg/day. Although this is above the adult AI for EFSA or IOM, it is noteworthy that the exposure calculation is extremely conservative, as it assumes that 100% of the numerous intended use food products in the market will contain the maximum intended use levels of the ingredient. The cumulative 90th percentile "user" total choline exposure does not exceed the tolerable upper limit of 3500 mg/day for adults.

Question/Comment 12. ***Since L-alpha-GPC is an important endogenous compound found in brain, please identify the pivotal animal study and its toxicological endpoint(s) that you selected as representing the most significant (i.e., sensitive) adverse effect levels associated with long-term oral exposure to alpha-GPC.***

a) Please <u>briefly</u> include the reasoning for the selection of the study and associated endpoint(s) as being pivotal. Also please clearly indicate whether the test substance administered in the pivotal study was L- alpha-GPC or not.

b) Please compare the selected no observable adverse effect level (NOAEL) and/or lowest observable adverse effect level (LOAEL) values expressed as mg choline/day to the 90th percentile <u>total</u> dietary choline intake across age groups and briefly discuss.

c) Please compare the selected NOAEL and/or LOAEL values expressed as mg choline/day to established reference values for choline intake (e.g., IOM AI and UL) and briefly discuss.

d) What do the margins of safety associated with the comparisons made in parts b and c above mean?

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In several animal studies described in Part 6 of the notice, behavioral effects were observed after the administration of alpha-GPC. These effects were not acknowledged as relevant or significant adverse effects by you. The effects routinely seen were reduced activity and mobility, and/or reduced reactivity to stimulation, bradypnea or dyspnea. The alpha-GPC-induced responses were consistent across different species (i.e., mice, rats, dogs) and after exposures of acute, subchronic or chronic durations. The severity and length of the response were dose dependent and absent after removal of alpha-GPC treatment. Because this alpha-GPC-related effect emerged in a consistent manner, affected animals negatively, and is likely biologically based (e.g., via neurotransmitters), it should be considered an adverse effect.

a) Please identify a study NOAEL and/or LOAEL that best represents the threshold level for adverse behavioral responses for long-term consumption of alpha-GPC. Also please clearly indicate whether the test substance administered in the selected NOAEL/LOAEL study was L-alpha-GPC or not.

b) Please compare the selected NOAEL and/or LOAEL values expressed as mg choline/day to the 90th percentile <u>total</u> dietary choline intake across age groups and briefly discuss.

c) Please compare the selected NOAEL and/or LOAEL values expressed as mg choline/day to established reference values for choline intake (e.g., IOM AI and UL) and briefly discuss.

<u>Response:</u>

The "Questions/Comments for GRN 1141", dated October 12, 2023, included two Questions/Comments identified as "12". Because both are discussions that impact the NOAEL and/or LOAEL and comparisons to the established reference values for choline intake, they are combined in this response.

The notifier wants to be very clear that there was no overt intention to have a reviewer of the notification reach a conclusion that behavioral effects were "not acknowledged as relevant or significant adverse effects". In the consideration of the NOAEL all effects were considered and assessed in terms of significance. In addition, the test substance for all the studies reviewed for consideration of the NOAEL was alpha-GPC.

Toxicity data conducted on alpha-GPC includes *in vitro* studies (bacterial reverse mutation, yeast forward mutation, yeast gene conversion, yeast host mediated gene conversion and mouse micronucleus assay), acute oral toxicity studies in rats, mice, and dogs, sub-chronic oral toxicity studies in rats, and chronic oral toxicity studies in rats and dogs has been published (Brownawell et al., 2011). In establishing the NOAEL of alpha-GPC, the chronic, oral toxicity studies of alpha-GPC in rats and beagle dogs were considered as pivotal. Rats in the low-dose (100 mg/kg bw alpha-GPC)

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and mid-dose (300 mg/kg bw alpha-GPC) dose groups exhibited no change in behavior and no differences in food consumption and body weight gain after treatment with oral alpha-GPC for 26 weeks. After 3-4 weeks of oral treatment with A-GPC, rats that received the high dose (1,000 mg/kg bw) of alpha-GPC experienced a variable, but generally mild to moderate, decrease in spontaneous motor activity and reactivity to stimulation within 1 - 2 hours of dosing. These effects persisted for 3-5 hours, however, the activity of the rats returned to normal during the recovery period. Rats in the 1,000 mg/kg bw dosing group also exhibited reduced food consumption and body weight gain. Alterations in clinical chemistry that may have been related to decreased activity and reduced body weight were observed. These alterations included reduced plasma triglycerides in both sexes and decreased plasma bilirubin, ALT, and creatinine. Body weight gain of animals in the high dose group was similar to that of controls by the end of the 4-week recovery period. Urinalysis, necropsy, and histopathological studies revealed no effects related to alpha-GPC treatment. Brownawell et al. (2011) concluded that the type and frequency of the pathologies were generally mild and similar across the experimental groups. Some of the 10 animal deaths in the study were due to problematic gavage manipulation. Other deaths, which lacked common organ toxicity, were not considered attributable to the dose of alpha-GPC.

In the oral, chronic study with beagle dogs dosed with 75, 150, or 300 mg/kg bw alpha-GPC the oral route resulted in no deaths. Administration of 75 mg/kg bw and 150 mg/kg bw alpha-GPC for 26 weeks did not affect behavior, body weight, or hematology, clinical chemistry, or urinalysis measurements. The 300 mg/kg bw dose elicited a mild reduction in activity that lasted for 2-5 hours. Body weight gain was reduced at week 13. Increased plasma cholesterol and decreased alkaline phosphatase were observed at week 13, but not at week 26. Decreased liver and heart weights were observed, however, there were no histopathological correlates. Clinical chemistry analyses also revealed an increase in plasma bilirubin, triglycerides, and alkaline phosphatase, which was suggestive of reduced liver function. However, these changes may have been related to decreases in activity and body weight gain. Overall, these effects were minor.

The NOAEL for alpha-GPC is greater than 150 mg/kg bw in dogs and 300 mg/kg bw in rats. A number of clinical studies have been conducted on alpha-GPC, and the literature updated from the date of the GRN419, which received an FDA letter of “no questions”, to present was summarized in Table 27 of the notification. The large number of clinical trials where alpha-GPC was well-tolerated and with no reported adverse events lead to a conclusion of safety at the dose of 1,200 mg/person/day.

This notification, GRN1141, has identified conditions of intended use in fewer categories than those identified in GRN419 and the assessment of the margin of safety was presented in the notification based on the specific intentions of GRN1141 as a partial replacement of GRN419 intended uses. However, at the specific request of Questions/Comments 12, the table below will also include the total dietary choline, using the analysis outlined and presented in the response to Question/Comment 5, noting again that GRN419 did not provide specific food codes for the conditions of intended use resulting in the response to Question/Comment 5 being based on best available understanding and expertise on the use of alpha-GPC.

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Comments Table 5: alpha-GPC Intake Comparisons for 2+ Population vs. alpha-GPC NOAEL

	GRN1141	**GRN1141+GRN419**
	90th Percentile "User"	**90th Percentile "User"**
alpha-GPC mg/day	113	142
alpha-GPC mg/kg bw/day	1.6	2.8
alpha-GPC NOAEL, mg/kg bw/d	150	150
alpha-GPC MOS	94X	54X

The margin of safety for the conditions of intended use at 90th percentile "user" for GRN1141 is slightly under 100-fold. The margin of safety for the combined conditions of intended use, as best that can be derived, for GRN1141 and GRN419 combined is slightly over 50. The 90th percentile users are extremely conservative, as it assumes that 100% of the numerous intended use food products in the market will contain the maximum intended use levels of the ingredient. The Expert Panel for GRN419, which received an FDA letter of "no questions", concluded that the level is lower than the doses found to be safe in clinical studies, 1200 mg/day, and reached a GRAS conclusion with a 50-fold margin of safety.

Both Questions/Comments 12, ask for a comparison of the NOAL and/or LOAEL values expressed as mg choline per day against the reference values for choline intake, e.g., IOM AI and UL. As the NOAEL discussed above is based on oral administration of alpha-GPC, not choline, and the IOM AI and UL are not based on NOAEL, this response has tried to interpret the intent of the request.

The IOM considered 7.5 g/day of choline as the Lowest Observed Adverse Effect Level (LOAEL), and after the application of an uncertainty factor of 2 and rounding, set a UL of 3.5 g choline/day for adults. No UL was established for infants and ULs for children were derived from the adult value by allometric scaling (exponent 0.75) according to reference body weights (EFSA, 2016). alpha-GPC contributes 40% choline, resulting in 45 and 57 mg choline/day for 90th percentile "users" of GRN1141 and GRN1141+GRN419, respectively. These levels are 166 and 132 times less than the LOAEL for choline. The table below was developed to assess the "total dietary choline intake across age groups" and "compare … to established reference values for choline intake". The report for choline intake from cumulative alpha-GPC (GRN1141+GRN419) was re-run, using DaDiet software, to match the age groups used by IOM for AI and UL determinations. These age ranges are slightly different in the USDA report of choline intake 2017-2018 so some assumptions need to be made to determine the total choline by age group.

Comments Table 6: Total Choline Compared to Reference Values

Age	**AI, mg/day (both genders)**	**UL, mg/day (both genders)**	**Choline from food, mg/day Pseudo 90th percentile (female-male)**	**Choline from aGPC, mg/day 90th Percentile Users (both genders)**	**Total Choline, mg/day 90th Percentile Users (female-male)**	**>AI**	**>UL**
1–3 years	200	1,000		35.2	445-479	Yes	No
2-5 years			410-444				
4–8 years	250	1,000		42.4	500-560	Yes	No
6-11 years			458-518				
9–13 years	375	2,000		50.4	298-656	No-Yes	No
12-19			248-606				

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14–18 years	400-450	3,000		55.2	303-661	No-Yes	No
19+ years	425-550	3,500		60	724	Yes	No
20+			664				

The total choline for 90th percentile users is higher than the AI, with the exception of teenage females. The total choline for 90th percentile users does not exceed the UL in any age group. The 90th percentile assumes that all of the intended uses include alpha-GPC at the maximum use and, therefore, is an exaggerated consumption number. The availability of choline in the diet from alpha-GPC does not result in consumption that would be above the IOM upper limit which is based on the LOAEL for choline.

We hope this response letter adequately addresses the Agency's questions on GRN 1141, all Attachments, Exhibits, and the Reference are on the following pages. If you require any further information or have additional inquiries, please do not hesitate to reach out to us at 631-670-3646 or Jimmy@summit-life-science.com

Sincerely,

[redacted]

Jimmy Wang, Ph. D
Chief Scientific Officer
Summit Life Science, Inc.

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Question/Comment Attachment 1

JYOUKI JYOUKI PHARMACEUTICAL CO. , Ltd.

Analytical method of ChP2020 Vol.4, Chap.0801 for chloride in L-alpha-GPC

1. **Analytical method for chloride in L-alpha-GPC**

Preparation of standard sodium chloride solution :weigh 0.165g of sodium chloride, put it into a 1000ml volumetric flask. Add water to dilute it to the scale, and shake it well to get the stock solution. Before use, accurately measure 10ml of standard sodium chloride stock solution, put it into a 100ml volumetric flask, add water to dilute it to the scale, and shake it well to get the solution (every 1ml is equivalent to 10μg CL).

Preparation of test solution:Take 0.25g of the test sample, put it into a 50ml Nessler colorimetric tube and add water to dissolve it into 25ml. Then add 10ml diluted nitric acid(take 105ml of nitric acid and dilute it to 1000ml with water), add water to make it into 40ml solution, shake well and get the test solution.

Preparation of control solution:accurately measure 5.00ml of standard sodium chloride solution and put it into a 50ml Nessler colorimetric tube, add 10ml of diluted nitric acid and add water to make it into 40ml solution, and shake well and get the control solution.

Add 1.0ml silver nitrate solution(take 17.5g of silver nitrate, dilute it to 1000ml with water, and shake it well) into test solution and control solution respectively, and dilute with water to make 50ml. Shake well, place in dark place for 5 minutes and place on same black background, observe and compare from up to down of colorimetric tube.Any opalescence in the test solution is not more intense than that in the control solution (0.02%).

2. **Overview of method validation for chloride in L-alpha-GPC**

We established the analytical method of chloride in L-alpha-GPC according to the "ChP2020 Vol.4, Chap.0801" , and is determined by physical-chemical method. To ensure the test results are accurate and reliable, we carried out the method validation.

According to ICH Q2 (R1): "validation of analytical procedure: Text and Methodology ", the method of a limit method for impurities, the validation should at least include: specificity, limit of detection. Therefore, we validate the specificity, limit of detection limit and robustness.

3. Validation results for chloride in L-alpha-GPC

Table: Test results summary of Method validation for Chloride

Test item	Acceptance criteria	Validation results
Specificity	The blank should be clear.	The blank is clear.

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LOD	For three testings at the measured concentration, the visible turbidity was the detection limit of chloride, and the detection limit should be far less than the limit of chloride (50μg).	The LOD of chloride is 5μg, which is far less than the limit (50μg）.
Robustness	When the experimental conditions are slightly changed, the results of sample are the same as the experimental results under the specified parameters, which proved that the robustness of method is good.	Different batches of silver nitrate TS had no effect on test results. The test solution and control solution had no effect on the test results observed within 30 minutes of preparation.

Signed by QC manager: [redacted] 2023.10.21 Signed by QA manager: [redacted] 2023.10.21

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Question/Comment Attachment 2

JYOUKI PHARMACEUTICAL CO. , Ltd.

Analytical method of In-house method (# SOP-QC1-318-01) for phosphate in L-alpha-GPC

1. **Analytical method for phosphate in L-alpha-GPC**

Preparation of standard phosphate solution: accurately weigh 0.286g of potassium dihydrogen phosphate dried to constant weight at 105 °C, put it into a 1000ml volumetric flask, add water to dissolve and dilute to the scale as standard phosphate stock solution.

Before use, take 5.00 ml of the above standard phosphate stock solution, put it into 100ml volumetric flask, add water to dilute to the scale, shake well and use it as phosphate standard solution.(Every 1ml of this solution is equivalent to 10 μg of PO_4^{3-})

Preparation of test solution :take 1.0g of test sample, put it into 25ml Nessler colorimetric tube, and add 10ml of water to dissolve it.

Preparation of control solution :take 5.0ml of standard phosphate solution, put it into 25ml Nessler colorimetric tube, and add water to 10ml.

Preparation of ammonium molybdate solution :weigh 1g of ammonium molybdate and dissolve it with 40ml of 0.5mol/L sulfuric acid solution.

Preparation of 1-amino-2-naphthol-4-sulfonic acid solution: take 5g of anhydrous sodium sulfite, 94.3g of sodium bisulfite and 0.7g of 1-amino-2-naphthol-4-sulfonic acid, and mix well, before use take the 1.5 g of above mixture, dissolve it with 10ml of water.and filter it if necessary)

Add 1.0ml of ammonium molybdate and 0.5ml of 1-amino-2-naphthol-4-sulfonic acid solution to to the test solution and the control solution respectively. Dilute them with water to 25ml respectively. Shake well, place them for 10 minutes, and place them on the same white background. Observe and compare from the top to the bottom of the colorimetric tube. The color of test solution should not be deeper than the color of control solution (0.005%).

2. Overview of method validation for phosphate in L-alpha-GPC

We developed the analytical method of phosphate in L-alpha-GPC by ourselves, and is determined by physical-chemical method. To ensure the test results are accurate and reliable, we carried out the method validation.

According to ICH Q2 (R1): "validation of analytical procedure: Text and Methodology ", the method of a limit method for impurities, the validation should at least include: specificity, limit of detection. Therefore, we validate the specificity, limit of detection limit, linearity and range, repeatability, solution stability and robustness.

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3. Validation results for Method validation for phosphate in L-alpha-GPC

Table: Test results summary of Method validation for phosphate

Test item	Acceptance criteria	Validation results
Specificity	The blank should be colorless. For the test solution interference experiment, the color of tube A should not be lighter than tube B.	The blank and sample had no interference to the phosphate test results.
LOD	At the measured concentration, three parallel experiments showed that the visually obvious blue color was the detection limit of phosphate, and the detection limit should be far less than the limit requirement of phosphate (50μg).	The LOD of phosphate is 2μg, which is equivalent to 40% the limit of phosphate (50μg), and prove that the sensitivity of method is good.
线性与范围 Linearity and range	The correlation coefficient r between phosphate concentration and absorbance should be not less than 0.998, and the range is at least 10% to 120% of the limit concentration (5μg to 60μg) .	The linear relationship between phosphate mass (between 2μg and 70μg) and absorbance is good, the correlation coefficient r is 0.9999, and the range is equivalent to 4% to 140% of the limit
Solution stability	If the change in absorbance of the stability solution during the investigation period is within ±10%, it is judged that the solution is stable, otherwise it should be immediately compared and observed 10 minutes after color development.	The test solution and control solution observed within 1 hour after preparation had no effect on the test results.
耐用性	When the experimental conditions	The using of different batches of

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Robustness	are slightly changed, if the results of samples are the same as the experimental results under the given parameters, it is judged that the robustness of method is good.	ammonium molybdate solution had no effect on the test results, and the using of 1-amino-2-naphthol-4-sulfonic acid solution within 24 hours had no effect on the test results.

Signed by QC manager: [redacted] 2023.10.21

Signed by QA manager: [redacted] 2023.10.21

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Question/Comment Attachment 3

JYOUKI JYOUKI PHARMACEUTICAL CO. , Ltd.

Analytical method of ChP2020 Vol.4, Chap.0802 for sulfate in L-alpha-GPC

1. Analytical method for sulfate in L-alpha-GPC

Preparation of standard potassium sulfate solution: weigh 0.181g of potassium sulfate, put it into a 1000ml volumetric flask, add appropriate amount of water to dissolve it, dilute it to the scale, and shake it evenly (every 1ml is equivalent to 100 μ g of SO_4)

Preparation of test solution:Take 1.0g of the test sample, put it into a 50ml Nessler colorimetric tube and add water to make it into 40ml solution . Add 2.0ml diluted hydrochloric acid (take 234ml of hydrochloric acid and dilute it to 1000ml with water) and shake well to get the test solution.

Preparation of control solution:accurately measure 2.00ml of standard potassium sulfate solution and put it into a 50ml Nessler colorimetric tube and add water to make it into 40ml solution .Add 2.0ml of diluted hydrochloric acid and shake well to get control solution.

Add 5.0ml 25% barium chloride solution into the test solution and the control solution respectively, and dilute to 50ml with water. Shake well, place them for 10 minutes, and place them on the same black background. Observe and compare from the top to the bottom of the colorimetric tube.Any opalescence in the test solution is not more intense than that in the control solution (0.02%).

2. Overview of method validation for sulfate in L-alpha-GPC

We established the analytical method of sulfate in L-alpha-GPC according to the "ChP2020 Vol.4, Chap.0802" , and is determined by physical-chemical method. To ensure the test results are accurate and reliable, we carried out the method validation.

According to ICH Q2 (R1): "validation of analytical procedure: Text and Methodology ", the method of a limit method for impurities, the validation should at least include: specificity, limit of detection. Therefore, we validate the specificity, limit of detection limit and robustness.

3. Validation results for sulfate in L-alpha-GPC

Table: Test results summary of Method validation for sulfate

Test item	Acceptance criteria	Validation results
Specificity	The blank should be clear.	The blank is clear.
LOD	For three testings at the measured concentration, the visible turbidity was the detection limit of sulfate, and	The LOD of sulfate is 70μg, which is far less than the limit (200μg).

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	the detection limit should be far less than the limit requirement of sulfate (200μg).	
Robustness	When the experimental conditions are slightly changed, the results of samples are the same as the experimental results under the specified parameters, which proved that the robustness of method is good.	Different batches of 25% barium chloride solution had no effect on the test results. The test solution and control solution had no effect on the test results observed within 30 minutes of preparation .

Signed by QC manager: [redacted] 2023.10.21 Signed by QA manager: [redacted] 2023.10.21

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Question/Comment Attachment 4

JYOUKI JYOUKI PHARMACEUTICAL CO. , Ltd.

Analytical method of USP43-NF38 (HPLC) for glycerol in L-alpha-GP

1. Analytical method for glycerol in L-alpha-GP

Take 4g of the test sample, put it into a 10ml volumetric flask,, add water to dissolve and dilute to the scale, shake well, and use it as the test solution. Take an appropriate amount of glycerol reference substance and dilute it with water to form a solution containing 2mg glycerol per 1ml as the control solution.Take appropriate amount of control solution and test solution respectively, and dilute them with water to get one solution containing 2mg glycerol per 1mland anther solution containing 400mg of choline alfoscerate per 1ml, as the System suitability solution. Use Zorbax Sax column (4.6mm × 25cm, 5μm) as the analytical column, acetonitrile-water (55:45) as the mobile phase, the flow rate : 0.5 ml per minute, the column temperature : 40°C, and the detector: the differential detector. Injection volume: 20μl.

Take the blank solution (water) and the system suitability solution for injection once respectively, and record the chromatogram. The resolution of Glycerol and L-α- glycerophosphoryl choline in the chromatogram of the system suitability solution shall not be less than 2.0.Take the control solution for 6 consecutive injections, and calculate from the last injection of the control solution. the bracketing standard solution (that is, System suitability solution) is respectively injected once after every 12 times injection and ending the sequence. and record the chromatogram.The RSD should not exceed 5.0%, base on the chromatographic peak area of glycerol for 6 consecutive injections .The RSD should not exceed 5.0% ,based on chromatographic peak area of each substance adding with bracketing standard solution, Inject the test solution and record the chromatogram. According to the external standard method, the content of glycerol was calculated by peak area,the content of glycerol in the test sample shall not exceed 0.50%

Calculation formula:

$$\text{Glycerol (\%)} = \frac{m_{\text{对}} \times \text{purity of reference substance} \times A_{\text{供}} \times \text{dilution ratio of test solution}}{V_{\text{供}} \times A_{\text{对}} \times m \times 1000} \times 100$$

Where,

$m_{\text{对}}$: the weight of glycerol reference substance, mg;

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$A_{试}$, the peak area of glycerol in the test solution;

$V_{对}$, diluted volume of glycerol reference substance, ml;

$A_{对}$, peak area of glycerol reference substance;

m. weight of the test sample, g.

2. Overview of method verification for glycerol in L-alpha-GPC

The glycerol test method for L-α-choline glycyrrheate was developed by our company according to We formulated the analytical procedure of glycerol for L-alpha-GPC according to the monograph of L-alpha-GPC in USP43-NF38, and was determined by HPLC. The chromatographic column, mobile phase, detector and other information in the method were the same as those in USP. In order to ensure the applicability of the method in our QC lab, we carried out the method verification.

After evaluation, we determined to verify the following items: specificity, limit of detection, limit of quantitation and solution stability.

3. Verification results for glycerol in L-alpha-GPC

Table: Verification Results summary of analytical method for glycerol

Items	Acceptance Criteria	Validation Results
Specificity	1. The blank solution should not interfere with the test of glycerol; 2. The resolution between glycerol and adjacent peaks in the chromatogram of system suitability solution shall be not less than 2.0.	There is no interference in the blank; The minimum resolution between glycerol and adjacent peaks in the chromatogram of system suitability solution is 3.29.
Limit of Detection (LOD)	In the chromatograms of 3 injections, the ratio of glycerol signal to noise (S/N) shall be not less than 3	42 μg/ml glycerol standard solution; Equivalent to about 2.1% of the limit.
Limit of Quantification (LOQ)	S/N ≥10; The RSD of peak area for glycerol is ≤ 5.0%.	125 μg/ml glycerol standard solution; RSD: 3.5% (n=6); LOQ is equivalent to 6.0% of the

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		limit.
Solution Stability	If new peaks are present in system suitability solution for suitability study during the study time period, they shall not interfere with glycerol testing, and the resolution between glycerol and adjacent impurity peaks shall be not less than 2.0. If the ratio of the concentration of glycerol to that at 0 h is between 90.0%~108.0%, it indicates that the system suitability solution and sample solution are stable in this time period. If the ratio of the concentration of glycerol to that at 0 h in standard solution for suitability study during this time period is between 90.0%~108.0%, it indicates that the solution is stable in this time period.	Standard solution, system suitability solution, and sample solution are stable in refrigerator for 8 days.

Signed by QC manager: [redacted] 2023.10.21 Signed by QA manager: [redacted] 2023.10.21

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Question/Comment Attachment 5

JYOUKI JYOUKI PHARMACEUTICAL CO. , Ltd.

Analytical method of In-house method(GC, # SOP-QC1-318-01)for residual solvents in L-alpha-GPC

1. Analytical method for residual solvents in L-alpha-GPC

Sample solution: Transfer 50 mg of sample into a 20ml headspace vial, add 5.00 ml of water, and seal. Standard solution: Accurately weigh suitable amounts of ethanol and n-butanol respectively, dilute with water to obtain a mixture with a concentration of 0.05 mg of ethanol and 0.05 mg of n-butanol per ml.

Chromatographic condtion:

Column: DB-WAX capillary column (60 m × 0.32 mm × 0.5 μm);

Column temperature: 120 °C; flow rate: 1 ml/min; inlet temperature: 200 °C, split ratio: 10:1;

Detector: FID; Detector temperature: 200°C;

Headspace vial equilibrium temperature: 85°C, Equilibrium time: 15 minutes.

Procedure: Transfer accurately 5 ml of the sample solution and 5 ml of the standard solution into 20 ml headspace vial and seal. Determine by the residual solvent test method, A standard solution was taken as the solution for system suitability, headspace injection was made and the chromatogram was recorded. Inject control solution (consistent with the system suitability solution) once every 12 injections starting from the last injection of system suitability solution and at the end of the sequence and record the chromatogram. The RSD of chromatographic peak area for each solvent in six consecutive injections of the system suitability solution should meet the requirements, and that in injections including the control solution should still meet the above requirements; the resolution between ethanol and n-Butanol should meet the requirements, and the theoretical plate of ethanol should be not less than 5000. Then take the headspace injection of sample solution and record the chromatogram. The contents of ethanol and n-Butanol are calculated by the external standard method with the peak area. Ethanol should be not more than 5000ppm, and n-Butanol should be not more than 5000ppm.

The content of ethanol or n-Butanol in the sample is calculated separately according to the following formula.

$$\text{Residual solvent (ppm)} = \frac{m_{std} \times \text{standard purity} \times A_{spl} \times \text{dilution factor of the sample}}{V_{std} \times A_{std} \times 1000} \times 100$$

In which,

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m_{std}, weight of ethanol RS or n-Butanol RS, mg;

A_{spl}, peak area of ethanol or n-Butanol in the sample;

V_{std}, dilution factor of ethanol or n-Butanol RS;

A_{std}, average value of the peak areas of ethanol or n-Butanol in standard solution.

m, the weight of sample, g.

2. Analytical method for residual solvents in L-alpha-GPC

The test method for residual solvent of L-alpha-Glycerylphosphorylcholine was developed by our company according to ICH Q3C (R7): impurities: residual solvents guideline, which is tested by headspace-gas chromatography. In order to ensure the suitability of this method in our laboratory, method validation of the analytical method was carried out.

Carry out the method validation according to ICH Q2(R1)"Validation of Analytical Procedures: Text and Methodology ". As a quantitative testing of impurities, method validation should include at least: Specificity, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy and Intermediate Precision. This validation includes: Specificity, Limit of Detection, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy, Intermediate Precision and Robustness.

3. Validation results for residual solvents in L-alpha-GPC

Table: Summary of Validation Results of Residual Solvent of L-alpha-Glycerylphosphorylcholine

Items	Acceptance Criteria	Validation Results
System Suitability	RSD ≤ 10.0% (n=6). Resolution between ethanol and n-Butanol≥ 1.5. In terms of ethanol, the number of theoretical plates should be not less than 5000.	The system suitability is qualified and the test data is valid.
Specificity	The analysis system should be free of interference. The components in the sample do not interfere with the inspection of ethanol	No interference in the analysis system The components in the sample do not interfere with the inspection of ethanol and n-Butanol.

	and n-Butanol. The resolution between ethanol, n-Butanol and other components in the resolution solution shall be not less than 1.5.	The resolution between ethanol, n-Butanol and other components in the resolution solution is 16.31, which meets the requirements.
LOD (Limit of Detection)	S/N ≥ 3.	0.5μg/ml of standard solution is equivalent to 1.0% of the limit of impurity.
LOQ	S/N ≥ 10. RSD ≤ 10.0% (n=6). Limit of quantification: ≤ 50% of the impurity limit	1.5μg/ml standard solution, corresponding to 3.0% of the impurity limit. The RSD of Ethanol is 3.1% (n=6). The RSD of n-Butanol is 2.2% (n=6).
Linearity and Range	The correlation coefficient r of the regression equation should be not less than 0.999. The absolute value of the Y-axis intercept should be not more than 5.0% of the peak area of the 100% limit concentration. The residual standard deviation should be not more than 5.0% of the peak area of the 100% limit concentration. The range is at least 80% to 120% of the limit.	Ethanol: correlation coefficient r: 0.9997. Y-axis intercept: the absolute value is equivalent to 0.23% of the peak area of 100% limit concentration. Residual standard deviation is equivalent to 1.3% of peak area of 100% limit concentration. Range: 1.5μg/ml to 71.8μg/ml, equivalent to 3.0% to 143.6% of the limit. n-Butanol: correlation coefficient r: 0.9993. Y-axis intercept: the absolute value is equivalent to 0.84% of the peak area of 100% limit concentration. Residual standard deviation:

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		equivalent to 2.0% of the peak area of 100% of limit concentration. Range: 1.5μg/ml to 71.9μg/ml, equivalent to 3.0% to 143.8% of the limit.
Repeatability and Accuracy	Recovery: 75.0% to 120.0%. RSD: ≤10.0% (n=9)	Recovery of ethanol: 83.0%~102.7% with an RSD of 8.4% (n=9). Recovery of n-Butanol: 80.3%~104.3% with RSD of 9.8% (n=9).
Intermediate Precision	Recovery: 75.0% to 120.0%. RSD: ≤10.0% (n=18)	Recovery of ethanol: 96.1%~101.8% with RSD of 6.0% (n=18). Recovery of n-Butanol: 95.4%~103.9% with RSD of 7.0% (n=18).
Solution Stability	If the concentration of 100% sample during this time is within 90% ~ 108% compared with the 0h concentration, which indicates that the solution is stable during this time.	The standard solution is stable for 48 hours at room temperature.
Robustness	When the chromatographic conditions change slightly (±2°C), the system suitability should meet the requirements, meanwhile the resolution of ethanol and n-Butanol in the test solution for resolution should meet the requirements.	Column temperature: 120±2°C, gas flow rate: 1.0±0.1ml/min, headspace equilibrium temperature: 85±5°C. It shows that the robustness of this method is good.

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Question/Comment Attachment 6

JYOUKI JYOUKI PHARMACEUTICAL CO. , Ltd.

Analytical method (in-house) for Arsenic, Lead, mercury and cadmium in L-alpha-GPC

1. **Analytical method for Arsenic, Lead, mercury and cadmium in L-alpha-GPC**

1.1 Instrument and parameters

Instrument information

Instrument	Model	Manufacturer	Instrument No.
Inductively coupled plasma mass spectrometer (ICP-MS)	7800	Agilent	KC-YX-YQ-458
Electrical balance	BSA224S-CW	Sartorius Scientific Instruments (Beijing) Co., LTD	KC-YX-YQ-006

Testing parameters of ICP-MS

Instrument parameters	Reference value
Radio frequency power	1600W
Flow rate of plasma gas	15.00L/min
Flow rate of auxiliary gas	0.9L/min
Sampling depth	10mm
Speed of pump	0.1rps
Flow rate of Atomizing gas	0.57L/min
Atomizing chamber temperature	2.0℃

1.2、Solution Preparation

（1）Standard solution preparation

Intermediate solution A: precisely measure 15ml of multiple elements (15) Kf into a 100ml volumetric flask, dilute with 2% nitric acid to scale, shake well. Each 1ml solution contains Cd: 125ng; Pb: 125ng; As: 375ng; Hg: 750ng.

Standard solution (system suitability solution) : accurately measure 4ml of intermediate solution A, into a 250ml volumetric flask, add 1ml of hydrochloric acid, then dilute with 2% nitric acid to the

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scale, shake well.

Internal standard solution: Accurately measure 5ml of Bi, Ge, In, Lu, Rh, Sc, Tb, Y multi-element standard solution into a 1000ml volumetric flask, then dilute with 2% nitric acid to the scale, shake well.

（2）Test solution preparation

Take 0.1g of the substance being examined, accurately weighed, into a polytetrafluoroethylene beaker, add 0.1ml of hydrochloric acid, dissolve completely with appropriate amount of 2% nitric acid, transfer it to a 25ml volumetric flask, wash the beaker with a small amount of 2% nitric acid, combine the washing solution into the volumetric flask, dilute with 2% nitric acid to the scale, shake well.

2. **Overview of method validation for Arsenic, Lead, mercury and cadmium in L-alpha-GPC**

The analytical method for Arsenic, Lead, mercury and cadmium of L-alpha-GPC was developed by the entrusted third party, and was determined by ICP-MS. In order to ensure the suitability of this method in our laboratory, method validation of the analytical method was carried out.

This method is established based on the ICH Q3D: guideline for elemental impurities, USP <233> elemental impurities - procedures, USP <730> plasma spectrochemistry, and the ChP2020, volume IV <9101 Guidelines for validation of Analytical Methods, California Act 65, etc. This validation includes: system suitability, specificity, accuracy, precision, limit of detection, limit of quantitation, linearity and range, and solution stability.

3. **Validation results for Arsenic, Lead, mercury and cadmium in L-alpha-GPC**

<table>
<tr><th>Items</th><th>Validation Method</th><th>Acceptance criteria</th><th colspan="2">Validation results</th></tr>
<tr><td rowspan="5">System suitability</td><td rowspan="5">Inject the standard solution for consecutively 6 times</td><td rowspan="5">RSD of the element response value ratio (the ratio of the response value of the element examined to the</td><td>Element</td><td>RSD(%)</td></tr>
<tr><td>As</td><td>1.5</td></tr>
<tr><td>Pb</td><td>1.0</td></tr>
<tr><td>Hg</td><td>1.0</td></tr>
<tr><td>Cd</td><td>1.1</td></tr>
</table>

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		response value of the internal standard element) ≤10.0%	
Specificity	Inject the blank solution, test solution, 100% concentration standard solution and 100% concentration spikked test solution for i time, respectively.	The concentration of blank solution is less than 15% of the concentration of 100% standard solution; The determination of each element has its own mass-charge ratio, and does not interfere with each other. The recovery of each element sipked solution was in the range of 70%-150%.	The concentration of blank element solution is less than 15% of the concentration of level 2 standard solution, so the interference of blank solution to the method can be ignored. The determination of each element has its own mass-charge ratio and does not interfere with each other. The recoveries of each element level 2 spiked solution were in the range of 102%-109%, so the matrix of the test product had no strong interference to the determination of this method
Accuracy	Prepare 25%, 100% and 150% of spiked test solution, and each is 3 solutions and total is 9 solutions, then inject	Recovery is 70%-150%; the recovery RSD≤20.0%。	Element / Recovery (%) / RSD(%) As / 90-110 / 6.0 Pb / 104-111 / 2.1

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	each solution for once		Hg 105-107 0.6 Cd 95-108 4.3
Repeatability	Prepare 6 samples of 100% spiked test solution in parallel, and inject each solution once.	RSD≤20.0%。	Element RSD(%) As 5.4 Pb 1.0 Hg 0.7 Cd 2.9
Intermediate precision	Another analyst independently prepares 6 samples of 100% spiked test solution with the same method, and inject each sample once.	RSD≤25.0% (n=12)	Element RSD(%) As 4.1 Pb 2.6 Hg 2.5 Cd 3.5
LOD and LOQ	Take 7 portions of blank solutions and inject each once. The LOD and LOQ were calculated based on the response values. Seven blank solutions were taken and each was injected once. The detection limit and theoretical quantitation limit were calculated based on the response values. The linear lowest point that is not lower than the theoretical quantitative limit and meets the	LOD: ≤10% the limit concentration.	LOD of each element is less than 10% the limit concentration.
		LOQ is less than 25% the limit concentration, and the RSD is not more than 20.0%.	LOQ of each element is less than 25% the limit concentration. Element RSD(%) As 7.0 Pb 3.0 Hg 1.7 Cd 57

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	quantitative needs of methodology is taken as the quantitative limit. Morcover, 25% of the spiked test solution with the same content as the limit of quantification was injected for 6 consecutive times to verify the repeatability of the limit of quantification.		
Linearity and range	Prepare at least 5 parts pf linear solution, and consecutively inject each sample once.	Linearity relative coefficient (r): ≥0.990	Element / Range (ng/ml) / Linear coefficient As / 1.5-18 / 0.999 Pb / 0.5-6 / 0.999 Hg / 3-36 / 0.999 Cd / 0.5-6 / 0.999
Solution stability	During the validation of this method, the time of 100% spiked test solution injection under the specificity is defined as 0 hours, and and the test is repeated within 8-48 hours.	The change rate of element concentration in the solution of spiked test solution is less than 20%.	Test the same spiked solution at 22 hours, the concentration change rate of each element was less than 20%. and the solution had good stability.

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Question/Comment Attachment 7

JYOUKI JYOUKI PHARMACEUTICAL CO. , Ltd.

Analytical method of PVA-R-2020-101.01 for 2-chlorethanol in L-alpha-GPC

1. Analytical method for 2-chlorethanol in L-alpha-GPC

1250 ng/mL standard stock solution preparation： Precisely measure 0.25 mL of chloroethanol standard (2.0 mg/mL) into a 10 mL volumetric flask containing a certain amount of solvent, dilute with water to the scale, mix well, and label it as standard stock solution I. Accurately transfer 0.5mL standard stock solution I into a 20 mL volumetric flask containing a certain amount of solvent, dilute to the volume to the scale and mix.

125ng/ml standard solution (system suitability solution)preparation: accurately measure 5.0ml of standard stock solution into a 50ml volumetric flask, dilute to the scale with water and mix well.

62.50ng/ml standard solution preparation: accurately measure 1.0ml of standard stock solution into a 20ml volumetric flask, dilute to the scale with water and mix well.

Test solution preparation: accurately weigh 200mg of L-alpha-GPC sample into a 20ml headspace vial, dissolve with 2.0ml of water, then cover.

Chromatographic condition:

Chromatographic column	DB-WAX (30 m× 0.250 mm ×0.50 μm)		
Carrier gas	He		
Detector	MS EI (70eV)		
Injection port temperature	150℃		
Split ratio	10 :1		
Flow rate	1.5mL/min		
Control method	Constant current		
Heating procedure	Rate (℃/min)	Temperature (℃)	Remaining time (min)
	-	35	5
	30	230	0
Ion source temperature	250 ℃		
Quadrupole rod temperature	200 ℃		
Transmission temperature	250 ℃		
Sampling mode	Solvent delay 8.00 min 8.00~10.00 min, SIM m/z=31.0		
Dwell time	100 ms		

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Headspace injector parameters	
Oven temperature	85℃
Loop temperature	95℃
Transfer temperature	105℃
Headspace vial equilibrium time	12 min

Procedure: inject each of the blank (water), sensitivity solution, reference solution (that is, system suitability solution, 6 consecutive times of injection) and test solution for analysis. For the sensitivity solution, the signal-to-noise ratio (S/N) of impurity to be examined should not be less than 10. The peak area RSD of system suitable solution for 6 consecutive samples should be not more than 15.0%, and the retention time RSD should be not more than 1.0%. Calculate the content of impurity in sample by external standard method. The 2-chloroethanol should not exceed 1.25ppm.

2. **Overview of method validation for 2-chloroethanol in L-alpha-GPC**

The test method for 2-chloroethanol of L-alpha-GPC was developed by the entrusted third party, and was determined by GC-MS. In order to ensure the suitability of this method in our laboratory, method validation of the analytical method was carried out.

Carry out the method validation according to ICH Q2(R1)"Validation of Analytical Procedures: Text and Methodology ". As a quantitative testing of impurities, method validation should include at least: Specificity, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy and Intermediate Precision. This validation includes: Specificity, Limit of Detection, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy, Intermediate Precision and Robustness.

3. **Validation results for 2-chloroethanol in L-alpha-GPC**

Table: Summary of Method Validation for Residual of Chloroethanol

Validation Item	Acceptance Criteria	Validation Results

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System Suitability	The system is clean and stable, there is no interference at the position of the peak of each component. If there is interference, the interfering peak area should be no greater than the main peak area in the sensitivity solution. The signal-to-noise (S/N) of target peak in the sensitivity solution should be not less than 10. The RSD of the target peak area of six consecutive injections should be not more than 15.0%, and the RSD of retention time should be not more than 1.0%.	All reported validation results are based on the premise that the system suitability meets the requirements.
Specificity	There is no obvious interference at the target peak in the blank solution chromatogram. If there is interference, the peak area of the interference peak should be not greater than the main peak area of LOQ; The standard solution of 100% limit shows the target peak; In the spiked sample of 100% limit, the resolution between all adjacent peaks greater than LOQ and the target peak should be greater than 1.5.	There is no interference in Blank; The standard solution of 100% limit shows the target peak, and RT=9.325 min. In the spiked sample of 100% limit, the resolution between all adjacent peaks of greater than LOQ and the target peak is 12.4.
LOD	The signal-to-noise (S/N) of each injection of LOD solution should be not less than 3.	

Name	S/N
LOD1	12
LOD2	13
LOD3	16

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LOQ	The signal-to-noise (S/N) of each injection of LOQ solution should be not less than 10. The RSD of target peak area of six consecutive injections in LOQ solution should be not more than 30.0%.	Name: S/N LOQ1: 26 LOQ2: 25 LOQ3: 25 LOQ4: 24 LOQ5: 24 LOQ6: 25 Peak area RSD: 5.9%
Linearity	Regression coefficient (r) ≥0.990; Report the Y-axis intercept and the residual sum of squares.	(r): 0.999 Y intercept: 0.186 Residual sum of squares: 11163.486
Accuracy	The average recovery of spiked solution at each concentration level should be between 70% and 130%; The RSD of recovery of nine spiked sample solutions should be not more than 15.0%.	Name: Recovery 50%Spiked: 105% 100%Spiked: 108% 150%Spiked: 103% RSD: 4.0%
Repeatability	The RSD of recovery of six spiked solutions should be not more than 15.0%.	Name: RSD 100%Spiked 01 to 06: 4.9%
Intermediate Precision	The RSD of recovery of six 100% spiked sample solutions prepared by the second researcher should be not more than 15.0%; The RSD of recovery of twelve spiked sample solutions should be not more than 30.0%.	Name: RSD Spiked solution for 6 injections: 2.5% Spiked solution for 13 injections: 5.1%

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Solution Stability	The content of the stability solution should be between 70% and 130% of the initial content.	Name	Content VS initial
		STD Assay% (vs initial)33.5h	111%
		100%Spiked Assay% (vs initial)31.0h	113%
Robustness	Under single condition, the RSD of six test solution peak areas shall be not more than 20.0%. If any robustness method that does not meet the requirements, an explanation should be provided.	Name	Peak area RSD
		Injection port temperature ±2°C	2.9%
		Initial column temperature ±2°C	3.9%
		Flow rate ±0.02mL/min	2.6%

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Analytical method of ICAS "prior art" for test research or reference for glycidol and R-3-chloro-1, 2-propanediol in L-alpha-GPC

1. Analytical method for glycidol and R-3-chloro-1, 2-propanediol in L-alpha-GPC

Solvent 1 preparation: weigh 20g of sodium chloride into a 100ml volumetric flask, add ultra-pure water to dissolve ultrasonic, and dilute with the same solvent to the volume.

Solvent 2 preparation: measure 1ml of glacial acetic acid and 30ml of solvent 1 into a centrifuge tube and mix well.

Solvent 3 preparation: measure 1ml of ultra-pure water and 19ml of acetone into a centrifuge tube

Derivative reagent solution preparation: weigh 2.5g of phenylboric acid into a 20ml volumetric flask, adding solvent 3 o dissolve ultrasonic, adding solvent 3 to the scale, and shaking well.

Blank solution preparation: Precisely measure 1ml of solvent 2 and 0,5ml of derivative reagent in a centrifuge tube, sealed and swirled for 5 minutes, and then place in a water bath at 80°C for 30 minutes. After derivatization, remove and cool to room temperature, add 5ml of n-hexane, swirl for 10 minutes, extract, centrifuge and take the upper organic phase, add an appropriate amount of anhydrous sodium sulfate, filter and label as blank solution.

Standard stock solution 1 preparation: take 20mg of 3-chloro-1, 2-propanediol RS, accurately weighed,into a 20ml volumetric flask containing a certain amount of ultra-pure water, dilute to the scale with ultra-pure water, shake well.

2.5μg/ml standard mixture stock solution preparation: accurately measure 1.0ml of each of Standard stock solution 1 into a 10ml volumetric flask containing a certain amount of solvent 2, and dilute to the scale with solvent 2, shake well. Precisely measure the above 1.0ml of above solution and 0.5ml of derivative reagent into a centrifuging tube, sealed and swirl for 5min, and then place in a water bath at 80°C for 30 minutes. After derivatization, remove and cool to room temperature, add 5ml of n-hexane, swirl for 10 minutes, extract, centrifuge and take the upper organic phase, add an appropriate amount of anhydrous sodium sulfate, filter. Precisely measure 1.25ml of above solution into a 10ml volumetric flask, dilute to the scale with n-hexane.

0.25μg/ml standard solution (system suitability solution) preparation: precisely measure 1.0ml of standard stock solution into a 10ml volumetric flask, dilute to the scale with n-hexane and shake well.

0.125μg/ml sensitivity solution preparation: precisely measure 0,5ml of standard stock solution into a 10ml volumetric flask, dilute to the scale with n-hexane and shake well.

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Test solution preparation: accurately weigh 1.0g of the substance being examined into a centrifuge tube, add 1.0ml of solvent 2, after vortex dissolution, add 0.5ml of derivative reagent solution, sealed and vortex for 5 minutes, and then place in a water bath at 80℃ for 30 minutes to derive. After derivatization, remove and cool to room temperature, add 5ml of n-hexane 5ml, vortex oscillation for 10 minutes, extract, centrifuge, take the upper organic phase, add a appropriate amount of anhydrous sodium sulfate, filter. Prepare another solution in parallel.

Chromatographic condition:

Chromatographic column	DB-624(30 m× 0.32 mm × 1.8μm)		
Carrier gas	He		
Detector	MS EI (70eV)		
Injection port temperature	230℃		
Split ratio	10:1		
Flow rate	1.8 ml/min		
Control method	Constant current		
Heating procedure	Rate (℃/min)	Temperature (℃)	Remaining time (min)
	-	80	1
	40	240	3
Running time (min)	8min		
MS parameters			
Ion source temperature	230℃		
Quadrupole rod temperature	150℃		
Transmission temperature	280℃		
Sampling mode	Solvent delay: 5.0 min 5.0~8.0 min，SIM m/z=196		
Dwell time	100 ms		

Procedure inject each of the blank, sensitivity solution, reference solution (that is, system suitability solution, 6 consecutive times of injection) and test solution for analysis. For the sensitivity solution, the signal-to-noise ratio (S/N) of each impurity to be examined should not be less than 10. The peak

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area RSD of the system suitable solution for 6 consecutive samples should be not more than 15.0%, and the retention time RSD should be not more than 1.0%. Calculate the content of each impurity in sample by external standard method. The glycidol and R-3-chloro-1, 2-propanediol should not exceed 1.25ppm.

2. **Overview of method validation for glycidol and R-3-chloro-1, 2-propanediol in L-alpha-GPC**

The test method for glycidol and R-3-chloro-1, 2-propanediol of L-alpha-GPC was developed by the entrusted third party, and was determined by GC-MS. In order to ensure the suitability of this method in our laboratory, method validation of the analytical method was carried out.

Carry out the method validation according to ICH Q2(R1)"Validation of Analytical Procedures: Text and Methodology ". As a quantitative testing of impurities, method validation should include at least: Specificity, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy and Intermediate Precision. This validation includes: Specificity, Limit of Detection, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy, Intermediate Precision and Robustness.

3. **Validation results for glycidol and R-3-chloro-1, 2-propanediol in L-alpha-GPC**

Table: Summary of Method Validation for Residual of Glycidol and R-3-chloro-1, 2-propanediol

Items	Acceptance criteria	Validation results
System Suitability	The system has no interference with the analysis; S/N of sensitivity should be not less than 10; The peak area RSD of 100% limit of standard solution should be not more than 15.0%（n=6）	The system is conformed, and the test results is valid.
Specificity	There is no obvious interference at the target peak in the blank solution chromatogram. If there is interference, the peak area of the interference peak should be not greater than the main peak area of LOQ;	The blank has no interference with the impurity determination. The peaks of the glycidyl derived reactants were consistent with that of 3-chloro-1, 2-propanediol

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	In the spiked sample of 100% limit, the resolution between all adjacent peaks greater than LOQ and the target peak should be greater than 1.5.	The mini resolution of resolution test solution between each impurity and adjacent peak is 5.6.
LOD	S/N≥3;	R-3-chloro-1,2-propanediol: 62.38ng/ml; Which is equivalent to 25% of the impurity limit。
LOQ	S/N≥10; RSD: ≤30.0% (n=6); LOQ: not more than 50% the impurity limit.	R-3-chloro-1,2-propanediol: 124.77ng/ml, RSD is 3.6% (n=6); Which is not more than 30.4% of the impurity limit.
Linearity and range	Correlation coefficient, r≥0.990;	R-3-chloro-1,2-propanediol: 125.0～375.0ng/ml, correlation coefficient (r) is 1.000; The range is equivalent to 50% to 150% of the !00% limit.
Repeatability	RSD≤15.0% (n=6)。	RSD of R-3-chloro-1,2-propanediol: 1.5% (n=6);
Intermediate precision	RSD≤15.0% (n=6); RSD≤30.0% (n=12)。	RSD of R-3-chloro-1,2-propanediol: 3.4% (n=6), 3.7% (n=12);
Accuracy	Recovery: 70%～130%; RSD: ≤15.0% (n=9)。	R-3-chloro-1,2-propanediol: 103%~108%, RSD is 2.5% (n=9);
Solution stability	The content of the stability solution should be between 70% and 130% of the initial content.	The standard solution at room temperature is stable within 59 hours ; The 100% spiked test solution at room temperature is stable within 55 hours.

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Robustness	Under single condition, the RSD of six test solution peak areas shall be not more than 20.0%. If any robustness method that does not meet the requirements, an explanation should be provided.	When there are slightly changes, such as the change of the transmission temperature is between 280℃±2℃, the change of the initial column temperature is between 80℃±2℃, and the change of the flow rate is between 1.8ml/min±0.02 mL/min, the method has good robustness.

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Analytical method of PVA-R-2020-078.01 for epichlorohydrin, 1,3-dichloropropanol and 2,3-dichloropropanol in L-alpha-GPC

1. Analytical method for epichlorohydrin, 1,3-dichloropropanol and 2,3-dichloropropanol in L-alpha-GPC

500ng/ml standard stock solution preparation: Take 20mg of epichlorohydrin, 1, 3-dichloropropanol and 2, 3-dichloropropanol reference standard, respectively, accurately weighed, into a 20ml volumetric flask containing certain methanol, add methanol to the scale, and shake well. Take 0.1ml of the above solution into a 10ml volumetric flask, add methanol to the scale, and shake well. Take 0.5ml of the above solution into a 10ml volumetric flask certain methanol, add methanol to the scale, and shake well.

50ng/ml standard solution (system suitability solution) preparation: take 1.0ml of standard stock solution into a 10 volumetric flask, add methanol to the scale, and shake well.

15ng/ml sensitivity solution preparation: take 0.3ml of standard stock solution into a 10ml volumetric flask, add methanol to the scale, and shake well.

Test solution preparation: accurately weigh 40mg of the substance being examined into 15ml centrifuging tube, add 1ml of methanol to dissolve, prepare another solution in parallel.

Chromatographic condition:

Chromatographic parameters			
Chromatographic column	DB-WAX(30 m× 0.25 mm × 0.5 μm)		
Carrier gas	He		
Detector	MS EI (70eV)		
Injection port temperature	150°C		
Split ratio	10:1		
Flow rate	1.5 ml/min		
Control method	Constant current		
Heating procedure	Rate (°C/min)	Temperature (°C)	Remaining time (min)
	-	70	1
	20	160	4
	35	230	0
Running time (min)	11.5 min		
MS parameters			

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Ion source temperature	230°C
Quadruple rod temperature	150°C
Transmission temperature	250°C
Sampling model	Solvent delay: 3.0 min 3.0~4.2 min, SIM m/z=57(epichlorohydrin), 4.2~9.5 min, SIM m/z=79(1,3-dichloropropanol), 9.5~10.5 min, SIM m/z=62(2,3-dichloropropanol) 10.5~11.5min Close detector.

Procedure: inject 1μl of each of the blank (methanol), sensitivity solution, reference solution (that is, system suitability solution, 6 consecutive times of injection) and test solution for analysis. For the sensitivity solution, the signal-to-noise ratio (S/N) of each impurity to be examined should not be less than 10. The peak area RSD of the system suitable solution for 6 consecutive samples should be not more than 15.0%, and the retention time RSD should be not more than 1.0%. Calculate the content of each impurity in sample by external standard method. Epichlorohydrin, 1, 3-dichloropropanol and 2, 3-dichloropropanol should not exceed 1.25ppm.

2. Overview of method validation for Epichlorohydrin, 1, 3-dichloropropanol and 2, 3-dichloropropanol in L-alpha-GPC

The test method for epichlorohydrin, 1,3-dichloropropanol and 2,3-dichloropropanol of L-alpha-Glycerylphosphorylcholine was developed by the entrusted third party, and was determined by GC-MS. In order to ensure the suitability of this method in our laboratory, method validation of the analytical method was carried out.

Carry out the method validation according to ICH Q2(R1)"Validation of Analytical Procedures: Text and Methodology ". As a quantitative testing of impurities, method validation should include at least: Specificity, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy and Intermediate Precision. This validation includes: Specificity, Limit of Detection, Limit of Quantitation, Linearity and Range, Repeatability, Accuracy, Intermediate Precision and Robustness.

3. Validation results for epichlorohydrin, 1,3-dichloropropanol and 2,3-dichloropropanol in L-alpha-GPC

Table: Summary of Method Validation for Epichlorohydrin, 1, 3-dichloropropanol and 2, 3-dichloropropanol

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Items	Acceptance criteria	Validation results
System Suitability	The system has no interference with the analysis; S/N of sensitivity should be not less than 10; The peak area RSD of 100% limit of standard solution should be not more than 15.0%（n=6）	The system is conformed. and the test results is valid.
Specificity	There is no obvious interference at the target peak in the blank solution chromatogram. If there is interference, the peak area of the interference peak should be not greater than the main peak area of LOQ; In the spiked sample of 100% limit, the resolution between all adjacent peaks greater than LOQ and the target peak should be greater than 1.5.	The blank has no interference with the impurity determination. The mini resolution of resolution test solution between each impurity and adjacent peak is 20.7.
LOD	S/N≥3;	Epichlorohydrin：7.6ng/ml; 1, 3-dichloropropanol：7.5μg/ml; 2, 3-dichloropropanol：7.5μg/ml; Which are all not more than 15.2% the impurity limit.
LOQ	S/N≥10; RSD：≤30.0%（n=6）; LOQ ： not more than 50% the impurity limit.	Epichlorohydrin：15.2ng/ml，RSD 为 9.0%（n=6）; 1, 3-dichloropropanol：15.0ng/ml，RSD 为 2.3%（n=6）; 2, 3-dichloropropanol：15.0ng/ml，RSD 为

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		2.1%（n=6）; Which are all not more than 30.4% the impurity limit.
Linearity and range	Correlation coefficient, r≥0.990;	Epichlorohydrin： 25.0～75.0ng/ml， and correlation coefficient (r) is 1.000; 1, 3-dichloropropanol: 25.0～75.0ng/ml, and correlation coefficient (r) is 0.999; 2, 3-dichloropropanol: 25.0～75.0ng/ml, and correlation coefficient (r) is 1.000; The range is equivalent to 50% to 150% of 100% limit.
Repeatability	RSD≤15.0%（n=6）。	Epichlorohydrin RSD：1.9%（n=6）; 1, 3-dichloropropanol RSD：2.7%（n=6）; 2, 3-dichloropropanol RSD：1.4%（n=6）。
Intermediate precision	RSD≤15.0%（n=6）; RSD≤30.0%（n=12）。	Epichlorohydrin RSD：1.8%（n=6），3.6%（n=12）; 1, 3-dichloropropanol RSD：1.6%（n=6），2.2%（n=12）; 2, 3-dichloropropanol RSD：1.9%（n=6），1.6%（n=12）。
Accuracy	Recovery：70%～130%; RSD：≤15.0%（n=9）。	Epichlorohydrin: recovery: 85%~97%, RSD is 6.3%（n=9）; 1, 3-dichloropropanol: recovery: 86%~95%, RSD is 5.1%（n=9）; 2, 3-dichloropropanol: recovery: 88%~96%, RSD is 3.8%（n=9）。
Solution stability	The content of the stability solution should be between 70% and 130% of the initial content.	The standard solution at room temperature is stable within 29.7 hours ; The spiked test solution at room temperature is stable within 28.25 hours.

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Robustness	Under single condition, the RSD of six test solution peak areas shall be not more than 20.0%. If any robustness method that does not meet the requirements, an explanation should be provided.	When there are slightly changes, such as the change of the injection port temperature is between 150°C±2°C, the change of the initial column temperature is between 70°C±2°C, and the change of the flow rate is between 1.5ml/min±0.02 mL/min, the method has good robustness.

Signed by QC manager: 2023.10.21 Signed by QA manager: 2023.10.21

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Question/Comment Exhibit A Food Codes for Cumulative a-GPC Dietary Exposure

WWEIA Category number	WWEIA Category description	Food code	Main food description
1004	Milk, reduced fat	11100000	Milk, NFS
1002	Milk, whole	11111000	Milk, whole
1002	Milk, whole	11111100	Milk, low sodium, whole
1002	Milk, whole	11111150	Milk, calcium fortified, whole
1006	Milk, lowfat	11111160	Milk, calcium fortified, low fat (1%)
1008	Milk, nonfat	11111170	Milk, calcium fortified, fat free (skim)
1004	Milk, reduced fat	11112110	Milk, reduced fat (2%)
1006	Milk, lowfat	11112120	Milk, acidophilus, low fat (1%)
1004	Milk, reduced fat	11112130	Milk, acidophilus, reduced fat (2%)
1006	Milk, lowfat	11112210	Milk, low fat (1%)
1008	Milk, nonfat	11113000	Milk, fat free (skim)
1006	Milk, lowfat	11114300	Milk, lactose free, low fat (1%)
1008	Milk, nonfat	11114320	Milk, lactose free, fat free (skim)
1004	Milk, reduced fat	11114330	Milk, lactose free, reduced fat (2%)
1002	Milk, whole	11114350	Milk, lactose free, whole
1008	Milk, nonfat	11115000	Buttermilk, fat free (skim)
1006	Milk, lowfat	11115100	Buttermilk, low fat (1%)
1004	Milk, reduced fat	11115200	Buttermilk, reduced fat (2%)
1002	Milk, whole	11115300	Buttermilk, whole
1006	Milk, lowfat	11115400	Kefir, NS as to fat content
1002	Milk, whole	11116000	Goat's milk, whole
1008	Milk, nonfat	11120000	Milk, dry, reconstituted, NS as to fat content
1002	Milk, whole	11121100	Milk, dry, reconstituted, whole
1006	Milk, lowfat	11121210	Milk, dry, reconstituted, low fat (1%)
1008	Milk, nonfat	11121300	Milk, dry, reconstituted, fat free (skim)
1002	Milk, whole	11210050	Milk, evaporated, NS as to fat content
1002	Milk, whole	11211050	Milk, evaporated, whole
1004	Milk, reduced fat	11211400	Milk, evaporated, reduced fat (2%)
1008	Milk, nonfat	11212050	Milk, evaporated, fat free (skim)
1202	Flavored milk, whole	11220000	Milk, condensed, sweetened
1820	Yogurt, regular	11400000	Yogurt, NFS
1822	Yogurt, Greek	11400010	Yogurt, Greek, NS as to type of milk or flavor
1820	Yogurt, regular	11410000	Yogurt, NS as to type of milk or flavor
1820	Yogurt, regular	11411010	Yogurt, NS as to type of milk, plain
1820	Yogurt, regular	11411100	Yogurt, whole milk, plain
1820	Yogurt, regular	11411200	Yogurt, low fat milk, plain
1820	Yogurt, regular	11411300	Yogurt, nonfat milk, plain
1822	Yogurt, Greek	11411390	Yogurt, Greek, NS as to type of milk, plain
1822	Yogurt, Greek	11411400	Yogurt, Greek, whole milk, plain
1822	Yogurt, Greek	11411410	Yogurt, Greek, low fat milk, plain
1822	Yogurt, Greek	11411420	Yogurt, Greek, nonfat milk, plain
1820	Yogurt, regular	11430000	Yogurt, NS as to type of milk, fruit
1820	Yogurt, regular	11431000	Yogurt, whole milk, fruit
1820	Yogurt, regular	11432000	Yogurt, low fat milk, fruit
1820	Yogurt, regular	11433000	Yogurt, nonfat milk, fruit
1822	Yogurt, Greek	11433990	Yogurt, Greek, NS as to type of milk, fruit
1822	Yogurt, Greek	11434000	Yogurt, Greek, whole milk, fruit
1822	Yogurt, Greek	11434010	Yogurt, Greek, low fat milk, fruit
1822	Yogurt, Greek	11434020	Yogurt, Greek, nonfat milk, fruit
1820	Yogurt, regular	11434090	Yogurt, NS as to type of milk, flavors other than fruit
1820	Yogurt, regular	11434100	Yogurt, whole milk, flavors other than fruit
1820	Yogurt, regular	11434200	Yogurt, low fat milk, flavors other than fruit
1820	Yogurt, regular	11434300	Yogurt, nonfat milk, flavors other than fruit

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WWEIA Category number	WWEIA Category description	Food code	Main food description
1822	Yogurt, Greek	11435000	Yogurt, Greek, NS as to type of milk, flavors other than fruit
1822	Yogurt, Greek	11435010	Yogurt, Greek, whole milk, flavors other than fruit
1822	Yogurt, Greek	11435020	Yogurt, Greek, low fat milk, flavors other than fruit
1822	Yogurt, Greek	11435030	Yogurt, Greek, nonfat milk, flavors other than fruit
1822	Yogurt, Greek	11435100	Yogurt, Greek, with oats
1820	Yogurt, regular	11436000	Yogurt, liquid
8412	Dips, gravies, other sauces	11440010	Chipotle dip, yogurt based
8412	Dips, gravies, other sauces	11440020	Dill dip, yogurt based
8412	Dips, gravies, other sauces	11440030	Onion dip, yogurt based
8412	Dips, gravies, other sauces	11440040	Ranch dip, yogurt based
8412	Dips, gravies, other sauces	11440050	Spinach dip, yogurt based
8412	Dips, gravies, other sauces	11440070	Vegetable dip, yogurt based
1820	Yogurt, regular	11446000	Yogurt parfait, low fat, with fruit
5802	Ice cream and frozen dairy desserts	11459990	Frozen yogurt, NFS
5802	Ice cream and frozen dairy desserts	11460000	Frozen yogurt, vanilla
5802	Ice cream and frozen dairy desserts	11460100	Frozen yogurt, chocolate
5802	Ice cream and frozen dairy desserts	11460500	Frozen yogurt, soft serve, vanilla
5802	Ice cream and frozen dairy desserts	11460510	Frozen yogurt, soft serve, chocolate
5802	Ice cream and frozen dairy desserts	11461200	Frozen yogurt sandwich
5802	Ice cream and frozen dairy desserts	11461210	Frozen yogurt bar, vanilla
5802	Ice cream and frozen dairy desserts	11461220	Frozen yogurt bar, chocolate
5802	Ice cream and frozen dairy desserts	11461250	Frozen yogurt cone, chocolate
5802	Ice cream and frozen dairy desserts	11461260	Frozen yogurt cone, vanilla
5802	Ice cream and frozen dairy desserts	11461300	Frozen yogurt cone, vanilla, waffle cone
5802	Ice cream and frozen dairy desserts	11461320	Frozen yogurt cone, chocolate, waffle cone
1208	Flavored milk, nonfat	11511000	Chocolate milk, NFS
1202	Flavored milk, whole	11511100	Chocolate milk, ready to drink, whole
1204	Flavored milk, reduced fat	11511200	Chocolate milk, ready to drink, reduced fat
1208	Flavored milk, nonfat	11511300	Chocolate milk, ready to drink, fat free
1206	Flavored milk, lowfat	11511400	Chocolate milk, ready to drink, low fat
1206	Flavored milk, lowfat	11511550	Chocolate milk, ready to drink, reduced sugar, NS as to milk
1206	Flavored milk, lowfat	11511600	Chocolate milk, ready to drink, low fat (Nesquik)
1208	Flavored milk, nonfat	11511610	Chocolate milk, ready to drink, fat free (Nesquik)
1206	Flavored milk, lowfat	11511700	Chocolate milk, ready to drink, low fat, no sugar added (Nesquik)
1204	Flavored milk, reduced fat	11512010	Hot chocolate / Cocoa, ready to drink
1208	Flavored milk, nonfat	11512020	Hot chocolate / Cocoa, ready to drink, made with nonfat milk
1204	Flavored milk, reduced fat	11512100	Hot chocolate / Cocoa, ready to drink, with whipped cream
1208	Flavored milk, nonfat	11512110	Hot chocolate / Cocoa, ready to drink, made with nonfat milk and whipped cream
1204	Flavored milk, reduced fat	11513000	Chocolate milk, made from dry mix, NS as to type of milk
1202	Flavored milk, whole	11513100	Chocolate milk, made from dry mix with whole milk
1204	Flavored milk, reduced fat	11513150	Chocolate milk, made from dry mix with reduced fat milk
1206	Flavored milk, lowfat	11513200	Chocolate milk, made from dry mix with low fat milk
1208	Flavored milk, nonfat	11513300	Chocolate milk, made from dry mix with fat free milk

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WWEIA Category number	WWEIA Category description	Food code	Main food description
1204	Flavored milk, reduced fat	11513350	Chocolate milk, made from reduced sugar mix, NS as to type of milk
1202	Flavored milk, whole	11513355	Chocolate milk, made from reduced sugar mix with whole milk
1204	Flavored milk, reduced fat	11513360	Chocolate milk, made from reduced sugar mix with reduced fat milk
1206	Flavored milk, lowfat	11513365	Chocolate milk, made from reduced sugar mix with low fat milk
1208	Flavored milk, nonfat	11513370	Chocolate milk, made from reduced sugar mix with fat free milk
1204	Flavored milk, reduced fat	11513380	Chocolate milk, made from dry mix, NS as to type of milk (Nesquik)
1202	Flavored milk, whole	11513381	Chocolate milk, made from dry mix with whole milk (Nesquik)
1204	Flavored milk, reduced fat	11513382	Chocolate milk, made from dry mix with reduced fat milk (Nesquik)
1206	Flavored milk, lowfat	11513383	Chocolate milk, made from dry mix with low fat milk (Nesquik)
1208	Flavored milk, nonfat	11513384	Chocolate milk, made from dry mix with fat free milk (Nesquik)
1204	Flavored milk, reduced fat	11513390	Chocolate milk, made from no sugar added dry mix, NS as to type of milk (Nesquik)
1202	Flavored milk, whole	11513391	Chocolate milk, made from no sugar added dry mix with whole milk (Nesquik)
1204	Flavored milk, reduced fat	11513392	Chocolate milk, made from no sugar added dry mix with reduced fat milk (Nesquik)
1206	Flavored milk, lowfat	11513393	Chocolate milk, made from no sugar added dry mix with low fat milk (Nesquik)
1208	Flavored milk, nonfat	11513394	Chocolate milk, made from no sugar added dry mix with fat free milk (Nesquik)
1204	Flavored milk, reduced fat	11513400	Chocolate milk, made from syrup, NS as to type of milk
1202	Flavored milk, whole	11513500	Chocolate milk, made from syrup with whole milk
1204	Flavored milk, reduced fat	11513550	Chocolate milk, made from syrup with reduced fat milk
1206	Flavored milk, lowfat	11513600	Chocolate milk, made from syrup with low fat milk
1208	Flavored milk, nonfat	11513700	Chocolate milk, made from syrup with fat free milk
1204	Flavored milk, reduced fat	11513800	Chocolate milk, made from light syrup, NS as to type of milk
1202	Flavored milk, whole	11513801	Chocolate milk, made from light syrup with whole milk
1204	Flavored milk, reduced fat	11513802	Chocolate milk, made from light syrup with reduced fat milk
1206	Flavored milk, lowfat	11513803	Chocolate milk, made from light syrup with low fat milk
1208	Flavored milk, nonfat	11513804	Chocolate milk, made from light syrup with fat free milk
1204	Flavored milk, reduced fat	11513850	Chocolate milk, made from sugar free syrup, NS as to type of milk
1202	Flavored milk, whole	11513851	Chocolate milk, made from sugar free syrup with whole milk
1204	Flavored milk, reduced fat	11513852	Chocolate milk, made from sugar free syrup with reduced fat milk
1206	Flavored milk, lowfat	11513853	Chocolate milk, made from sugar free syrup with low fat milk
1208	Flavored milk, nonfat	11513854	Chocolate milk, made from sugar free syrup with fat free milk
1208	Flavored milk, nonfat	11514100	Hot chocolate / Cocoa, made with dry mix and water
1202	Flavored milk, whole	11514110	Hot chocolate / Cocoa, made with dry mix and whole milk
1204	Flavored milk, reduced fat	11514120	Hot chocolate / Cocoa, made with dry mix and reduced fat milk
1206	Flavored milk, lowfat	11514130	Hot chocolate / Cocoa, made with dry mix and low fat milk
1208	Flavored milk, nonfat	11514140	Hot chocolate / Cocoa, made with dry mix and fat free milk
1208	Flavored milk, nonfat	11514310	Hot chocolate / Cocoa, made with no sugar added dry mix and water
1202	Flavored milk, whole	11514320	Hot chocolate / Cocoa, made with no sugar added dry mix and whole milk
1204	Flavored milk, reduced fat	11514330	Hot chocolate / Cocoa, made with no sugar added dry mix and reduced fat milk
1206	Flavored milk, lowfat	11514340	Hot chocolate / Cocoa, made with no sugar added dry mix and low fat milk
1208	Flavored milk, nonfat	11514350	Hot chocolate / Cocoa, made with no sugar added dry mix and fat free milk

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WWEIA Category number	WWEIA Category description	Food code	Main food description
1204	Flavored milk, reduced fat	11519040	Strawberry milk, NFS
1202	Flavored milk, whole	11519050	Strawberry milk, whole
1204	Flavored milk, reduced fat	11519105	Strawberry milk, reduced fat
1206	Flavored milk, lowfat	11519200	Strawberry milk, low fat
1208	Flavored milk, nonfat	11519205	Strawberry milk, fat free
1206	Flavored milk, lowfat	11519210	Strawberry milk, reduced sugar
1204	Flavored milk, reduced fat	11526000	Milk, malted
1402	Milk shakes and other dairy drinks	11531000	Eggnog
1402	Milk shakes and other dairy drinks	11541110	Milk shake, home recipe, chocolate
1402	Milk shakes and other dairy drinks	11541120	Milk shake, home recipe, flavors other than chocolate
1402	Milk shakes and other dairy drinks	11541130	Milk shake, home recipe, chocolate, light
1402	Milk shakes and other dairy drinks	11541135	Milk shake, home recipe, flavors other than chocolate, light
1402	Milk shakes and other dairy drinks	11541400	Milk shake with malt
1402	Milk shakes and other dairy drinks	11542100	Milk shake, fast food, chocolate
1402	Milk shakes and other dairy drinks	11542200	Milk shake, fast food, flavors other than chocolate
1402	Milk shakes and other dairy drinks	11543000	Milk shake, bottled, chocolate
1402	Milk shakes and other dairy drinks	11543010	Milk shake, bottled, flavors other than chocolate
1402	Milk shakes and other dairy drinks	11560000	Chocolate milk drink
9999	Not included in a food category	11810000	Milk, dry, not reconstituted, NS as to fat content
9999	Not included in a food category	11811000	Milk, dry, not reconstituted, whole
9999	Not included in a food category	11812000	Milk, dry, not reconstituted, low fat (1%)
9999	Not included in a food category	11813000	Milk, dry, not reconstituted, fat free (skim)
1402	Milk shakes and other dairy drinks	13120800	Ice cream soda, flavors other than chocolate
1402	Milk shakes and other dairy drinks	13120810	Ice cream soda, chocolate
1820	Yogurt, regular	42401100	Yogurt, coconut milk
5704	Candy not containing chocolate	44201000	Carob chips
5402	Cereal bars	53710400	Cereal or granola bar (General Mills Fiber One Chewy Bar)
5402	Cereal bars	53710500	Cereal or granola bar (Kellogg's Nutri-Grain Cereal Bar)
5402	Cereal bars	53710502	Cereal or granola bar (Kellogg's Nutri-Grain Yogurt Bar)
5402	Cereal bars	53710504	Cereal or granola bar (Kellogg's Nutri-Grain Fruit and Nut Bar)
5402	Cereal bars	53710600	Milk 'n Cereal bar
5402	Cereal bars	53710700	Cereal or granola bar (Kellogg's Special K bar)
5404	Nutrition bars	53710800	Cereal or granola bar (Kashi Chewy)
5404	Nutrition bars	53710802	Cereal or granola bar (Kashi Crunchy)
5402	Cereal bars	53710810	Cereal or granola bar (KIND Fruit and Nut Bar)
5402	Cereal bars	53710900	Cereal or granola bar (General Mills Nature Valley Chewy Trail Mix)
5402	Cereal bars	53710902	Cereal or granola bar, with yogurt coating (General Mills Nature Valley Chewy Granola Bar)
5402	Cereal bars	53710904	Cereal or granola bar (General Mills Nature Valley Sweet and Salty Granola Bar)
5402	Cereal bars	53710906	Cereal or granola bar (General Mills Nature Valley Crunchy Granola Bar)

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WWEIA Category number	WWEIA Category description	Food code	Main food description
5402	Cereal bars	53711000	Cereal or granola bar (Quaker Chewy Granola Bar)
5402	Cereal bars	53711002	Cereal or granola bar (Quaker Chewy 90 Calorie Granola Bar)
5402	Cereal bars	53711004	Cereal or granola bar (Quaker Chewy 25% Less Sugar Granola Bar)
5402	Cereal bars	53711006	Cereal or granola bar (Quaker Chewy Dipps Granola Bar)
5402	Cereal bars	53711100	Cereal or granola bar (Quaker Granola Bites)
5402	Cereal bars	53712000	Snack bar, oatmeal
5402	Cereal bars	53712100	Cereal or Granola bar, NFS
5402	Cereal bars	53712200	Cereal or granola bar, lowfat, NFS
5402	Cereal bars	53712210	Cereal or granola bar, nonfat
5402	Cereal bars	53713000	Cereal or granola bar, reduced sugar, NFS
5402	Cereal bars	53713010	Cereal or granola bar, fruit and nut
5402	Cereal bars	53713100	Cereal or granola bar, peanuts , oats, sugar, wheat germ
5402	Cereal bars	53714200	Cereal or granola bar, chocolate coated, NFS
5402	Cereal bars	53714210	Cereal or granola bar, with coconut, chocolate coated
5402	Cereal bars	53714220	Cereal or granola bar with nuts, chocolate coated
5402	Cereal bars	53714230	Cereal or granola bar, oats, nuts, coated with non-chocolate coating
5402	Cereal bars	53714250	Cereal or granola bar, coated with non-chocolate coating
5402	Cereal bars	53714300	Cereal or granola bar, high fiber, coated with non-chocolate yogurt coating
5402	Cereal bars	53714400	Cereal or granola bar, with rice cereal
5402	Cereal bars	53714500	Breakfast bar, NFS
5402	Cereal bars	53714510	Breakfast bar, date, with yogurt coating
5402	Cereal bars	53714520	Breakfast bar, cereal crust with fruit filling, lowfat
5404	Nutrition bars	53720100	Nutrition bar (Balance Original Bar)
5404	Nutrition bars	53720200	Nutrition bar (Clif Bar)
5404	Nutrition bars	53720210	Nutrition bar (Clif Kids Organic Zbar)
5404	Nutrition bars	53720300	Nutrition bar (PowerBar)
5404	Nutrition bars	53720400	Nutrition bar (Slim Fast Original Meal Bar)
5404	Nutrition bars	53720500	Nutrition bar (Snickers Marathon Protein Bar)
5404	Nutrition bars	53720600	Nutrition bar (South Beach Living Meal Bar)
5404	Nutrition bars	53720610	Nutrition bar (South Beach Living High Protein Bar)
5404	Nutrition bars	53720700	Nutrition bar (Tiger's Milk)
5404	Nutrition bars	53720800	Nutrition bar (Zone Perfect Classic Crunch)
5404	Nutrition bars	53729000	Nutrition bar or meal replacement bar, NFS
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57000100	Cereal, oat, NFS
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57100100	Cereal, ready-to-eat, NFS
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57101000	Cereal (Kellogg's All-Bran)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57103000	Cereal (Post Alpha-Bits)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57103100	Cereal, O's, flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57104000	Cereal (Kellogg's Apple Jacks)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57106050	Cereal (Post Great Grains Banana Nut Crunch)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57106060	Cereal (General Mills Cheerios Banana Nut)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57106260	Cereal (General Mills Cheerios Berry Burst)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57117000	Cereal (Quaker Cap'n Crunch)

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WWEIA Category number	WWEIA Category description	Food code	Main food description
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57117500	Cereal (Quaker Christmas Crunch)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57119000	Cereal, crunch
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57120000	Cereal (Quaker Cap'n Crunch's Peanut Butter Crunch)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57123000	Cereal, O's, plain
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124030	Cereal (General Mills Chex Chocolate)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124050	Cereal (General Mills Chex Cinnamon)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124100	Cereal (General Mills Cheerios Chocolate)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124200	Cereal, chocolate puffs
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124300	Cereal (General Mills Lucky Charms Chocolate)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57125000	Cereal, cinnamon toast
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57125010	Cereal (General Mills 25% Less Sugar Cinnamon Toast Crunch)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57125900	Cereal (General Mills Honey Nut Clusters)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57126000	Cereal, chocolate crispy
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57127000	Cereal (Post Cocoa Pebbles)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57128000	Cereal (General Mills Cocoa Puffs)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57130000	Cereal (General Mills Cookie Crisp)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57132000	Cereal, corn squares
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57134000	Cereal, corn flakes, plain
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57135000	Cereal (Kellogg's Corn Flakes)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57137000	Cereal, corn puffs
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57139000	Cereal (General Mills Count Chocula)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57143000	Cereal (Kellogg's Cracklin' Oat Bran)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57143500	Cereal (Post Great Grains, Cranberry Almond Crunch)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57148000	Cereal (Kellogg's Crispix)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57151000	Cereal, rice crispy, plain
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57206700	Cereal (General Mills Fiber One)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57206710	Cereal (General Mills Fiber One Honey Clusters)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57206715	Cereal (General Mills Fiber One Raisin Bran Clusters)

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4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57207000	Cereal, bran flakes, plain
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57208000	Cereal (Kellogg's All-Bran Complete Wheat Flakes)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57209000	Cereal (Post Bran Flakes)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57211000	Cereal (General Mills Frankenberry)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57213000	Cereal (Kellogg's Froot Loops)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57213010	Cereal (Kellogg's Froot Loops Marshmallow)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57213850	Cereal (General Mills Cheerios Frosted)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57214000	Cereal, shredded wheat, flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57216000	Cereal, rice crispy, flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57221700	Cereal, fruit rings
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57221810	Cereal (General Mills Cheerios Fruity)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57223000	Cereal, fruit crispy
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57224000	Cereal (General Mills Golden Grahams)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57227000	Cereal, granola
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57228000	Granola, homemade
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57229000	Cereal (Kellogg's Low Fat Granola)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57230000	Cereal (Post Grape-Nuts)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57231200	Cereal (Post Great Grains Raisins, Dates, and Pecans)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57237100	Cereal, oat bunches
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57237200	Cereal (Post Honey Bunches of Oats with Vanilla Bunches)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57237300	Cereal (Post Honey Bunches of Oats with Almonds)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57238000	Cereal (Post Honeycomb)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57240100	Cereal, corn squares, flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57241000	Cereal, O's, honey nut
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57241200	Cereal (Post Shredded Wheat Honey Nut)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57243000	Cereal (Kellogg's Honey Smacks)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301500	Cereal (Kashi 7 Whole Grain Puffs)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301505	Cereal (Kashi Autumn Wheat)

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4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301510	Cereal (Kashi GOLEAN)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57301511	Cereal (Kashi GOLEAN Crunch)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57301512	Cereal (Kashi GOLEAN Crunch Honey Almond Flax)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301530	Cereal (Kashi Heart to Heart Honey Toasted Oat)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301600	Cereal, multigrain
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57303100	Cereal (General Mills Kix)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57303105	Cereal (General Mills Honey Kix)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57303200	Cereal (Kellogg's Krave)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57304100	Cereal, oat squares
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305100	Cereal (General Mills Lucky Charms)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305150	Cereal, frosted oats with marshmallows
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57305160	Cereal (Malt-O-Meal Blueberry Muffin Tops)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305165	Cereal (Malt-O-Meal Cinnamon Toasters)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305170	Cereal (Malt-O-Meal Coco-Roos)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305174	Cereal (Malt-O-Meal Colossal Crunch)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305175	Cereal (Malt-O-Meal Cocoa Dyno-Bites)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305180	Cereal (Malt-O-Meal Corn Bursts)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305210	Cereal (Malt-O-Meal Frosted Flakes)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305300	Cereal (Malt-O-Meal Fruity Dyno-Bites)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305400	Cereal (Malt-O-Meal Honey Graham Squares)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305500	Cereal (Malt-O-Meal Honey Nut Toasty O's)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305600	Cereal (Malt-O-Meal Marshmallow Mateys)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57306500	Cereal (Malt-O-Meal Golden Puffs)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57306700	Cereal (Malt-O-Meal Toasted Oat Cereal)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57306800	Cereal (Malt-O-Meal Tootie Fruities)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57308190	Cereal, muesli
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57308400	Cereal, O's, multigrain
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57309100	Cereal (Nature Valley Granola)

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4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316380	Cereal (General Mills Cheerios Oat Cluster Crunch)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316385	Cereal (General Mills Cheerios Protein)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316450	Cereal (General Mills Oatmeal Crisp with Almonds)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316710	Cereal (Quaker Honey Graham Oh's)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57320500	Cereal (Quaker Granola with Oats, Honey, and Raisins)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57321900	Cereal (Nature's Path Organic Flax Plus)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57326000	Cereal (Barbara's Puffins)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57327450	Cereal (Quaker Toasted Oat Bran)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57327500	Cereal (Quaker Oatmeal Squares)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57329000	Cereal, bran flakes, flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57330000	Cereal (Kellogg's Raisin Bran)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57330010	Cereal (Kellogg's Raisin Bran Crunch)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57331000	Cereal (Post Raisin Bran)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57332100	Cereal (General Mills Raisin Nut Bran)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57335550	Cereal (General Mills Reese's Puffs)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57336000	Cereal, rice squares
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57337000	Cereal, rice flakes
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57339000	Cereal (Kellogg's Rice Krispies)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57339500	Cereal (Kellogg's Rice Krispies Treats Cereal)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57340000	Cereal, puffed rice
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57341200	Cereal (Kellogg's Smart Start Strong)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57341300	Cereal (Kellogg's Smorz)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57344000	Cereal, K's, plain
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344001	Cereal (Kellogg's Special K Blueberry)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344005	Cereal (Kellogg's Special K Chocolatey Delight)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344010	Cereal, K's, flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344015	Cereal (Kellogg's Special K Fruit & Yogurt)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344020	Cereal (Kellogg's Special K Vanilla Almond)

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4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344025	Cereal (Kellogg's Special K Cinnamon Pecan)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57347000	Cereal, flavored puffs
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57348000	Cereal, corn flakes, flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57349000	Cereal (Kellogg's Frosted Flakes)
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57355000	Cereal (Post Golden Crisp)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57401100	Cereal, O's, NFS
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57407100	Cereal (General Mills Trix)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57408100	Cereal (Uncle Sam)
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57411000	Cereal, wheat squares
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57416000	Cereal, plain puffs
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57416010	Cereal, puffed wheat, sweetened
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57417000	Cereal, shredded wheat, plain
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57418000	Cereal, wheat flakes
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420100	Cereal, other, NFS
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57420110	Cereal, other, plain
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420120	Cereal, other, fruit flavored
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420130	Cereal, other, chocolate
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420140	Cereal, other, peanut butter
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420150	Cereal, other, honey
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57420160	Cereal, reduced sugar
9999	Not included in a food category	57602500	Cereal, oat bran, ready-to-eat
5704	Candy not containing chocolate	91700010	Candy, NFS
5702	Candy containing chocolate	91700500	M&M's Almond Chocolate Candies
5702	Candy containing chocolate	91701010	Almonds, chocolate covered candy
5704	Candy not containing chocolate	91701020	Almonds, sugar-coated
5704	Candy not containing chocolate	91701030	Almonds, yogurt-covered
5704	Candy not containing chocolate	91702010	Butterscotch morsels
5704	Candy not containing chocolate	91703010	Caramel, chocolate-flavored roll
5704	Candy not containing chocolate	91703020	Caramel, flavor other than chocolate
5704	Candy not containing chocolate	91703030	Caramel, with nuts
5702	Candy containing chocolate	91703040	Caramel candy, chocolate covered
5702	Candy containing chocolate	91703050	Caramel with nuts and cereal, chocolate covered
5702	Candy containing chocolate	91703060	Caramel with nuts, chocolate covered
5702	Candy containing chocolate	91703070	Rolo
5704	Candy not containing chocolate	91703080	Caramel, all flavors, sugar free
5702	Candy containing chocolate	91703150	Toblerone, milk chocolate with honey and almond nougat

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Website: www.summit-life-science.com

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5702	Candy containing chocolate	91703200	TWIX Caramel Cookie Bars
5702	Candy containing chocolate	91703250	TWIX Chocolate Fudge Cookie Bars
5702	Candy containing chocolate	91703300	TWIX Peanut Butter Cookie Bars
5702	Candy containing chocolate	91703400	Whatchamacallit
5704	Candy not containing chocolate	91703500	Nuts, carob-coated
5702	Candy containing chocolate	91703600	Espresso coffee beans, chocolate-covered
5702	Candy containing chocolate	91705005	Chocolate candy, other, NFS
5702	Candy containing chocolate	91705010	Chocolate candy
5702	Candy containing chocolate	91705012	Chocolate candy with nuts, other, NFS
5702	Candy containing chocolate	91705015	Chocolate candy with nuts
5702	Candy containing chocolate	91705020	Chocolate candy with cereal
5702	Candy containing chocolate	91705030	Kit Kat
5702	Candy containing chocolate	91705040	Chocolate, milk, with nuts, not almond or peanuts
5702	Candy containing chocolate	91705050	Milk chocolate candy, with fruit and nuts
5702	Candy containing chocolate	91705060	Milk chocolate candy, with almonds
5702	Candy containing chocolate	91705070	Chocolate, milk, with peanuts
5702	Candy containing chocolate	91705080	Chocolate candy, cookie filled
5702	Candy containing chocolate	91705090	Chocolate candy with fondant and caramel
5702	Candy containing chocolate	91705200	Chocolate chips
5704	Candy not containing chocolate	91705250	Candy, sprinkles
5702	Candy containing chocolate	91705290	Dark chocolate candy, other, NFS
5702	Candy containing chocolate	91705300	Dark chocolate candy
5702	Candy containing chocolate	91705310	Chocolate, sweet or dark, with almonds
5702	Candy containing chocolate	91705312	Dark chocolate candy with nuts, other, NFS
5702	Candy containing chocolate	91705315	Dark chocolate candy with nuts
5704	Candy not containing chocolate	91705400	White chocolate candy
5704	Candy not containing chocolate	91705410	Chocolate, white, with almonds
5704	Candy not containing chocolate	91705420	Chocolate, white, with cereal
5704	Candy not containing chocolate	91705430	Kit Kat White
5702	Candy containing chocolate	91705440	Chocolate candy, fudge
5702	Candy containing chocolate	91705450	Chocolate candy, caramel filled
5702	Candy containing chocolate	91705460	Chocolate candy, caramel filled with nuts
5702	Candy containing chocolate	91705470	Chocolate candy, coconut filled
5702	Candy containing chocolate	91705480	Chocolate candy, cream filled
5702	Candy containing chocolate	91705500	Mexican chocolate, tablet
5702	Candy containing chocolate	91705510	Chocolate candy, nougat filled
5702	Candy containing chocolate	91705520	Chocolate candy, nougat filled with nuts
5702	Candy containing chocolate	91705530	Chocolate candy, peanut butter filled
5702	Candy containing chocolate	91705550	Chocolate candy with dried fruit
5702	Candy containing chocolate	91706000	Coconut candy, chocolate covered
5702	Candy containing chocolate	91706010	Chocolate candy, sugar free
5704	Candy not containing chocolate	91706020	Candy, non chocolate, other, NFS
5704	Candy not containing chocolate	91706100	Coconut candy, no chocolate covering
5704	Candy not containing chocolate	91706400	Coconut candy, Puerto Rican style
5704	Candy not containing chocolate	91707000	Fondant
5702	Candy containing chocolate	91707010	Fondant, chocolate covered
5704	Candy not containing chocolate	91708000	Fruit peel, candied
5704	Candy not containing chocolate	91708010	Date candy
5704	Candy not containing chocolate	91708020	Soft fruit confections
5704	Candy not containing chocolate	91708030	Fruit leather and fruit snacks candy
5704	Candy not containing chocolate	91708040	Fun Fruits Creme Supremes
5704	Candy not containing chocolate	91708070	Tamarind candy
5704	Candy not containing chocolate	91708100	Fruit snacks candy, with high vitamin C
5704	Candy not containing chocolate	91708150	Yogurt covered fruit snacks candy, with added vitamin C
5704	Candy not containing chocolate	91708160	Yogurt covered fruit snacks candy rolls, with high vitamin C
5702	Candy containing chocolate	91709000	Gumdrops, chocolate covered

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Website: www.summit-life-science.com

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5702	Candy containing chocolate	91713010	Fudge, chocolate, chocolate-coated
5702	Candy containing chocolate	91713020	Fudge, chocolate, chocolate-coated, with nuts
5702	Candy containing chocolate	91713030	Fudge, chocolate
5702	Candy containing chocolate	91713040	Fudge, chocolate, with nuts
5704	Candy not containing chocolate	91713050	Fudge, peanut butter
5704	Candy not containing chocolate	91713060	Fudge, peanut butter, with nuts
5704	Candy not containing chocolate	91713070	Fudge, vanilla
5704	Candy not containing chocolate	91713080	Fudge, vanilla, with nuts
5704	Candy not containing chocolate	91713090	Fudge, divinity
5704	Candy not containing chocolate	91713100	Fudge, brown sugar, penuche
5702	Candy containing chocolate	91715000	Fudge, caramel and nut, chocolate-coated candy
5702	Candy containing chocolate	91715100	SNICKERS Bar
5702	Candy containing chocolate	91715200	Baby Ruth
5702	Candy containing chocolate	91715300	100 GRAND Bar
5704	Candy not containing chocolate	91716010	Halvah, plain
5702	Candy containing chocolate	91716110	Halvah, chocolate covered
5704	Candy not containing chocolate	91718000	Honey-combed hard candy with peanut butter
5702	Candy containing chocolate	91718050	Honey-combed hard candy with peanut butter, chocolate covered
5702	Candy containing chocolate	91718100	Butterfinger
5702	Candy containing chocolate	91718110	Butterfinger Crisp
5702	Candy containing chocolate	91718200	Chocolate-flavored sprinkles
5704	Candy not containing chocolate	91718300	Ladoo, round ball
5704	Candy not containing chocolate	91721000	Candy, licorice
5704	Candy not containing chocolate	91723000	Candy, marshmallow
5702	Candy containing chocolate	91723010	Marshmallow, chocolate covered
5704	Candy not containing chocolate	91723020	Marshmallow, candy-coated
5704	Candy not containing chocolate	91723030	Candy, caramel
5704	Candy not containing chocolate	91726000	Nougat, plain
5702	Candy containing chocolate	91726110	Nougat, with caramel, chocolate covered
5702	Candy containing chocolate	91726130	MILKY WAY Bar
5702	Candy containing chocolate	91726140	MILKY WAY MIDNIGHT Bar
5702	Candy containing chocolate	91726150	MARS Almond Bar
5702	Candy containing chocolate	91726410	Nougat, chocolate covered
5702	Candy containing chocolate	91726420	3 MUSKETEERS Bar
5702	Candy containing chocolate	91726425	3 Musketeers Truffle Crisp Bar
5702	Candy containing chocolate	91727010	Nuts, chocolate covered, not almonds or peanuts
5704	Candy not containing chocolate	91728000	Candy, nougat with nuts
5704	Candy not containing chocolate	91728500	Sugared pecans, sugar and egg white coating
5702	Candy containing chocolate	91731000	Peanuts, chocolate covered candy
5702	Candy containing chocolate	91731010	M&M's Peanut Chocolate Candies
5702	Candy containing chocolate	91731060	M&M's Peanut Butter Chocolate Candies
5704	Candy not containing chocolate	91731100	Peanuts, sugar-coated
5704	Candy not containing chocolate	91731150	Peanuts, yogurt covered
5704	Candy not containing chocolate	91732000	Peanut bar
5704	Candy not containing chocolate	91732100	Planters Peanut Bar
5704	Candy not containing chocolate	91733000	Candy, peanut brittle
5702	Candy containing chocolate	91733200	Peanut Bar, chocolate covered candy
5702	Candy containing chocolate	91734000	Peanut butter, chocolate covered
5702	Candy containing chocolate	91734100	Reese's Peanut Butter Cup
5704	Candy not containing chocolate	91734200	Reese's Pieces
5702	Candy containing chocolate	91734300	Reese's Sticks
5702	Candy containing chocolate	91734400	Reese's Fast Break
5702	Candy containing chocolate	91734450	Reese's Crispy Crunchy Bar
5704	Candy not containing chocolate	91734500	Peanut butter morsels
5704	Candy not containing chocolate	91735000	Pralines
5704	Candy not containing chocolate	91736000	Pineapple candy, Puerto Rican style

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WWEIA Category number	WWEIA Category description	Food code	Main food description
5702	Candy containing chocolate	91739010	Raisins, chocolate covered
5704	Candy not containing chocolate	91739600	Raisins, yogurt covered
5704	Candy not containing chocolate	91742010	Sesame Crunch, Sahadi
5704	Candy not containing chocolate	91745000	Candy, mint
5704	Candy not containing chocolate	91745010	Candy, gummy
5704	Candy not containing chocolate	91745020	Hard candy
5704	Candy not containing chocolate	91745025	Candy, hard
5704	Candy not containing chocolate	91745030	Candy, lollipop
5704	Candy not containing chocolate	91745035	Cough drops
5704	Candy not containing chocolate	91745040	Butterscotch hard candy
5704	Candy not containing chocolate	91745050	Candy, cotton
5704	Candy not containing chocolate	91745100	Skittles
5704	Candy not containing chocolate	91745110	Candy, fruit flavored pieces
5702	Candy containing chocolate	91746010	Sugar-coated chocolate discs
5702	Candy containing chocolate	91746100	Chocolate candy, candy shell
5702	Candy containing chocolate	91746110	Chocolate candy, candy shell with nuts
5702	Candy containing chocolate	91746120	Sixlets
5702	Candy containing chocolate	91746150	Easter egg, candy coated chocolate
5702	Candy containing chocolate	91746200	M&M's Pretzel Chocolate Candies
5704	Candy not containing chocolate	91746300	Candy, fruit snacks
5704	Candy not containing chocolate	91746350	Candy, fruit leather
5704	Candy not containing chocolate	91750000	Candy, taffy
5704	Candy not containing chocolate	91760000	Toffee, plain
5702	Candy containing chocolate	91760100	Toffee, chocolate covered
5702	Candy containing chocolate	91760200	Toffee, chocolate-coated, with nuts
5702	Candy containing chocolate	91760500	Truffles
5704	Candy not containing chocolate	91760700	Wax candy, liquid filled
5704	Candy not containing chocolate	91770000	Dietetic or low calorie candy, NFS
5704	Candy not containing chocolate	91770010	Dietetic or low calorie gumdrops
5704	Candy not containing chocolate	91770020	Dietetic or low calorie hard candy
5702	Candy containing chocolate	91770030	Dietetic or low calorie candy, chocolate covered
5704	Candy not containing chocolate	91770050	Dietetic or low calorie mints
5704	Candy not containing chocolate	91770060	Candy, non chocolate, sugar free
5704	Candy not containing chocolate	91800100	Chewing gum, NFS
5704	Candy not containing chocolate	91801000	Chewing gum
5704	Candy not containing chocolate	91802000	Chewing gum, sugar free
7302	Coffee	92100000	Coffee, NS as to type
7302	Coffee	92100500	Coffee, NS as to brewed or instant
7302	Coffee	92101000	Coffee, brewed
7302	Coffee	92101500	Coffee, brewed, blend of regular and decaffeinated
7302	Coffee	92101600	Coffee, Turkish
7302	Coffee	92101610	Coffee, espresso
7302	Coffee	92101630	Coffee, espresso, decaffeinated
7302	Coffee	92101700	Coffee, brewed, flavored
7302	Coffee	92101800	Coffee, Cuban
7302	Coffee	92101810	Coffee, macchiato
7302	Coffee	92101820	Coffee, macchiato, sweetened
7302	Coffee	92101850	Coffee, cafe con leche
7302	Coffee	92101851	Coffee, cafe con leche, decaffeinated
7302	Coffee	92101900	Coffee, Latte
7302	Coffee	92101901	Coffee, Latte, nonfat
7302	Coffee	92101903	Coffee, Latte, with non-dairy milk
7302	Coffee	92101904	Coffee, Latte, flavored
7302	Coffee	92101905	Coffee, Latte, nonfat, flavored
7302	Coffee	92101906	Coffee, Latte, with non-dairy milk, flavored
7302	Coffee	92101910	Coffee, Latte, decaffeinated

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7302	Coffee	92101911	Coffee, Latte, decaffeinated, nonfat
7302	Coffee	92101913	Coffee, Latte, decaffeinated, with non-dairy milk
7302	Coffee	92101917	Coffee, Latte, decaffeinated, flavored
7302	Coffee	92101918	Coffee, Latte, decaffeinated, nonfat, flavored
7302	Coffee	92101919	Coffee, Latte, decaffeinated, with non-dairy milk, flavored
7302	Coffee	92101920	Frozen coffee drink
7302	Coffee	92101921	Frozen coffee drink, nonfat
7302	Coffee	92101923	Frozen coffee drink, with non-dairy milk
7302	Coffee	92101925	Frozen coffee drink, with whipped cream
7302	Coffee	92101926	Frozen coffee drink, nonfat, with whipped cream
7302	Coffee	92101928	Frozen coffee drink, with non-dairy milk and whipped cream
7302	Coffee	92101930	Frozen coffee drink, decaffeinated
7302	Coffee	92101931	Frozen coffee drink, decaffeinated, nonfat
7302	Coffee	92101933	Frozen coffee drink, decaffeinated, with non-dairy milk
7302	Coffee	92101935	Frozen coffee drink, decaffeinated, with whipped cream
7302	Coffee	92101936	Frozen coffee drink, decaffeinated, nonfat, with whipped cream
7302	Coffee	92101938	Frozen coffee drink, decaffeinated, with non-dairy milk and whipped cream
7302	Coffee	92101950	Coffee, Cafe Mocha
7302	Coffee	92101955	Coffee, Cafe Mocha, nonfat
7302	Coffee	92101960	Coffee, Cafe Mocha, with non-dairy milk
7302	Coffee	92101965	Coffee, Cafe Mocha, decaffeinated
7302	Coffee	92101970	Coffee, Cafe Mocha, decaffeinated, nonfat
7302	Coffee	92101975	Coffee, Cafe Mocha, decaffeinated, with non-dairy milk
7302	Coffee	92102000	Frozen mocha coffee drink
7302	Coffee	92102010	Frozen mocha coffee drink, nonfat
7302	Coffee	92102020	Frozen mocha coffee drink, with non-dairy milk
7302	Coffee	92102030	Frozen mocha coffee drink, with whipped cream
7302	Coffee	92102040	Frozen mocha coffee drink, nonfat, with whipped cream
7302	Coffee	92102050	Frozen mocha coffee drink, with non-dairy milk and whipped cream
7302	Coffee	92102060	Frozen mocha coffee drink, decaffeinated
7302	Coffee	92102070	Frozen mocha coffee drink, decaffeinated, nonfat
7302	Coffee	92102080	Frozen mocha coffee drink, decaffeinated, with non-dairy milk
7302	Coffee	92102090	Frozen mocha coffee drink, decaffeinated, with whipped cream
7302	Coffee	92102100	Frozen mocha coffee drink, decaffeinated, nonfat, with whipped cream
7302	Coffee	92102110	Frozen mocha coffee drink, decaffeinated, with non-dairy milk and whipped cream
7302	Coffee	92102400	Iced Coffee, brewed
7302	Coffee	92102401	Iced Coffee, brewed, decaffeinated
7302	Coffee	92102450	Iced Coffee, pre-lightened and pre-sweetened
7302	Coffee	92102500	Coffee, Iced Latte
7302	Coffee	92102501	Coffee, Iced Latte, nonfat
7302	Coffee	92102502	Coffee, Iced Latte, with non-dairy milk
7302	Coffee	92102503	Coffee, Iced Latte, flavored
7302	Coffee	92102504	Coffee, Iced Latte, nonfat, flavored
7302	Coffee	92102505	Coffee, Iced Latte, with non-dairy milk, flavored
7302	Coffee	92102510	Coffee, Iced Latte, decaffeinated
7302	Coffee	92102511	Coffee, Iced Latte, decaffeinated, nonfat
7302	Coffee	92102512	Coffee, Iced Latte, decaffeinated, with non-dairy milk
7302	Coffee	92102513	Coffee, Iced Latte, decaffeinated, flavored
7302	Coffee	92102514	Coffee, Iced Latte, decaffeinated, nonfat, flavored
7302	Coffee	92102515	Coffee, Iced Latte, decaffeinated, with non-dairy milk, flavored
7302	Coffee	92102600	Coffee, Iced Cafe Mocha
7302	Coffee	92102601	Coffee, Iced Cafe Mocha, nonfat

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WWEIA Category number	WWEIA Category description	Food code	Main food description
7302	Coffee	92102602	Coffee, Iced Cafe Mocha, with non-dairy milk
7302	Coffee	92102610	Coffee, Iced Cafe Mocha, decaffeinated
7302	Coffee	92102611	Coffee, Iced Cafe Mocha, decaffeinated, nonfat
7302	Coffee	92102612	Coffee, Iced Cafe Mocha, decaffeinated, with non-dairy milk
7302	Coffee	92103000	Coffee, instant, reconstituted
7302	Coffee	92104000	Coffee, instant, 50% less caffeine, reconstituted
7302	Coffee	92111000	Coffee, NS as to brewed or instant, decaffeinated
7302	Coffee	92111010	Coffee, brewed, decaffeinated
7302	Coffee	92114000	Coffee, instant, decaffeinated, reconstituted
7302	Coffee	92121000	Coffee, instant, pre-lightened and pre-sweetened with sugar, reconstituted
7302	Coffee	92121001	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, reconsitituted
7302	Coffee	92121010	Coffee, instant, pre-sweetened with sugar, reconstituted
7302	Coffee	92121020	Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, reconstituted
7302	Coffee	92121030	Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted
7302	Coffee	92121040	Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted
7302	Coffee	92121041	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted
7302	Coffee	92121050	Coffee, mocha, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted
7302	Coffee	92130000	Coffee, pre-lightened and pre-sweetened with sugar
7302	Coffee	92130001	Coffee, decaffeinated, pre-lightened and pre-sweetened with sugar
7302	Coffee	92130005	Coffee, pre-lightened and pre-sweetened with low calorie sweetener
7302	Coffee	92130006	Coffee, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener
7302	Coffee	92130010	Coffee, pre-lightened
7302	Coffee	92130011	Coffee, decaffeinated, pre-lightened
7302	Coffee	92130020	Coffee, pre-sweetened with sugar
7302	Coffee	92130021	Coffee, decaffeinated, pre-sweetened with sugar
7302	Coffee	92130030	Coffee, pre-sweetened with low calorie sweetener
7302	Coffee	92130031	Coffee, decaffeinated, pre-sweetened with low calorie sweetener
7302	Coffee	92152000	Coffee and chicory, brewed
7302	Coffee	92152010	Coffee and chicory, brewed, decaffeinated
7302	Coffee	92161000	Coffee, Cappuccino
7302	Coffee	92161001	Coffee, Cappuccino, nonfat
7302	Coffee	92161002	Coffee, Cappuccino, with non-dairy milk
7302	Coffee	92162000	Coffee, Cappuccino, decaffeinated
7302	Coffee	92162001	Coffee, Cappuccino, decaffeinated, nonfat
7302	Coffee	92162002	Coffee, Cappuccino, decaffeinated, with non-dairy milk
7302	Coffee	92171000	Coffee, bottled/canned
7302	Coffee	92171010	Coffee, bottled/canned, light
9999	Not included in a food category	92191100	Coffee, instant, not reconstituted
9999	Not included in a food category	92191105	Coffee, instant, 50% less caffeine, not reconstituted
9999	Not included in a food category	92191200	Coffee, instant, decaffeinated, not reconstituted
9999	Not included in a food category	92191400	Coffee, instant, pre-sweetened with sugar, not reconstituted
9999	Not included in a food category	92192000	Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, not reconstituted
9999	Not included in a food category	92192030	Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted

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9999	Not included in a food category	92192040	Coffee, mocha, instant, decaffeinated, pre-lightened and pre-sweetend with low calorie sweetener, not reconstituted
9999	Not included in a food category	92193000	Coffee, instant, pre-lightened and pre-sweetened with sugar, not reconstituted
9999	Not included in a food category	92193005	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, not reconstituted
9999	Not included in a food category	92193020	Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted
9999	Not included in a food category	92193025	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted
7302	Coffee	92201010	Coffee substitute
7302	Coffee	92202010	Chicory beverage
7302	Coffee	92203000	Cereal beverage
7302	Coffee	92203110	Cereal beverage with beet roots, from powdered instant
7304	Tea	92302000	Tea, hot, leaf, black
7304	Tea	92302500	Tea, hot, leaf, black, decaffeinated
7304	Tea	92303010	Tea, hot, leaf, green
7304	Tea	92303100	Tea, hot, leaf, green, decaffeinated
7304	Tea	92304100	Tea, hot, leaf, oolong
7304	Tea	92305010	Tea, iced, instant, black, unsweetened
7304	Tea	92305040	Tea, iced, instant, black, pre-sweetened with sugar
7304	Tea	92305050	Tea, iced, instant, black, decaffeinated, pre-sweetened with sugar
7304	Tea	92305090	Tea, iced, instant, black, pre-sweetened with low calorie sweetener
7304	Tea	92305110	Tea, iced, instant, black, decaffeinated, pre-sweetened with low calorie sweetener
7304	Tea	92305180	Tea, iced, instant, black, decaffeinated, unsweetened
7304	Tea	92305900	Tea, iced, instant, green, unsweetened
7304	Tea	92305910	Tea, iced, instant, green, pre-sweetened with sugar
7304	Tea	92305920	Tea, iced, instant, green, pre-sweetened with low calorie sweetener
7304	Tea	92306000	Tea, hot, herbal
7304	Tea	92306090	Tea, hot, hibiscus
7304	Tea	92306700	Tea, hot, chamomile
7304	Tea	92306800	Tea, hot, with milk
7304	Tea	92306850	Tea, ginger
7304	Tea	92306910	Tea, bubble
7304	Tea	92306920	Tea, kombucha
9999	Not included in a food category	92307000	Tea, iced, instant, black, unsweetened, dry
9999	Not included in a food category	92307400	Tea, iced, instant, black, pre-sweetened, dry
7304	Tea	92307500	Iced Tea / Lemonade juice drink
7304	Tea	92307510	Iced Tea / Lemonade juice drink, light
7304	Tea	92307520	Iced Tea / Lemonade juice drink, diet
7304	Tea	92308000	Tea, iced, brewed, black, pre-sweetened with sugar
7304	Tea	92308010	Tea, iced, brewed, black, pre-sweetened with low calorie sweetener
7304	Tea	92308020	Tea, iced, brewed, black, unsweetened
7304	Tea	92308030	Tea, iced, brewed, black, decaffeinated, pre-sweetened with sugar
7304	Tea	92308040	Tea, iced, brewed, black, decaffeinated, pre-sweetened with low calorie sweetener
7304	Tea	92308050	Tea, iced, brewed, black, decaffeinated, unsweetened
7304	Tea	92308500	Tea, iced, brewed, green, pre-sweetened with sugar
7304	Tea	92308510	Tea, iced, brewed, green, pre-sweetened with low calorie sweetener
7304	Tea	92308520	Tea, iced, brewed, green, unsweetened

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WWEIA Category number	WWEIA Category description	Food code	Main food description
7304	Tea	92308530	Tea, iced, brewed, green, decaffeinated, pre-sweetened with sugar
7304	Tea	92308540	Tea, iced, brewed, green, decaffeinated, pre-sweetened with low calorie sweetener
7304	Tea	92308550	Tea, iced, brewed, green, decaffeinated, unsweetened
7304	Tea	92309000	Tea, iced, bottled, black
7304	Tea	92309010	Tea, iced, bottled, black, decaffeinated
7304	Tea	92309020	Tea, iced, bottled, black, diet
7304	Tea	92309030	Tea, iced, bottled, black, decaffeinated, diet
7304	Tea	92309040	Tea, iced, bottled, black, unsweetened
7304	Tea	92309050	Tea, iced, bottled, black, decaffeinated, unsweetened
7304	Tea	92309500	Tea, iced, bottled, green
7304	Tea	92309510	Tea, iced, bottled, green, diet
7304	Tea	92309520	Tea, iced, bottled, green, unsweetened
7202	Soft drinks	92400000	Soft drink, NFS
7102	Diet soft drinks	92400100	Soft drink, NFS, diet
7802	Flavored or carbonated water	92410110	Water, tonic
7802	Flavored or carbonated water	92410210	Water, carbonated, plain
7802	Flavored or carbonated water	92410250	Water, carbonated, flavored
7202	Soft drinks	92410310	Soft drink, cola
7202	Soft drinks	92410315	Soft drink, cola, reduced sugar
7102	Diet soft drinks	92410320	Soft drink, cola, diet
7202	Soft drinks	92410340	Soft drink, cola, decaffeinated
7102	Diet soft drinks	92410350	Soft drink, cola, decaffeinated, diet
7202	Soft drinks	92410360	Soft drink, pepper type
7102	Diet soft drinks	92410370	Soft drink, pepper type, diet
7202	Soft drinks	92410390	Soft drink, pepper type, decaffeinated
7102	Diet soft drinks	92410400	Soft drink, pepper type, decaffeinated, diet
7202	Soft drinks	92410410	Soft drink, cream soda
7102	Diet soft drinks	92410420	Soft drink, cream soda, diet
7202	Soft drinks	92410510	Soft drink, fruit flavored, caffeine free
7102	Diet soft drinks	92410520	Soft drink, fruit flavored, diet, caffeine free
7202	Soft drinks	92410550	Soft drink, fruit flavored, caffeine containing
7102	Diet soft drinks	92410560	Soft drink, fruit flavored, caffeine containing, diet
7202	Soft drinks	92410610	Soft drink, ginger ale
7102	Diet soft drinks	92410620	Soft drink, ginger ale, diet
7202	Soft drinks	92410710	Soft drink, root beer
7102	Diet soft drinks	92410720	Soft drink, root beer, diet
7202	Soft drinks	92410810	Soft drink, chocolate flavored
7102	Diet soft drinks	92410820	Soft drink, chocolate flavored, diet
7202	Soft drinks	92411510	Soft drink, cola, fruit or vanilla flavored
7202	Soft drinks	92411520	Soft drink, cola, chocolate flavored
7102	Diet soft drinks	92411610	Soft drink, cola, fruit or vanilla flavored, diet
7102	Diet soft drinks	92411620	Soft drink, cola, chocolate flavored, diet
7204	Fruit drinks	92432000	Fruit juice drink, citrus, carbonated
7204	Fruit drinks	92433000	Fruit juice drink, noncitrus, carbonated
7204	Fruit drinks	92541010	Fruit flavored drink, powdered, reconstituted
7204	Fruit drinks	92542000	Fruit flavored drink, with high vitamin C, powdered, reconstituted
7106	Other diet drinks	92552000	Fruit flavored drink, with high vitamin C, powdered, reconstituted, diet
7106	Other diet drinks	92552010	Fruit flavored drink, powdered, reconstituted, diet
9999	Not included in a food category	92900100	Fruit flavored drink, with high vitamin C, powdered, not reconstituted
9999	Not included in a food category	92900110	Fruit flavored drink, powdered, not reconstituted
9999	Not included in a food category	92900200	Fruit flavored drink, powdered, not reconstituted, diet

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WWEIA Category number	WWEIA Category description	Food code	Main food description
9999	Not included in a food category	92900300	Sports drink, dry concentrate, not reconstituted
7802	Flavored or carbonated water	94100200	Water, non-carbonated, flavored
7802	Flavored or carbonated water	94100300	Water beverage, fruit flavored
7208	Nutritional beverages	95101000	Nutritional drink or shake, ready-to-drink (Boost)
7208	Nutritional beverages	95101010	Nutritional drink or shake, ready-to-drink (Boost Plus)
7208	Nutritional beverages	95102000	Nutritional drink or shake, ready-to-drink (Carnation Instant Breakfast)
7208	Nutritional beverages	95103000	Nutritional drink or shake, ready-to-drink (Ensure)
7208	Nutritional beverages	95103010	Nutritional drink or shake, ready-to-drink (Ensure Plus)
7208	Nutritional beverages	95104000	Nutritional drink or shake, ready-to-drink, sugar free (Glucerna)
7208	Nutritional beverages	95105000	Nutritional drink or shake, ready-to-drink (Kellogg's Special K Protein)
7208	Nutritional beverages	95106000	Nutritional drink or shake, ready-to-drink (Muscle Milk)
7208	Nutritional beverages	95106010	Nutritional drink or shake, ready-to-drink, light (Muscle Milk)
7208	Nutritional beverages	95110000	Nutritional drink or shake, ready-to-drink (Slim Fast)
7208	Nutritional beverages	95110010	Nutritional drink or shake, ready-to-drink, sugar free (Slim Fast)
7208	Nutritional beverages	95110020	Nutritional drink or shake, high protein, ready-to-drink (Slim Fast)
7208	Nutritional beverages	95120000	Nutritional drink or shake, ready-to-drink, NFS
7208	Nutritional beverages	95120010	Nutritional drink or shake, high protein, ready-to-drink, NFS
7208	Nutritional beverages	95120020	Nutritional drink or shake, high protein, light, ready-to-drink, NFS
7208	Nutritional beverages	95120050	Nutritional drink or shake, liquid, soy-based
9802	Protein and nutritional powders	95201000	Nutritional powder mix (Carnation Instant Breakfast)
9802	Protein and nutritional powders	95201010	Nutritional powder mix, sugar free (Carnation Instant Breakfast)
9802	Protein and nutritional powders	95201200	Nutritional powder mix (EAS Whey Protein Powder)
9802	Protein and nutritional powders	95201300	Nutritional powder mix (EAS Soy Protein Powder)
9802	Protein and nutritional powders	95201500	Nutritional powder mix, high protein (Herbalife)
9802	Protein and nutritional powders	95201600	Nutritional powder mix (Isopure)
9802	Protein and nutritional powders	95201700	Nutritional powder mix (Kellogg's Special K20 Protein Water)
9802	Protein and nutritional powders	95202000	Nutritional powder mix (Muscle Milk)
9802	Protein and nutritional powders	95202010	Nutritional powder mix, light (Muscle Milk)
9802	Protein and nutritional powders	95210000	Nutritional powder mix (Slim Fast)
9802	Protein and nutritional powders	95210010	Nutritional powder mix, sugar free (Slim Fast)
9802	Protein and nutritional powders	95210020	Nutritional powder mix, high protein (Slim Fast)
9802	Protein and nutritional powders	95220000	Nutritional powder mix, NFS
9802	Protein and nutritional powders	95220010	Nutritional powder mix, high protein, NFS
9802	Protein and nutritional powders	95230000	Nutritional powder mix, whey based, NFS
9802	Protein and nutritional powders	95230010	Nutritional powder mix, protein, soy based, NFS
9802	Protein and nutritional powders	95230020	Nutritional powder mix, protein, light, NFS
9802	Protein and nutritional powders	95230030	Nutritional powder mix, protein, NFS
7206	Sport and energy drinks	95310200	Energy drink (Full Throttle)
7206	Sport and energy drinks	95310400	Energy drink (Monster)
7206	Sport and energy drinks	95310500	Energy drink (Mountain Dew AMP)
7206	Sport and energy drinks	95310550	Energy drink (No Fear)
7206	Sport and energy drinks	95310555	Energy drink (No Fear Motherload)
7206	Sport and energy drinks	95310560	Energy drink (NOS)
7206	Sport and energy drinks	95310600	Energy drink (Red Bull)
7206	Sport and energy drinks	95310700	Energy drink (Rockstar)
7206	Sport and energy drinks	95310750	Energy drink (SoBe Energize Energy Juice Drink)
7206	Sport and energy drinks	95310800	Energy drink (Vault)
7206	Sport and energy drinks	95311000	Energy Drink
7206	Sport and energy drinks	95312560	Energy drink (Ocean Spray Cran-Energy Juice Drink)
7206	Sport and energy drinks	95312900	Energy drink (XS)
7206	Sport and energy drinks	95312905	Energy drink (XS Gold Plus)
7206	Sport and energy drinks	95320200	Sports drink (Gatorade G)

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WWEIA Category number	WWEIA Category description	Food code	Main food description
7206	Sport and energy drinks	95320500	Sports drink (Powerade)
7206	Sport and energy drinks	95321000	Sports drink, NFS
7206	Sport and energy drinks	95330100	Fluid replacement, electrolyte solution
7206	Sport and energy drinks	95330500	Fluid replacement, 5% glucose in water

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Question/Comment Exhibit B Depletion/Repletion Studies for Choline excerpted from Appendix D EFSA J 2016 14(8):4484

Appendix D – Depletion/repletion studies for choline

(choline intake per 70-kg body weight per day)

Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
Zeisel et al. (1991) **1***	Experimental choline deficiency in humans	Choline, PC in plasma; PC in red blood cells; liver and kidney function, blood lipids, liver size and density by CT	Male, n = 15, healthy **A controls** n = 6, mean age 26.8 years; **B depleted** n = 8, mean age 29.1 years One recruited control subject was excluded (abnormal liver function tests on day 1)	Metabolic unit;		Plasma choline, plasma PC and serum ALT activity expressed as a change from day 7 to day 28 Three-week depletion of dietary choline (513–13 mg choline/day) significantly decreased plasma choline and PC and increases serum ALT activity in all subjects. No effects on other hepatic or kidney function parameters
				Week 1: A and B: baseline diet (13 mg/70-kg bw per day) + 500 mg/day choline	**Week 1:** free choline in plasma 9.6–10.9 μmol/L; plasma PC 1.3–2.0 mmol/L	
				Week 2-4: **A:** baseline diet + 500 mg/day choline **B:** baseline diet + placebo	**Week 4**: **A**: no change in plasma choline/PC, increase by 14% in red blood cell PC, no change in ALT **B**: choline in plasma decreased by 30%, plasma PC (as % of day 7 value) decreased by 30%, decrease in red blood cell PC by 15%; significant **increase in ALT** by 50%; non-significant increase in liver size	
				Week 5 (i.e. 35 days): **A:** baseline diet + 500 mg/day choline **B:** baseline diet + 500 mg/day choline	**Week 5:** **A**: no change **B**: plasma choline, plasma PC, ALT return to baseline	
Kohlmeier et al. (2005) **2**	Influence of genetic variants of folate metabolism on susceptibility to choline deficiency	Liver fat by MRI, CK in serum, Plasma folate, plasma tHcy, SAM, SAH; tHcy response to methionine load before and after depletion; genotyping for *MTHFR*, *MTHFD1* and *RFC1*	n = 54, female n = 28, mean age 38.7 years, healthy	Metabolic unit **Baseline**: 10 days, 550 mg choline/70-kg bw per day + 400 μg folic acid **Depletion** (up to 42 days): < 50 mg choline/70-kg bw per day and 100 μg folate/ day	**Organ dysfunction** 12/54 subjects 5-fold increase in CK 24/54 increase (at least by 28%) in liver fat content, no effect of folate intake **Genotyping and %**	More than 50% of the participants developed signs of organ dysfunction when consuming < 50 mg/ 70-kg bw per day. Susceptibility to develop signs of choline deficiency on a 50 mg/70-kg bw per

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
				A plus 400 μg folic acid/day **B** placebo **Repletion** (increasing amount (137–550 mg/70-kg bw per day) up to > 550 mg choline per day for ≥ 3 days)	**symptomatic choline deficiency:** *MTHFD1* 1958 GG n = 20: 40% *MTHFD1* 1958 GA n = 28: 82% *MTHFD1* 1958 AA n = 6: 83% GG vs GA/AA **OR 7.0 (95% CI 2.0–25) p = 0.007** *RFC1* 80 AG n = 20: 70% *RFC1* 80 GG n = 15: 73% AA vs AG/GG OR 1.82 (95% CI 0.56-5.9) N.S Mean serum folate significantly lower in subjects with low folate intake (22.1 (B) vs 28.3 mmol/L (A)) without effect by genetic polymorphism	day-choline diet greater in carriers of the *MTHFD1* G1958A polymorphism: OR 7.0 (95% CI 2.0–25; p < 0.01) unless they received additional folic acid Susceptibility to develop signs of choline deficiency not influenced by polymorphism of *MTHFR* or *RFC1*
da Costa et al. (2005) **3**	Choline deficiency and capacity to methylate tHcy	Total plasma tHcy, before and after Met load (100 mg/kg bw) before and after choline depletion and repletion, plasma choline, betaine, PC, folate liver fat by MRI	n = 8 males, age 20-46 years, healthy	Standardised depletion/ repletion design **Baseline** diet (10 days): 550 mg choline/70-kg bw per day + 400 DFE/day **Depletion** diet (up to 42 days): < 50 mg choline/ 70-kg bw per day **Repletion** diet: 1) Subjects not clinically choline deficient: 550 mg choline diet for 3 days 2) Subjects clinically choline deficient: graded amounts	**Organ dysfunction** 4/8 increase in liver **fat tHcy in plasma Depletion** fasting tHcy significantly increased by 1.3 μmol/L in clinically choline-deficient participants (no significant change in the non-deficient subjects) **Free choline in plasma (mean)** Before depletion 10 μmol/L	Half of the participants developed signs of liver dysfunction when consuming < 50 mg choline/70-kg bw per day; no difference in change in plasma choline (or betaine) between those with and without organ dysfunction

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
				of choline sequentially in 10 days periods (138, 275, 413, 550 mg/70-kg bw per day until hepatic steatosis resolved)	Clinically depleted 7 μmol/L Not clinically depleted 7 μmol/L **PC in plasma (mean)** Before depletion 1,818 μmol/L Clinically depleted 1,564 μmol/L Not clinically depleted 1,834 μmol/L **Betaine in plasma (mean)** Before depletion 66 μmol/L Clinically depleted 36 μmol/L Not clinically depleted 34 μmol/L	
da Costa et al. (2006a) **3**	Choline deficiency and lymphocyte apoptosis and DNA damage	CK, liver fat by MRI, 24 h urine choline and betaine, plasma folate, peripheral lymphocytes at baseline, after depletion and repletion: DNA fragmentation (TUNEL) and strand breaks (COMET), activated caspase-3 (used as a marker for apoptosis)	n = 51, n = 31 female, age 18-70 years, healthy	Metabolic unit Standardised depletion/repletion design **Baseline** diet (10 days): 550 mg choline/70-kg bw per day + 400 DFE/day **Depletion** diet (up to 42 days): < 50 mg choline/70-kg bw per day and 100 DFE/day **A** plus 400 μg folic acid/day, n = 26 **B** placebo, n = 25 **Repletion** diet 1) Subjects not clinically choline deficient: 550 mg choline diet for 3 days 2) Subjects clinically choline	**Organ dysfunction** 33/51, including 26/51 liver dysfunction (18 females) 1/51 muscle dysfunction only 6/51 both liver and muscle dysfunction returning to normal after choline repletion **Plasma folate** Significant decrease during choline depletion without extra folic acid: 26.0–21.4 μmol/L (and p = 0.0003 without folate supplementation) **24 h urine choline**	Choline deficiency is associated with *in vitro* signs of DNA damage and of apoptosis in peripheral lymphocytes

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
				deficient: graded amounts of choline sequentially in 10 days periods (137.5, 275, 412.5 and 550 mg/70-kg bw per day and > 550 mg for 3 days	**and betaine** Decrease from about 25 to 10 and from 80 to about 30 μmol/g creatinine, respectively, with choline depletion **Activated caspase-3 assay in lymphocytes** Higher amounts in cells from clinically choline deficient subjects, compared to non-deficient subjects ($p < 0.05$) **TUNEL assay** More TUNEL-positive lymphocyte cells during choline depletion with or without organ dysfunction, without folic acid supplement ($p = 0.026$) **COMET assay** COMET-Tail moment increase during choline depletion compared to baseline	
Fischer et al. (2007) **3**	Dietary requirement in healthy men and women and clinical sequelae of choline deficiency	Plasma choline, PC, SAM, SAH, Met, tHcy, methylglycine and DMG CK, Liver fat by MRI	n = 57, n = 16 premenopausal women, n = 15 postmenopausal women, n = 26 men Age 18-70 years, healthy	Metabolic unit Standardised depletion/ repletion design **Baseline** diet (10 days): 550 mg choline/70-kg bw per day + 400 DFE/day **Depletion** diet (up to 42 days): < 50 mg choline/ 70-kg bw per day + 100 DFE/day	**Organ dysfunction** 39/57 as by changes in CK, AST, ALT, LDH or by hepatic steatosis, of which: 1) **6 while on 550 mg choline baseline diet (550 mg/70 kg bw per day)**, all men 2) **33 while on**	Most men and postmenopausal women (68.4%) developed clinical choline deficiency when on < 50 mg choline/day independent on folate intake 18/57 subjects did not develop signs of choline

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
				A plus 400 μg folic acid/day **B** placebo **Repletion** diet: 1) Subjects not clinically choline deficient: 550 mg choline diet for 3 days 2) Subjects clinically choline deficient: graded amounts of choline sequentially in 10 days periods (137.5, 275, 412.5 and 550 mg/70-kg bw per day, then > 550 mg for 3 days)	**low-choline diet (50 mg/70 kg bw per day):** 14/20 men (70%), 7/16 (44%) premenopausal women 12/15 (80%) postmenopausal women; with **liver steatosis** alone: in 8/20 men, 12/15 postmenopausal women and 6/16 premenopausal women **Choline (metabolites) in plasma on depletion**: Choline decrease by 28–33%, betaine by ≈50%, PC only in subjects with organ dysfunction, Met decreased only in subjects with organ dysfunction, DMG and MG decreased, tHcy increased, SAM and SAH did not change Serum uric acid increased in all subjects during depletion **Repletion of choline depleted subjects: see Table** 2, **Section** 5.1.1.3	deficiency with < 50 mg choline/day

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
Niculescu et al. (2007) **3**	Organ dysfunction on low-choline diet and SNPs in genes involved in choline and folate metabolism	Liver fat by MRI, CK in serum, Peripheral lymphocytes at 10 days and after depletion for genotyping *MTHFD1*, *PEMT*, *CHDH* and for change in expression with low-choline diet and DNA methylation	n = 33, age 20-67 years, 19 women, healthy	Metabolic unit Standardised depletion/ repletion design **Baseline** diet (10 days): 550 mg choline/70-kg bw/day + 400 DFE/day **Depletion** diet (up to 42 days): < 50 mg choline/70-kg bw per day **A** plus 400 µg folic acid/day **B** placebo **Repletion** diet	No outcome measurements indicative of choline requirement	Previous studies showed that the *PEMT* (rs12325817) and *MTHFD1* (rs2236225) SNPs predispose subjects to develop organ dysfunction when they consume a low-choline diet (Kohlmeier et al., 2005; da Costa et al., 2006a) At baseline, subjects with the *PEMT* (rs12325817) and *MTHFD1* (rs2236225) SNPs, compared with subjects without the SNPs, had a different expression of genes involved in apoptosis, the DNA damage checkpoint, and cell proliferation control This suggests that the presence of the *PEMT* and *MTHFD1* genotypes can lead to differences in the phenotypes at baseline (i.e. even before consuming a low-choline diet). Subjects may differ in their susceptibility to dietary choline deficiency. In women who are carriers of the *PEMT* allele, the risk of choline deficiency is higher

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
Fischer et al. (2010a) **4**	Low-choline related organ dysfunction, in relation to number of alleles of rs12325817 in premenopausal women, and in relation to oestrogen in postmenopausal women	Liver fat by MRI, CK, AST, ALT Plasma choline (metabolites) Genotyping for *PEMT* rs12325817	**A**: n = 27 premenopausal women, age 18–49 years. **B:** n = 22 postmenopausal women, age 50–73 years, randomised to receive oestrogen (**B1**) or placebo (**B2**). Healthy	Metabolic unit Standardised depletion/repletion **Baseline** diet (10 days): 550 mg choline/70-kg bw per day **Depletion** diet (up to 42 days): < 50 mg choline/70-kg bw per day **Repletion** diet: 550–850 mg/70-kg bw per day for up to 10 days. If signs of organ dysfunction did not resolve after 10 days of repletion diet: *ad libitum* diet for 2 weeks	**Among premenopausal women:** 11/27 developed choline deficiency/organ dysfunction. There was a dose–response effect of rs12325817 on the risk of choline related organ dysfunction: 80%, 43%, and 13% of women with 2, 1, or 0 alleles, respectively, developed organ dysfunction during the low-choline diet **Among postmenopausal women:** Only 2/11 (18%) who received oestrogen (B1) and 8/11 (73%) who received placebo (B2), developed organ dysfunction during the low-choline diet	Dietary requirement for choline is higher in postmenopausal women (because of their lower oestrogen concentrations) than in premenopausal women Choline requirements for both groups of women are further increased by rs12325817. 80% of homozygous women develop organ dysfunction on the depletion diet vs 43% of those with one copy and 13% of women homozygous for the wild-type No oestrogen vs oestrogen increases fourfold the risk for organ dysfunction on the depletion diet. Oestrogen mitigates the effect of the *PEMT* SNP. Oestrogen may decrease choline requirement in postmenopausal women
Sha et al. (2010) **3**	Metabolomic profiling to predict organ dysfunction with deficient choline intake	Liver fat by MRI CK, AST, ALT Plasma choline (metabolites), Met, Hcy, sarcosine, DMG, cysteine, cystathionine, Metabolomic analysis of plasma	n = 53, n = 30 women, age 18–70 years, healthy	Metabolic unit Standardised depletion/repletion design **Baseline** diet (10 days): 550 mg choline/70-kg bw per day **Depletion** diet (up to 42 days): < 50 mg choline/70-kg bw per day **Repletion** diet (≥ 3 days,	**Organ dysfunction** **Baseline diet:** 9 (17%) developed fatty liver (n = 4) or muscle dysfunction (n = 5), without special metabolome **Depletion** (n = 44): 23 fatty liver, 5 muscle dysfunction	Metabolomic profiles of subjects at baseline could predict the development of liver dysfunction when deprived of dietary choline

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
				(≥ 550 mg/70-kg bw per day)	Higher plasma Hcy, cysteine, cystathionine, keto-acids at baseline in subjects who later develop fatty liver Choline deficiency increased plasma carnitine and acyl-carnitine, decreased pyridoxate Baseline plasma choline has no predictive value	
Spencer et al. (2011) **4**	Choline deficiency and hepatic steatosis and gut microbiome	Liver fat by MRI CK AST, ALT Sequencing of the 16S RNA bacterial genes in stool; genotyping of *PEMT* promoter SNP rs12325817	n = 15 females, age not reported, healthy	Standardised depletion/ repletion design 2 months: **Baseline** diet (10 days): 550 mg choline/70-kg bw per day **Depletion** diet (up to 42 days): < 50 mg choline/ 70-kg bw per day **Repletion** diet (10 days, (≥ 850 mg/70-kg bw per day)	No statistically significant general microbial convergence with choline depletion	Host factors as well as gut bacteria respond to dietary choline deficiency, but individual microbiota persist although all subjects consumed the same diets
da Costa et al. (2011) **3+4**	PC-DHA plasma concentration used as a non-invasive marker of liver PEMT activity	Plasma DHA, PC-DHA, ratio PC-DHA/total PC	n = 72, age 18-70 years; n = 20 men; n = 52 women of which n = 25 postmenopausal and n = 27 premenopausal	Standardised depletion/ repletion design **Baseline** diet (10 days): 550 mg choline/70-kg bw per day **Depletion** diet (up to 42 days): < 50 mg choline/ 70-kg bw per day **Repletion** diet	70% of the subjects possess at least one *PEMT rs12325817* allele	Plasma ratio PC-DHA/total PC higher in premenopausal women than men or postmenopausal (at baseline and even when on a low-choline diet) Plasma PC-DHA/total PC at baseline and PEMT activity in liver: lower in premenopausal women homozygous for the *rs12325817* polymorphism in the *PEMT* gene

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Author	Aim of investigation	Outcome measurements	Participants	Design/duration	Results	Comment
da Costa et al. (2011) **3+4**	Identification of effect alleles of SNPs known to influence dietary requirement for choline	DNA concentration by spectrometry; genotyping of alleles	n = 79, 18-70 years old; n = 26 men n = 53 women of which n = 26 post and n = 27 premenopausal	Standardised depletion/ repletion design **Baseline** diet (10 days): 550 mg choline/70-kg bw per day **Depletion** diet (up to 42 days): < 50 mg choline/ 70-kg bw per day **Repletion** diet	Effect alleles identified of SNPs in genes for the choline transporter (SLC44A1) and choline kinase A and B (see Appendix C) Choline deficiency related organ dysfunction (liver or muscle: 50/79, including 20 of 26 postmenopausal women, 11 of 27 premenopausal women 19 of 26 men	29 of 79 healthy subjects did not develop organ dysfunction while consuming a low-choline diet for 6 weeks

*Same numbers in the column "author" indicate references providing data from the same cohort.
ALT: alanine aminotransferase; AST: aspartate aminotransferase; CHDH: choline dehydrogenase; CI: confidence interval; CK: creatine kinase; COMET: single-cell gel electrophoresis; CT: computerised tomography; DFE: dietary folate equivalent; DHA: docosahexaenoic acid; DMG: dimethylglycine; DNA: deoxyribonucleic acid; LDH: lactate dehydrogenase; Met: methionine; MG: methylglycine; MRI: magnetic resonance imaging; MTHFD1: 5,10-methylene-tetrahydrofolate dehydrogenase 1; MTHFR: Methylene-tetrahydrofolate reductase; N.S.: not significant; OR: odds ratio; PC: phosphatidylcholine; PEMT: phosphatidylethanolamine N-methyltransferase; RFC1: reduced folate carrier 1; RNA: ribonucleic acid; rs number: Reference SNP cluster ID; SAH: *S*-adenosylhomocysteine; SAM: *S*-adenosyl-methionine; SLC44A1: solute carrier family 44 member 1 (choline transporter); SNP: single-nucleotide polymorphism; tHcy: total homocysteine; TUNEL: terminal deoxynucleotidyl transferase mediated dUTP nick end labelling.

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Question/Comment References

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March 12, 2024

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Re: GRAS Notice No. GRN 1141

Dear Marissa,

It's our pleasure to have the call with you and your colleagues on March 8th. 2024, last Friday to go over our responses.

Regarding your concerns of food codes and use levels in the determination of EDI for both GRN no. 419 and GRN no. 1141, we generated a table to elaborate the data that contains the use level and food codes. Please see the attached excel sheet, ((*a-GPC Intended Use Level and Food Codes Table (03082024).xlsx).*

We would like to clarify that we do not intend on putting a-GPC into fruit drinks, that's why we do not consider them under "beverages" since (35) processed fruits and fruit juices, including all commercially processed fruits, citrus, berries, and mixtures; salads, juices and juice punches, concentrates, dilutions, "ades", and drink substitutes made therefrom.

If you require any further information, please feel free to reach out to me.

Sincerely,

[redacted]

Jimmy Wang, Ph. D
Chief Scientific Officer
Summit Life Science, Inc.

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WWEIA Category number	WWEIA Category description	Food code	Main food description	GRAS Food Group	GRAS Substance (g/100g)	Ingredient Fraction	Concentration in Substance
1004	Milk, reduced fat	11100000	Milk, NFS	Milk, whole, and skim (170.3(n)(30))	0.008		
1002	Milk, whole	11111000	Milk, whole	Milk, whole, and skim (170.3(n)(30))	0.008		
1002	Milk, whole	11111100	Milk, low sodium, whole	Milk, whole, and skim (170.3(n)(30))	0.008		
1002	Milk, whole	11111150	Milk, calcium fortified, whole	Milk, whole, and skim (170.3(n)(30))	0.008		
1006	Milk, lowfat	11111160	Milk, calcium fortified, low fat (1%)	Milk, whole, and skim (170.3(n)(30))	0.008		
1008	Milk, nonfat	11111170	Milk, calcium fortified, fat free (skim)	Milk, whole, and skim (170.3(n)(30))	0.008		
1004	Milk, reduced fat	11112110	Milk, reduced fat (2%)	Milk, whole, and skim (170.3(n)(30))	0.008		
1006	Milk, lowfat	11112120	Milk, acidophilus, low fat (1%)	Milk, whole, and skim (170.3(n)(30))	0.008		
1004	Milk, reduced fat	11112130	Milk, acidophilus, reduced fat (2%)	Milk, whole, and skim (170.3(n)(30))	0.008		
1006	Milk, lowfat	11112210	Milk, low fat (1%)	Milk, whole, and skim (170.3(n)(30))	0.008		
1008	Milk, nonfat	11113000	Milk, fat free (skim)	Milk, whole, and skim (170.3(n)(30))	0.008		

1006	Milk, lowfat	11114300	Milk, lactose free, low fat (1%)	Milk, whole, and skim (170.3(n)(30))	0.008
1008	Milk, nonfat	11114320	Milk, lactose free, fat free (skim)	Milk, whole, and skim (170.3(n)(30))	0.008
1004	Milk, reduced fat	11114330	Milk, lactose free, reduced fat (2%)	Milk, whole, and skim (170.3(n)(30))	0.008
1002	Milk, whole	11114350	Milk, lactose free, whole	Milk, whole, and skim (170.3(n)(30))	0.008
1008	Milk, nonfat	11115000	Buttermilk, fat free (skim)	Milk, whole, and skim (170.3(n)(30))	0.008
1006	Milk, lowfat	11115100	Buttermilk, low fat (1%)	Milk, whole, and skim (170.3(n)(30))	0.008
1004	Milk, reduced fat	11115200	Buttermilk, reduced fat (2%)	Milk, whole, and skim (170.3(n)(30))	0.008
1002	Milk, whole	11115300	Buttermilk, whole	Milk, whole, and skim (170.3(n)(30))	0.008
1006	Milk, lowfat	11115400	Kefir, NS as to fat content	Milk, whole, and skim (170.3(n)(30))	0.008
1002	Milk, whole	11116000	Goat's milk, whole	Milk, whole, and skim (170.3(n)(30))	0.008
1008	Milk, nonfat	11120000	Milk, dry, reconstituted, NS as to fat content	Milk products (170.3(n)(31))	0.008
1002	Milk, whole	11121100	Milk, dry, reconstituted, whole	Milk products (170.3(n)(31))	0.008
1006	Milk, lowfat	11121210	Milk, dry, reconstituted, low fat (1%)	Milk products (170.3(n)(31))	0.008

1008	Milk, nonfat	11121300	Milk, dry, reconstituted, fat free (skim)	Milk products (170.3(n)(31))	0.008
1820	Yogurt, regular	11400000	Yogurt, NFS	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11400010	Yogurt, Greek, NS as to type of milk or flavor	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11410000	Yogurt, NS as to type of milk or flavor	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11411010	Yogurt, NS as to type of milk, plain	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11411100	Yogurt, whole milk, plain	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11411200	Yogurt, low fat milk, plain	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11411300	Yogurt, nonfat milk, plain	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11411390	Yogurt, Greek, NS as to type of milk, plain	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11411400	Yogurt, Greek, whole milk, plain	Milk products (170.3(n)(31))	0.024

1822	Yogurt, Greek	11411410	Yogurt, Greek, low fat milk, plain	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11411420	Yogurt, Greek, nonfat milk, plain	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11430000	Yogurt, NS as to type of milk, fruit	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11431000	Yogurt, whole milk, fruit	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11432000	Yogurt, low fat milk, fruit	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11433000	Yogurt, nonfat milk, fruit	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11433990	Yogurt, Greek, NS as to type of milk, fruit	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11434000	Yogurt, Greek, whole milk, fruit	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11434010	Yogurt, Greek, low fat milk, fruit	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11434020	Yogurt, Greek, nonfat milk, fruit	Milk products (170.3(n)(31))	0.024

1820	Yogurt, regular	11434090	Yogurt, NS as to type of milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11434100	Yogurt, whole milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11434200	Yogurt, low fat milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	11434300	Yogurt, nonfat milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11435000	Yogurt, Greek, NS as to type of milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11435010	Yogurt, Greek, whole milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024
1822	Yogurt, Greek	11435020	Yogurt, Greek, low fat milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024

1822	Yogurt, Greek	11435030	Yogurt, Greek, nonfat milk, flavors other than fruit	Milk products (170.3(n)(31))	0.024		
1822	Yogurt, Greek	11435100	Yogurt, Greek, with oats	Milk products (170.3(n)(31))	0.024		
1820	Yogurt, regular	11436000	Yogurt, liquid	Milk products (170.3(n)(31))	0.024		
8412	Dips, gravies, other sauces	11440010	Chipotle dip, yogurt based	Milk products (170.3(n)(31))	0.0185	0.77	0.024
8412	Dips, gravies, other sauces	11440020	Dill dip, yogurt based	Milk products (170.3(n)(31))	0.0185	0.77	0.024
8412	Dips, gravies, other sauces	11440030	Onion dip, yogurt based	Milk products (170.3(n)(31))	0.0185	0.77	0.024
8412	Dips, gravies, other sauces	11440040	Ranch dip, yogurt based	Milk products (170.3(n)(31))	0.0185	0.77	0.024
8412	Dips, gravies, other sauces	11440050	Spinach dip, yogurt based	Milk products (170.3(n)(31))	0.0185	0.77	0.024
8412	Dips, gravies, other sauces	11440070	Vegetable dip, yogurt based	Milk products (170.3(n)(31))	0.0185	0.77	0.024
1820	Yogurt, regular	11446000	Yogurt parfait, low fat, with fruit	Milk products (170.3(n)(31))	0.024		
1208	Flavored milk, nonfat	11511000	Chocolate milk, NFS	Milk products (170.3(n)(31))	0.008		
1202	Flavored milk, whole	11511100	Chocolate milk, ready to drink, whole	Milk products (170.3(n)(31))	0.008		

1204	Flavored milk, reduced fat	11511200	Chocolate milk, ready to drink, reduced fat	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11511300	Chocolate milk, ready to drink, fat free	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11511400	Chocolate milk, ready to drink, low fat	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11511550	Chocolate milk, ready to drink, reduced sugar, NS as to milk	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11511600	Chocolate milk, ready to drink, low fat (Nesquik)	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11511610	Chocolate milk, ready to drink, fat free (Nesquik)	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11511700	Chocolate milk, ready to drink, low fat, no sugar added (Nesquik)	Milk products (170.3(n)(31))	0.008

1204	Flavored milk, reduced fat	11512010	Hot chocolate / Cocoa, ready to drink	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11512020	Hot chocolate / Cocoa, ready to drink, made with nonfat milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11512100	Hot chocolate / Cocoa, ready to drink, with whipped cream	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11512110	Hot chocolate / Cocoa, ready to drink, made with nonfat milk and whipped cream	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513000	Chocolate milk, made from dry mix, NS as to type of milk	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11513100	Chocolate milk, made from dry mix with whole milk	Milk products (170.3(n)(31))	0.008

1204	Flavored milk, reduced fat	11513150	Chocolate milk, made from dry mix with reduced fat milk	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11513200	Chocolate milk, made from dry mix with low fat milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11513300	Chocolate milk, made from dry mix with fat free milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513350	Chocolate milk, made from reduced sugar mix, NS as to type of milk	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11513355	Chocolate milk, made from reduced sugar mix with whole milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513360	Chocolate milk, made from reduced sugar mix with reduced fat milk	Milk products (170.3(n)(31))	0.008

1206	Flavored milk, lowfat	11513365	Chocolate milk, made from reduced sugar mix with low fat milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11513370	Chocolate milk, made from reduced sugar mix with fat free milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513380	Chocolate milk, made from dry mix, NS as to type of milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11513381	Chocolate milk, made from dry mix with whole milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513382	Chocolate milk, made from dry mix with reduced fat milk (Nesquik)	Milk products (170.3(n)(31))	0.008

1206	Flavored milk, lowfat	11513383	Chocolate milk, made from dry mix with low fat milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11513384	Chocolate milk, made from dry mix with fat free milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513390	Chocolate milk, made from no sugar added dry mix, NS as to type of milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11513391	Chocolate milk, made from no sugar added dry mix with whole milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513392	Chocolate milk, made from no sugar added dry mix with reduced fat milk (Nesquik)	Milk products (170.3(n)(31))	0.008

1206	Flavored milk, lowfat	11513393	Chocolate milk, made from no sugar added dry mix with low fat milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11513394	Chocolate milk, made from no sugar added dry mix with fat free milk (Nesquik)	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513400	Chocolate milk, made from syrup, NS as to type of milk	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11513500	Chocolate milk, made from syrup with whole milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513550	Chocolate milk, made from syrup with reduced fat milk	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11513600	Chocolate milk, made from syrup with low fat milk	Milk products (170.3(n)(31))	0.008

1208	Flavored milk, nonfat	11513700	Chocolate milk, made from syrup with fat free milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513800	Chocolate milk, made from light syrup, NS as to type of milk	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11513801	Chocolate milk, made from light syrup with whole milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513802	Chocolate milk, made from light syrup with reduced fat milk	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11513803	Chocolate milk, made from light syrup with low fat milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11513804	Chocolate milk, made from light syrup with fat free milk	Milk products (170.3(n)(31))	0.008

1204	Flavored milk, reduced fat	11513850	Chocolate milk, made from sugar free syrup, NS as to type of milk	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11513851	Chocolate milk, made from sugar free syrup with whole milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11513852	Chocolate milk, made from sugar free syrup with reduced fat milk	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11513853	Chocolate milk, made from sugar free syrup with low fat milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11513854	Chocolate milk, made from sugar free syrup with fat free milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11514100	Hot chocolate / Cocoa, made with dry mix and water	Milk products (170.3(n)(31))	0.008

1202	Flavored milk, whole	11514110	Hot chocolate / Cocoa, made with dry mix and whole milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11514120	Hot chocolate / Cocoa, made with dry mix and reduced fat milk	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11514130	Hot chocolate / Cocoa, made with dry mix and low fat milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11514140	Hot chocolate / Cocoa, made with dry mix and fat free milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11514310	Hot chocolate / Cocoa, made with no sugar added dry mix and water	Milk products (170.3(n)(31))	0.008

1202	Flavored milk, whole	11514320	Hot chocolate / Cocoa, made with no sugar added dry mix and whole milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11514330	Hot chocolate / Cocoa, made with no sugar added dry mix and reduced fat milk	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11514340	Hot chocolate / Cocoa, made with no sugar added dry mix and low fat milk	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11514350	Hot chocolate / Cocoa, made with no sugar added dry mix and fat free milk	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11519040	Strawberry milk, NFS	Milk products (170.3(n)(31))	0.008
1202	Flavored milk, whole	11519050	Strawberry milk, whole	Milk products (170.3(n)(31))	0.008

1204	Flavored milk, reduced fat	11519105	Strawberry milk, reduced fat	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11519200	Strawberry milk, low fat	Milk products (170.3(n)(31))	0.008
1208	Flavored milk, nonfat	11519205	Strawberry milk, fat free	Milk products (170.3(n)(31))	0.008
1206	Flavored milk, lowfat	11519210	Strawberry milk, reduced sugar	Milk products (170.3(n)(31))	0.008
1204	Flavored milk, reduced fat	11526000	Milk, malted	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11531000	Eggnog	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11541110	Milk shake, home recipe, chocolate	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11541120	Milk shake, home recipe, flavors other than chocolate	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11541130	Milk shake, home recipe, chocolate, light	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11541135	Milk shake, home recipe, flavors other than chocolate, light	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11541400	Milk shake with malt	Milk products (170.3(n)(31))	0.008

1402	Milk shakes and other dairy drinks	11542100	Milk shake, fast food, chocolate	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11542200	Milk shake, fast food, flavors other than chocolate	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11543000	Milk shake, bottled, chocolate	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11543010	Milk shake, bottled, flavors other than chocolate	Milk products (170.3(n)(31))	0.008
1402	Milk shakes and other dairy drinks	11560000	Chocolate milk drink	Milk products (170.3(n)(31))	0.008
9999	Not included in a food category	11810000	Milk, dry, not reconstituted, NS as to fat content	Milk products (170.3(n)(31))	0.024
9999	Not included in a food category	11811000	Milk, dry, not reconstituted, whole	Milk products (170.3(n)(31))	0.024
9999	Not included in a food category	11812000	Milk, dry, not reconstituted, low fat (1%)	Milk products (170.3(n)(31))	0.024
9999	Not included in a food category	11813000	Milk, dry, not reconstituted, fat free (skim)	Milk products (170.3(n)(31))	0.024
1820	Yogurt, regular	42401100	Yogurt, coconut milk	Milk products (170.3(n)(31))	0.024

5704	Candy not containing chocolate	44201000	Carob chips	Soft candy 170.3 (n)(38))	0.067
5402	Cereal bars	53710400	Cereal or granola bar (General Mills Fiber One Chewy Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710500	Cereal or granola bar (Kellogg's Nutri-Grain Cereal Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710502	Cereal or granola bar (Kellogg's Nutri-Grain Yogurt Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710504	Cereal or granola bar (Kellogg's Nutri-Grain Fruit and Nut Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710600	Milk 'n Cereal bar	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710700	Cereal or granola bar (Kellogg's Special K bar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53710800	Cereal or granola bar (Kashi Chewy)	Snack foods (170.3 (n)(37))	0.25

5404	Nutrition bars	53710802	Cereal or granola bar (Kashi Crunchy)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710810	Cereal or granola bar (KIND Fruit and Nut Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710900	Cereal or granola bar (General Mills Nature Valley Chewy Trail Mix)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710902	Cereal or granola bar, with yogurt coating (General Mills Nature Valley Chewy Granola Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53710904	Cereal or granola bar (General Mills Nature Valley Sweet and Salty Granola Bar)	Snack foods (170.3 (n)(37))	0.25

5402	Cereal bars	53710906	Cereal or granola bar (General Mills Nature Valley Crunchy Granola Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53711000	Cereal or granola bar (Quaker Chewy Granola Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53711002	Cereal or granola bar (Quaker Chewy 90 Calorie Granola Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53711004	Cereal or granola bar (Quaker Chewy 25% Less Sugar Granola Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53711006	Cereal or granola bar (Quaker Chewy Dipps Granola Bar)	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53711100	Cereal or granola bar (Quaker Granola Bites)	Snack foods (170.3 (n)(37))	0.25

5402	Cereal bars	53712000	Snack bar, oatmeal	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53712100	Cereal or Granola bar, NFS	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53712200	Cereal or granola bar, lowfat, NFS	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53712210	Cereal or granola bar, nonfat	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53713000	Cereal or granola bar, reduced sugar, NFS	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53713010	Cereal or granola bar, fruit and nut	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53713100	Cereal or granola bar, peanuts , oats, sugar, wheat germ	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714200	Cereal or granola bar, chocolate coated, NFS	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714210	Cereal or granola bar, with coconut, chocolate coated	Snack foods (170.3 (n)(37))	0.25

5402	Cereal bars	53714220	Cereal or granola bar with nuts, chocolate coated	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714230	Cereal or granola bar, oats, nuts, coated with non-chocolate coating	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714250	Cereal or granola bar, coated with non-chocolate coating	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714300	Cereal or granola bar, high fiber, coated with non-chocolate yogurt coating	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714400	Cereal or granola bar, with rice cereal	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714500	Breakfast bar, NFS	Snack foods (170.3 (n)(37))	0.25

5402	Cereal bars	53714510	Breakfast bar, date, with yogurt coating	Snack foods (170.3 (n)(37))	0.25
5402	Cereal bars	53714520	Breakfast bar, cereal crust with fruit filling, lowfat	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720100	Nutrition bar (Balance Original Bar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720200	Nutrition bar (Clif Bar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720210	Nutrition bar (Clif Kids Organic Zbar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720300	Nutrition bar (PowerBar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720400	Nutrition bar (Slim Fast Original Meal Bar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720500	Nutrition bar (Snickers Marathon Protein Bar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720600	Nutrition bar (South Beach Living Meal Bar)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720610	Nutrition bar (South Beach Living High Protein Bar)	Snack foods (170.3 (n)(37))	0.25

5404	Nutrition bars	53720700	Nutrition bar (Tiger's Milk)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53720800	Nutrition bar (Zone Perfect Classic Crunch)	Snack foods (170.3 (n)(37))	0.25
5404	Nutrition bars	53729000	Nutrition bar or meal replacement bar, NFS	Snack foods (170.3 (n)(37))	0.25
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57000100	Cereal, oat, NFS	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57100100	Cereal, ready-to-eat, NFS	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57101000	Cereal (Kellogg's All-Bran)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57103000	Cereal (Post Alpha-Bits)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57103100	Cereal, O's, flavored	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57104000	Cereal (Kellogg's Apple Jacks)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57106050	Cereal (Post Great Grains Banana Nut Crunch)	Breakfast cereals (170.3 (n)(4))	0.133

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57106060	Cereal (General Mills Cheerios Banana Nut)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57106260	Cereal (General Mills Cheerios Berry Burst)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57117000	Cereal (Quaker Cap'n Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57117500	Cereal (Quaker Christmas Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57119000	Cereal, crunch	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57120000	Cereal (Quaker Cap'n Crunch's Peanut Butter Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57123000	Cereal, O's, plain	Breakfast cereals (170.3 (n)(4))	0.133

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124030	Cereal (General Mills Chex Chocolate)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124050	Cereal (General Mills Chex Cinnamon)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124100	Cereal (General Mills Cheerios Chocolate)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124200	Cereal, chocolate puffs	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57124300	Cereal (General Mills Lucky Charms Chocolate)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57125000	Cereal, cinnamon toast	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57125010	Cereal (General Mills 25% Less Sugar Cinnamon Toast Crunch)	Breakfast cereals (170.3 (n)(4))	0.067

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57125900	Cereal (General Mills Honey Nut Clusters)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57126000	Cereal, chocolate crispy	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57127000	Cereal (Post Cocoa Pebbles)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57128000	Cereal (General Mills Cocoa Puffs)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57130000	Cereal (General Mills Cookie Crisp)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57132000	Cereal, corn squares	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57134000	Cereal, corn flakes, plain	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57135000	Cereal (Kellogg's Corn Flakes)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57137000	Cereal, corn puffs	Breakfast cereals (170.3 (n)(4))	0.133

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57139000	Cereal (General Mills Count Chocula)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57143000	Cereal (Kellogg's Cracklin' Oat Bran)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57143500	Cereal (Post Great Grains, Cranberry Almond Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57148000	Cereal (Kellogg's Crispix)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57151000	Cereal, rice crispy, plain	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57206700	Cereal (General Mills Fiber One)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57206710	Cereal (General Mills Fiber One Honey Clusters)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57206715	Cereal (General Mills Fiber One Raisin Bran Clusters)	Breakfast cereals (170.3 (n)(4))	0.067

4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57207000	Cereal, bran flakes, plain	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57208000	Cereal (Kellogg's All-Bran Complete Wheat Flakes)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57209000	Cereal (Post Bran Flakes)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57211000	Cereal (General Mills Frankenberry)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57213000	Cereal (Kellogg's Froot Loops)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57213010	Cereal (Kellogg's Froot Loops Marshmallow)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57213850	Cereal (General Mills Cheerios Frosted)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57214000	Cereal, shredded wheat, flavored	Breakfast cereals (170.3 (n)(4))	0.133

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57216000	Cereal, rice crispy, flavored	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57221700	Cereal, fruit rings	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57221810	Cereal (General Mills Cheerios Fruity)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57223000	Cereal, fruit crispy	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57224000	Cereal (General Mills Golden Grahams)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57227000	Cereal, granola	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57228000	Granola, homemade	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57229000	Cereal (Kellogg's Low Fat Granola)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57230000	Cereal (Post Grape-Nuts)	Breakfast cereals (170.3 (n)(4))	0.133

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57231200	Cereal (Post Great Grains Raisins, Dates, and Pecans)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57237100	Cereal, oat bunches	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57237200	Cereal (Post Honey Bunches of Oats with Vanilla Bunches)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57237300	Cereal (Post Honey Bunches of Oats with Almonds)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57238000	Cereal (Post Honeycomb)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57240100	Cereal, corn squares, flavored	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57241000	Cereal, O's, honey nut	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57241200	Cereal (Post Shredded Wheat Honey Nut)	Breakfast cereals (170.3 (n)(4))	0.133

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57243000	Cereal (Kellogg's Honey Smacks)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301500	Cereal (Kashi 7 Whole Grain Puffs)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301505	Cereal (Kashi Autumn Wheat)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301510	Cereal (Kashi GOLEAN)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57301511	Cereal (Kashi GOLEAN Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57301512	Cereal (Kashi GOLEAN Crunch Honey Almond Flax)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301530	Cereal (Kashi Heart to Heart Honey Toasted Oat)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57301600	Cereal, multigrain	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57303100	Cereal (General Mills Kix)	Breakfast cereals (170.3 (n)(4))	0.133

4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57303105	Cereal (General Mills Honey Kix)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57303200	Cereal (Kellogg's Krave)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57304100	Cereal, oat squares	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305100	Cereal (General Mills Lucky Charms)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305150	Cereal, frosted oats with marshmallows	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57305160	Cereal (Malt-O-Meal Blueberry Muffin Tops)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305165	Cereal (Malt-O-Meal Cinnamon Toasters)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305170	Cereal (Malt-O-Meal Coco-Roos)	Breakfast cereals (170.3 (n)(4))	0.067

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305174	Cereal (Malt-O-Meal Colossal Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305175	Cereal (Malt-O-Meal Cocoa Dyno-Bites)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305180	Cereal (Malt-O-Meal Corn Bursts)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305210	Cereal (Malt-O-Meal Frosted Flakes)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305300	Cereal (Malt-O-Meal Fruity Dyno-Bites)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305400	Cereal (Malt-O-Meal Honey Graham Squares)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305500	Cereal (Malt-O-Meal Honey Nut Toasty O's)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57305600	Cereal (Malt-O-Meal Marshmallow Mateys)	Breakfast cereals (170.3 (n)(4))	0.067

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57306500	Cereal (Malt-O-Meal Golden Puffs)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57306700	Cereal (Malt-O-Meal Toasted Oat Cereal)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57306800	Cereal (Malt-O-Meal Tootie Fruities)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57308190	Cereal, muesli	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57308400	Cereal, O's, multigrain	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57309100	Cereal (Nature Valley Granola)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316380	Cereal (General Mills Cheerios Oat Cluster Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316385	Cereal (General Mills Cheerios Protein)	Breakfast cereals (170.3 (n)(4))	0.067

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316450	Cereal (General Mills Oatmeal Crisp with Almonds)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57316710	Cereal (Quaker Honey Graham Oh's)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57320500	Cereal (Quaker Granola with Oats, Honey, and Raisins)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57321900	Cereal (Nature's Path Organic Flax Plus)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57326000	Cereal (Barbara's Puffins)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57327450	Cereal (Quaker Toasted Oat Bran)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57327500	Cereal (Quaker Oatmeal Squares)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57329000	Cereal, bran flakes, flavored	Breakfast cereals (170.3 (n)(4))	0.067

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57330000	Cereal (Kellogg's Raisin Bran)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57330010	Cereal (Kellogg's Raisin Bran Crunch)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57331000	Cereal (Post Raisin Bran)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57332100	Cereal (General Mills Raisin Nut Bran)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57335550	Cereal (General Mills Reese's Puffs)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57336000	Cereal, rice squares	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57337000	Cereal, rice flakes	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57339000	Cereal (Kellogg's Rice Krispies)	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57339500	Cereal (Kellogg's Rice Krispies Treats Cereal)	Breakfast cereals (170.3 (n)(4))	0.067

4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57340000	Cereal, puffed rice	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57341200	Cereal (Kellogg's Smart Start Strong)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57341300	Cereal (Kellogg's Smorz)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57344000	Cereal, K's, plain	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344001	Cereal (Kellogg's Special K Blueberry)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344005	Cereal (Kellogg's Special K Chocolatey Delight)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344010	Cereal, K's, flavored	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344015	Cereal (Kellogg's Special K Fruit & Yogurt)	Breakfast cereals (170.3 (n)(4))	0.067

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344020	Cereal (Kellogg's Special K Vanilla Almond)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57344025	Cereal (Kellogg's Special K Cinnamon Pecan)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57347000	Cereal, flavored puffs	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57348000	Cereal, corn flakes, flavored	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57349000	Cereal (Kellogg's Frosted Flakes)	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57355000	Cereal (Post Golden Crisp)	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57401100	Cereal, O's, NFS	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57407100	Cereal (General Mills Trix)	Breakfast cereals (170.3 (n)(4))	0.067

4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57408100	Cereal (Uncle Sam)	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57411000	Cereal, wheat squares	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57416000	Cereal, plain puffs	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57416010	Cereal, puffed wheat, sweetened	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57417000	Cereal, shredded wheat, plain	Breakfast cereals (170.3 (n)(4))	0.133
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57418000	Cereal, wheat flakes	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420100	Cereal, other, NFS	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57420110	Cereal, other, plain	Breakfast cereals (170.3 (n)(4))	0.133
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420120	Cereal, other, fruit flavored	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420130	Cereal, other, chocolate	Breakfast cereals (170.3 (n)(4))	0.067

4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420140	Cereal, other, peanut butter	Breakfast cereals (170.3 (n)(4))	0.067
4602	Ready-to-eat cereal, higher sugar (>21.2g/100g)	57420150	Cereal, other, honey	Breakfast cereals (170.3 (n)(4))	0.067
4604	Ready-to-eat cereal, lower sugar (=<21.2g/100g)	57420160	Cereal, reduced sugar	Breakfast cereals (170.3 (n)(4))	0.133
9999	Not included in a food category	57602500	Cereal, oat bran, ready-to-eat	Breakfast cereals (170.3 (n)(4))	0.067
5704	Candy not containing chocolate	91700010	Candy, NFS	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91700500	M&M's Almond Chocolate Candies	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91701010	Almonds, chocolate covered candy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91701020	Almonds, sugar-coated	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91701030	Almonds, yogurt-covered	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91702010	Butterscotch morsels	Soft candy 170.3 (n)(38))	0.067

5704	Candy not containing chocolate	91703010	Caramel, chocolate-flavored roll	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91703020	Caramel, flavor other than chocolate	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91703030	Caramel, with nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703040	Caramel candy, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703050	Caramel with nuts and cereal, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703060	Caramel with nuts, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703070	Rolo	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91703080	Caramel, all flavors, sugar free	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703150	Toblerone, milk chocolate with honey and almond nougat	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91703200	TWIX Caramel Cookie Bars	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703250	TWIX Chocolate Fudge Cookie Bars	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703300	TWIX Peanut Butter Cookie Bars	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703400	Whatchamacallit	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91703500	Nuts, carob-coated	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91703600	Espresso coffee beans, chocolate-covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705005	Chocolate candy, other, NFS	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705010	Chocolate candy	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705012	Chocolate candy with nuts, other, NFS	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705015	Chocolate candy with nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705020	Chocolate candy with cereal	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91705030	Kit Kat	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705040	Chocolate, milk, with nuts, not almond or peanuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705050	Milk chocolate candy, with fruit and nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705060	Milk chocolate candy, with almonds	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705070	Chocolate, milk, with peanuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705080	Chocolate candy, cookie filled	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705090	Chocolate candy with fondant and caramel	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705200	Chocolate chips	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91705250	Candy, sprinkles	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705290	Dark chocolate candy, other, NFS	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91705300	Dark chocolate candy	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705310	Chocolate, sweet or dark, with almonds	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705312	Dark chocolate candy with nuts, other, NFS	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705315	Dark chocolate candy with nuts	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91705400	White chocolate candy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91705410	Chocolate, white, with almonds	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91705420	Chocolate, white, with cereal	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91705430	Kit Kat White	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705440	Chocolate candy, fudge	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705450	Chocolate candy, caramel filled	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91705460	Chocolate candy, caramel filled with nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705470	Chocolate candy, coconut filled	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705480	Chocolate candy, cream filled	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705500	Mexican chocolate, tablet	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705510	Chocolate candy, nougat filled	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705520	Chocolate candy, nougat filled with nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705530	Chocolate candy, peanut butter filled	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91705550	Chocolate candy with dried fruit	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91706000	Coconut candy, chocolate covered	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91706010	Chocolate candy, sugar free	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91706020	Candy, non chocolate, other, NFS	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91706100	Coconut candy, no chocolate covering	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91706400	Coconut candy, Puerto Rican style	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91707000	Fondant	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91707010	Fondant, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708000	Fruit peel, candied	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708010	Date candy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708020	Soft fruit confections	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708030	Fruit leather and fruit snacks candy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708040	Fun Fruits Creme Supremes	Soft candy 170.3 (n)(38))	0.067

5704	Candy not containing chocolate	91708070	Tamarind candy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708100	Fruit snacks candy, with high vitamin C	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708150	Yogurt covered fruit snacks candy, with added vitamin C	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91708160	Yogurt covered fruit snacks candy rolls, with high vitamin C	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91709000	Gumdrops, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91713010	Fudge, chocolate, chocolate-coated	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91713020	Fudge, chocolate, chocolate-coated, with nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91713030	Fudge, chocolate	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91713040	Fudge, chocolate, with nuts	Soft candy 170.3 (n)(38))	0.067

5704	Candy not containing chocolate	91713050	Fudge, peanut butter	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91713060	Fudge, peanut butter, with nuts	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91713070	Fudge, vanilla	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91713080	Fudge, vanilla, with nuts	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91713090	Fudge, divinity	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91713100	Fudge, brown sugar, penuche	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91715000	Fudge, caramel and nut, chocolate-coated candy	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91715100	SNICKERS Bar	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91715200	Baby Ruth	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91715300	100 GRAND Bar	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91716010	Halvah, plain	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91716110	Halvah, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91718000	Honey-combed hard candy with peanut butter	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91718050	Honey-combed hard candy with peanut butter, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91718100	Butterfinger	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91718110	Butterfinger Crisp	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91718200	Chocolate-flavored sprinkles	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91718300	Ladoo, round ball	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91721000	Candy, licorice	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91723000	Candy, marshmallow	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91723010	Marshmallow, chocolate covered	Soft candy 170.3 (n)(38))	0.067

5704	Candy not containing chocolate	91723020	Marshmallow, candy-coated	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91723030	Candy, caramel	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91726000	Nougat, plain	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91726110	Nougat, with caramel, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91726130	MILKY WAY Bar	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91726140	MILKY WAY MIDNIGHT Bar	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91726150	MARS Almond Bar	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91726410	Nougat, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91726420	3 MUSKETEERS Bar	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91726425	3 Musketeers Truffle Crisp Bar	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91727010	Nuts, chocolate covered, not almonds or peanuts	Soft candy 170.3 (n)(38))	0.067

5704	Candy not containing chocolate	91728000	Candy, nougat with nuts	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91728500	Sugared pecans, sugar and egg white coating	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91731000	Peanuts, chocolate covered candy	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91731010	M&M's Peanut Chocolate Candies	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91731060	M&M's Peanut Butter Chocolate Candies	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91731100	Peanuts, sugar-coated	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91731150	Peanuts, yogurt covered	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91732000	Peanut bar	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91732100	Planters Peanut Bar	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91733000	Candy, peanut brittle	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91733200	Peanut Bar, chocolate covered candy	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91734000	Peanut butter, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91734100	Reese's Peanut Butter Cup	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91734200	Reese's Pieces	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91734300	Reese's Sticks	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91734400	Reese's Fast Break	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91734450	Reese's Crispy Crunchy Bar	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91734500	Peanut butter morsels	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91735000	Pralines	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91736000	Pineapple candy, Puerto Rican style	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91739010	Raisins, chocolate covered	Soft candy 170.3 (n)(38))	0.067

5704	Candy not containing chocolate	91739600	Raisins, yogurt covered	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91742010	Sesame Crunch, Sahadi	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745000	Candy, mint	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745010	Candy, gummy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745020	Hard candy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745025	Candy, hard	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745030	Candy, lollipop	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745035	Cough drops	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745040	Butterscotch hard candy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745050	Candy, cotton	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91745100	Skittles	Soft candy 170.3 (n)(38))	0.067

5704	Candy not containing chocolate	91745110	Candy, fruit flavored pieces	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91746010	Sugar-coated chocolate discs	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91746100	Chocolate candy, candy shell	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91746110	Chocolate candy, candy shell with nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91746120	Sixlets	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91746150	Easter egg, candy coated chocolate	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91746200	M&M's Pretzel Chocolate Candies	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91746300	Candy, fruit snacks	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91746350	Candy, fruit leather	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91750000	Candy, taffy	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91760000	Toffee, plain	Soft candy 170.3 (n)(38))	0.067

5702	Candy containing chocolate	91760100	Toffee, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91760200	Toffee, chocolate-coated, with nuts	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91760500	Truffles	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91760700	Wax candy, liquid filled	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91770000	Dietetic or low calorie candy, NFS	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91770010	Dietetic or low calorie gumdrops	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91770020	Dietetic or low calorie hard candy	Soft candy 170.3 (n)(38))	0.067
5702	Candy containing chocolate	91770030	Dietetic or low calorie candy, chocolate covered	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91770050	Dietetic or low calorie mints	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91770060	Candy, non chocolate, sugar free	Soft candy 170.3 (n)(38))	0.067
5704	Candy not containing chocolate	91800100	Chewing gum, NFS	Chewing gum (170.3 (n)(6))	0.667

5704	Candy not containing chocolate	91801000	Chewing gum	Chewing gum (170.3 (n)(6))	0.667
5704	Candy not containing chocolate	91802000	Chewing gum, sugar free	Chewing gum (170.3 (n)(6))	0.667
7302	Coffee	92100000	Coffee, NS as to type	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92100500	Coffee, NS as to brewed or instant	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101000	Coffee, brewed	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101500	Coffee, brewed, blend of regular and decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101600	Coffee, Turkish	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101610	Coffee, espresso	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101630	Coffee, espresso, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101700	Coffee, brewed, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101800	Coffee, Cuban	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101810	Coffee, macchiato	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92101820	Coffee, macchiato, sweetened	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101850	Coffee, cafe con leche	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101851	Coffee, cafe con leche, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101900	Coffee, Latte	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101901	Coffee, Latte, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101903	Coffee, Latte, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101904	Coffee, Latte, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101905	Coffee, Latte, nonfat, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101906	Coffee, Latte, with non-dairy milk, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101910	Coffee, Latte, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101911	Coffee, Latte, decaffeinated, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101913	Coffee, Latte, decaffeinated, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92101917	Coffee, Latte, decaffeinated, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101918	Coffee, Latte, decaffeinated, nonfat, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101919	Coffee, Latte, decaffeinated, with non-dairy milk, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101920	Frozen coffee drink	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101921	Frozen coffee drink, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101923	Frozen coffee drink, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101925	Frozen coffee drink, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101926	Frozen coffee drink, nonfat, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92101928	Frozen coffee drink, with non-dairy milk and whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101930	Frozen coffee drink, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101931	Frozen coffee drink, decaffeinated, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101933	Frozen coffee drink, decaffeinated, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101935	Frozen coffee drink, decaffeinated, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101936	Frozen coffee drink, decaffeinated, nonfat, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92101938	Frozen coffee drink, decaffeinated, with non-dairy milk and whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101950	Coffee, Cafe Mocha	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101955	Coffee, Cafe Mocha, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101960	Coffee, Cafe Mocha, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101965	Coffee, Cafe Mocha, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101970	Coffee, Cafe Mocha, decaffeinated, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92101975	Coffee, Cafe Mocha, decaffeinated, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102000	Frozen mocha coffee drink	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102010	Frozen mocha coffee drink, nonfat	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92102020	Frozen mocha coffee drink, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102030	Frozen mocha coffee drink, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102040	Frozen mocha coffee drink, nonfat, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102050	Frozen mocha coffee drink, with non-dairy milk and whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102060	Frozen mocha coffee drink, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102070	Frozen mocha coffee drink, decaffeinated, nonfat	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92102080	Frozen mocha coffee drink, decaffeinated, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102090	Frozen mocha coffee drink, decaffeinated, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102100	Frozen mocha coffee drink, decaffeinated, nonfat, with whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102110	Frozen mocha coffee drink, decaffeinated, with non-dairy milk and whipped cream	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102400	Iced Coffee, brewed	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102401	Iced Coffee, brewed, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92102450	Iced Coffee, pre-lightened and pre-sweetened	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102500	Coffee, Iced Latte	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102501	Coffee, Iced Latte, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102502	Coffee, Iced Latte, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102503	Coffee, Iced Latte, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102504	Coffee, Iced Latte, nonfat, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102505	Coffee, Iced Latte, with non-dairy milk, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102510	Coffee, Iced Latte, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102511	Coffee, Iced Latte, decaffeinated, nonfat	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92102512	Coffee, Iced Latte, decaffeinated, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102513	Coffee, Iced Latte, decaffeinated, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102514	Coffee, Iced Latte, decaffeinated, nonfat, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102515	Coffee, Iced Latte, decaffeinated, with non-dairy milk, flavored	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102600	Coffee, Iced Cafe Mocha	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102601	Coffee, Iced Cafe Mocha, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102602	Coffee, Iced Cafe Mocha, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102610	Coffee, Iced Cafe Mocha, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92102611	Coffee, Iced Cafe Mocha, decaffeinated, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92102612	Coffee, Iced Cafe Mocha, decaffeinated, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92103000	Coffee, instant, reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92104000	Coffee, instant, 50% less caffeine, reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92111000	Coffee, NS as to brewed or instant, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92111010	Coffee, brewed, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92114000	Coffee, instant, decaffeinated, reconstituted	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92121000	Coffee, instant, pre-lightened and pre-sweetened with sugar, reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92121001	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, reconsitituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92121010	Coffee, instant, pre-sweetened with sugar, reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92121020	Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, reconstituted	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92121030	Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92121040	Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92121041	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92121050	Coffee, mocha, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130000	Coffee, pre-lightened and pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130001	Coffee, decaffeinated, pre-lightened and pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130005	Coffee, pre-lightened and pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92130006	Coffee, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130010	Coffee, pre-lightened	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130011	Coffee, decaffeinated, pre-lightened	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130020	Coffee, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130021	Coffee, decaffeinated, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130030	Coffee, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92130031	Coffee, decaffeinated, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92152000	Coffee and chicory, brewed	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92152010	Coffee and chicory, brewed, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92161000	Coffee, Cappuccino	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92161001	Coffee, Cappuccino, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92161002	Coffee, Cappuccino, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92162000	Coffee, Cappuccino, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92162001	Coffee, Cappuccino, decaffeinated, nonfat	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92162002	Coffee, Cappuccino, decaffeinated, with non-dairy milk	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92171000	Coffee, bottled/canned	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92171010	Coffee, bottled/canned, light	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92191100	Coffee, instant, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92191105	Coffee, instant, 50% less caffeine, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92191200	Coffee, instant, decaffeinated, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92191400	Coffee, instant, pre-sweetened with sugar, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92192000	Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003

9999	Not included in a food category	92192030	Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92192040	Coffee, mocha, instant, decaffeinated, pre-lightened and pre-sweetend with low calorie sweetener, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92193000	Coffee, instant, pre-lightened and pre-sweetened with sugar, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003

9999	Not included in a food category	92193005	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92193020	Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92193025	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92201010	Coffee substitute	Coffe & tea (170.3 (n)(7))	0.003

7302	Coffee	92202010	Chicory beverage	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92203000	Cereal beverage	Coffe & tea (170.3 (n)(7))	0.003
7302	Coffee	92203110	Cereal beverage with beet roots, from powdered instant	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92302000	Tea, hot, leaf, black	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92302500	Tea, hot, leaf, black, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92303010	Tea, hot, leaf, green	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92303100	Tea, hot, leaf, green, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92304100	Tea, hot, leaf, oolong	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92305010	Tea, iced, instant, black, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92305040	Tea, iced, instant, black, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003

7304	Tea	92305050	Tea, iced, instant, black, decaffeinated, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92305090	Tea, iced, instant, black, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92305110	Tea, iced, instant, black, decaffeinated, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92305180	Tea, iced, instant, black, decaffeinated, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92305900	Tea, iced, instant, green, unsweetened	Coffe & tea (170.3 (n)(7))	0.003

7304	Tea	92305910	Tea, iced, instant, green, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92305920	Tea, iced, instant, green, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92306000	Tea, hot, herbal	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92306090	Tea, hot, hibiscus	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92306700	Tea, hot, chamomile	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92306800	Tea, hot, with milk	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92306850	Tea, ginger	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92306910	Tea, bubble	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92306920	Tea, kombucha	Coffe & tea (170.3 (n)(7))	0.003
9999	Not included in a food category	92307000	Tea, iced, instant, black, unsweetened, dry	Coffe & tea (170.3 (n)(7))	0.003

9999	Not included in a food category	92307400	Tea, iced, instant, black, pre-sweetened, dry	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92307500	Iced Tea / Lemonade juice drink	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92307510	Iced Tea / Lemonade juice drink, light	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92307520	Iced Tea / Lemonade juice drink, diet	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308000	Tea, iced, brewed, black, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308010	Tea, iced, brewed, black, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308020	Tea, iced, brewed, black, unsweetened	Coffe & tea (170.3 (n)(7))	0.003

7304	Tea	92308030	Tea, iced, brewed, black, decaffeinated, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308040	Tea, iced, brewed, black, decaffeinated, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308050	Tea, iced, brewed, black, decaffeinated, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308500	Tea, iced, brewed, green, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308510	Tea, iced, brewed, green, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003

7304	Tea	92308520	Tea, iced, brewed, green, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308530	Tea, iced, brewed, green, decaffeinated, pre-sweetened with sugar	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308540	Tea, iced, brewed, green, decaffeinated, pre-sweetened with low calorie sweetener	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92308550	Tea, iced, brewed, green, decaffeinated, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92309000	Tea, iced, bottled, black	Coffe & tea (170.3 (n)(7))	0.003

7304	Tea	92309010	Tea, iced, bottled, black, decaffeinated	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92309020	Tea, iced, bottled, black, diet	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92309030	Tea, iced, bottled, black, decaffeinated, diet	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92309040	Tea, iced, bottled, black, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92309050	Tea, iced, bottled, black, decaffeinated, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92309500	Tea, iced, bottled, green	Coffe & tea (170.3 (n)(7))	0.003
7304	Tea	92309510	Tea, iced, bottled, green, diet	Coffe & tea (170.3 (n)(7))	0.003

7304	Tea	92309520	Tea, iced, bottled, green, unsweetened	Coffe & tea (170.3 (n)(7))	0.003
7202	Soft drinks	92400000	Soft drink, NFS	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92400100	Soft drink, NFS, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7802	Flavored or carbonated water	92410110	Water, tonic	Beverages & beverage bases (170.3 (n)(3)	0.006
7802	Flavored or carbonated water	92410210	Water, carbonated, plain	Beverages & beverage bases (170.3 (n)(3)	0.006
7802	Flavored or carbonated water	92410250	Water, carbonated, flavored	Beverages & beverage bases (170.3 (n)(3)	0.006
7202	Soft drinks	92410310	Soft drink, cola	Beverages & beverage bases (170.3 (n)(3)	0.006
7202	Soft drinks	92410315	Soft drink, cola, reduced sugar	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410320	Soft drink, cola, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410340	Soft drink, cola, decaffeinated	Beverages & beverage bases (170.3 (n)(3)	0.006

7102	Diet soft drinks	92410350	Soft drink, cola, decaffeinated, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410360	Soft drink, pepper type	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410370	Soft drink, pepper type, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410390	Soft drink, pepper type, decaffeinated	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410400	Soft drink, pepper type, decaffeinated, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410410	Soft drink, cream soda	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410420	Soft drink, cream soda, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410510	Soft drink, fruit flavored, caffeine free	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410520	Soft drink, fruit flavored, diet, caffeine free	Beverages & beverage bases (170.3 (n)(3)	0.008

7202	Soft drinks	92410550	Soft drink, fruit flavored, caffeine containing	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410560	Soft drink, fruit flavored, caffeine containing, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410610	Soft drink, ginger ale	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410620	Soft drink, ginger ale, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410710	Soft drink, root beer	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410720	Soft drink, root beer, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92410810	Soft drink, chocolate flavored	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92410820	Soft drink, chocolate flavored, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7202	Soft drinks	92411510	Soft drink, cola, fruit or vanilla flavored	Beverages & beverage bases (170.3 (n)(3)	0.006

7202	Soft drinks	92411520	Soft drink, cola, chocolate flavored	Beverages & beverage bases (170.3 (n)(3)	0.006
7102	Diet soft drinks	92411610	Soft drink, cola, fruit or vanilla flavored, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7102	Diet soft drinks	92411620	Soft drink, cola, chocolate flavored, diet	Beverages & beverage bases (170.3 (n)(3)	0.008
7106	Other diet drinks	92552000	Fruit flavored drink, with high vitamin C, powdered, reconstituted, diet	Beverages & beverage bases (170.3 (n)(3)	0.006
7106	Other diet drinks	92552010	Fruit flavored drink, powdered, reconstituted, diet	Beverages & beverage bases (170.3 (n)(3)	0.006
9999	Not included in a food category	92900300	Sports drink, dry concentrate, not reconstituted	Beverages & beverage bases (170.3 (n)(3)	0.006
7802	Flavored or carbonated water	94100200	Water, non-carbonated, flavored	Beverages & beverage bases (170.3 (n)(3)	0.006
7802	Flavored or carbonated water	94100300	Water beverage, fruit flavored	Beverages & beverage bases (170.3 (n)(3)	0.006

7208	Nutritional beverages	95101000	Nutritional drink or shake, ready-to-drink (Boost)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95101010	Nutritional drink or shake, ready-to-drink (Boost Plus)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95102000	Nutritional drink or shake, ready-to-drink (Carnation Instant Breakfast)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95103000	Nutritional drink or shake, ready-to-drink (Ensure)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95103010	Nutritional drink or shake, ready-to-drink (Ensure Plus)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95104000	Nutritional drink or shake, ready-to-drink, sugar free (Glucerna)	Beverages & beverage bases (170.3 (n)(3)	0.25

7208	Nutritional beverages	95105000	Nutritional drink or shake, ready-to-drink (Kellogg's Special K Protein)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95106000	Nutritional drink or shake, ready-to-drink (Muscle Milk)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95106010	Nutritional drink or shake, ready-to-drink, light (Muscle Milk)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95110000	Nutritional drink or shake, ready-to-drink (Slim Fast)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95110010	Nutritional drink or shake, ready-to-drink, sugar free (Slim Fast)	Beverages & beverage bases (170.3 (n)(3)	0.25

7208	Nutritional beverages	95110020	Nutritional drink or shake, high protein, ready-to-drink (Slim Fast)	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95120000	Nutritional drink or shake, ready-to-drink, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95120010	Nutritional drink or shake, high protein, ready-to-drink, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95120020	Nutritional drink or shake, high protein, light, ready-to-drink, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
7208	Nutritional beverages	95120050	Nutritional drink or shake, liquid, soy-based	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95201000	Nutritional powder mix (Carnation Instant Breakfast)	Beverages & beverage bases (170.3 (n)(3)	0.25

9802	Protein and nutritional powders	95201010	Nutritional powder mix, sugar free (Carnation Instant Breakfast)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95201200	Nutritional powder mix (EAS Whey Protein Powder)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95201300	Nutritional powder mix (EAS Soy Protein Powder)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95201500	Nutritional powder mix, high protein (Herbalife)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95201600	Nutritional powder mix (Isopure)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95201700	Nutritional powder mix (Kellogg's Special K20 Protein Water)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95202000	Nutritional powder mix (Muscle Milk)	Beverages & beverage bases (170.3 (n)(3)	0.25

9802	Protein and nutritional powders	95202010	Nutritional powder mix, light (Muscle Milk)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95210000	Nutritional powder mix (Slim Fast)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95210010	Nutritional powder mix, sugar free (Slim Fast)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95210020	Nutritional powder mix, high protein (Slim Fast)	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95220000	Nutritional powder mix, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95220010	Nutritional powder mix, high protein, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95230000	Nutritional powder mix, whey based, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95230010	Nutritional powder mix, protein, soy based, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
9802	Protein and nutritional powders	95230020	Nutritional powder mix, protein, light, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25

9802	Protein and nutritional powders	95230030	Nutritional powder mix, protein, NFS	Beverages & beverage bases (170.3 (n)(3)	0.25
7206	Sport and energy drinks	95310200	Energy drink (Full Throttle)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310400	Energy drink (Monster)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310500	Energy drink (Mountain Dew AMP)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310550	Energy drink (No Fear)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310555	Energy drink (No Fear Motherload)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310560	Energy drink (NOS)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310600	Energy drink (Red Bull)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310700	Energy drink (Rockstar)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310750	Energy drink (SoBe Energize Energy Juice Drink)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95310800	Energy drink (Vault)	Beverages & beverage bases (170.3 (n)(3)	0.006

7206	Sport and energy drinks	95311000	Energy Drink	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95312560	Energy drink (Ocean Spray Cran-Energy Juice Drink)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95312900	Energy drink (XS)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95312905	Energy drink (XS Gold Plus)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95320200	Sports drink (Gatorade G)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95320500	Sports drink (Powerade)	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95321000	Sports drink, NFS	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95330100	Fluid replacement, electrolyte solution	Beverages & beverage bases (170.3 (n)(3)	0.006
7206	Sport and energy drinks	95330500	Fluid replacement, 5% glucose in water	Beverages & beverage bases (170.3 (n)(3)	0.006