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EAS CONSULTING GROUP

Specializing in FDA Regulatory Matters

May 15, 2007

Office of Food Additive Safety (HFS-255)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

RE: Notification of GRAS Determination for Phosphatidylserine

Dear Sir/Madame:

In accordance with proposed 21 CFR § 170.36 (Notice of a claim for exemption based on a GRAS determination) published in the Federal Register (62 FR 18939-18964), I am submitting in triplicate, as the agent to the notifier, Enzymotec, a GRAS Notification for phosphatidylserine, formulated under the product name Sharp PS™, for use as a nutrient in milk, flavored milk, milk drinks (excluding milk, fluid), milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, and fruit flavored drink at levels of 100 mg phosphatidylserine *per* serving and in breakfast cereals and milk, fluid at 50 mg/serving.

Please let me know if you have any questions

Sincerely

Edward A. Steele
President

Enclosures

EAS Consulting Group, LLC
1940 Duke Street, Suite 200, Alexandria, Virginia 22314
(877) 327-9808 Toll Free • (703) 684-4408 Local • (703) 684-4428 Fax

EAS CONSULTING GROUP

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I. Claim of GRAS Status

A. Claim of Exemption from the Requirement for Premarket Approval Requirements Pursuant to Proposed 21 CFR § 170.36(c)(1)

Phosphatidylserine, for use as a nutrient, has been determined to be Generally Recognized As Safe, and therefore, exempt from the requirement of premarket approval, under the conditions of its intended use as described below. The basis for this finding is described in the following sections.

Signed,

Edward A. Steele

Agent for:

Enzymotec
P.O.Box 6, Migdal HaEmeq
Israel 23106

EAS Consulting Group, LLC
1940 Duke Street, Suite 200, Alexandria, Virginia 22314
(877) 327-9808 Toll Free • (703) 684-4408 Local • (703) 684-4428 Fax

B. Name and Address of Notifier:

Iris Meiri-Bendek
Regulatory Affairs Manager
Enzymotec
P.O.Box 6, Migdal HaEmeq
Israel 23106
Telephone: 972-4-6545112
Facsimile: 972-4-6443799
Email: irisb@enzymotec.com

C. Common or usual name of the notified substance:

The common name of the substance of this notification is phosphatidylserine

D. Conditions of use:

Phosphatidylserine (Sharp•PS™) is intended for use as a nutrient in milk, flavored milk, milk drinks (excluding milk, fluid), milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, and fruit flavored drink at use levels of 100 mg phosphatidylserine *per* serving and in breakfast cereals and milk, fluid at 50 mg/serving. The serving sizes are determined by the 1994-96, 1998 Continuing Survey of Food Intake by Individuals (CSFII, 2000) Based on these determinations, the intended use of phosphatidylserine in the above mentioned food categories resulted in estimated daily intake for "users only" at mean and 90th percentile of 44.75 mg/person (0.95 mg/kg body weight/day) and 98.73 mg/person (2.51 mg/kg body weight/day), respectively.

There is sufficient qualitative and quantitative scientific evidence, including human and animal data, to determine safety-in-use for phosphatidylserine. The safety determination of phosphatidylserine is primarily based on human clinical trials and a variety of animal as well as *in vitro* studies further corroborate the human data. Results from over 35 human clinical trials show that phosphatidylserine is well-tolerated at doses from 200 to 600 mg *per* day. In animal studies no significant toxicity was noted at doses of up to 1000 mg/kg body weight/day. The adverse effects noted in animal studies at 1000 mg/kg/day were considered minor as these changes were small in magnitude, not supported by any histological damage, and lack of dose-response. On the basis of scientific procedures [1], and history of exposure from natural sources, the consumption of phosphatidylserine as an added food ingredient is considered safe at levels up to 300 mg/day. Recently, FDA has agreed to

[1] 21 CFR §170.3 Definitions (h) Scientific procedures include those human, animal, analytical, and other scientific studies, whether published or unpublished, appropriate to establish the safety of a substance

exercise enforcement discretion with a Health Claim Petition [2] on phosphatidylserine, in which the petitioner demonstrated that soy-derived phosphatidylserine is safe at levels up to 500 mg/day.[3]

The estimated daily intake of phosphatidylserine from its intended uses at the 90th percentile of 98.73 mg/person (2.51 mg/kg/day) is below the safe levels of intake in humans of 300 mg of phosphatidylserine/person *per* day (5 mg/kg/day). The estimated daily intake, if ingested daily over a lifetime, is considered safe.

E. Basis for GRAS Determination:

In accordance with 21 CFR § 170.30, the intended use of phosphatidylserine has been determined to be generally recognized as safe (GRAS) based on scientific procedures. A comprehensive search of the scientific literature was also utilized for this review.

F. Availability of Information:

The data and information that forms the basis for this GRAS determination will be provided to Food and Drug Administration upon request and are located at the offices of:

Iris Meiri-Bendek
Regulatory Affairs Manager
Enzymotec
P.O.Box 6, Migdal HaEmeq
Israel 23106
Telephone: 972-4-6545112
Facsimile: 972-4-6443799
Email: irisb@enzymotec.com

II. Detailed Information About the Identity of the Notified Substance:

A. Chemical name

Phosphatidylserine. Per IUPAC-CBN nomenclature, it is a 1,2-diacyl-*sn*-glycero-3-phospho-L-serine.

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[2] Letter Regarding Dietary Supplement Health Claim for Phosphatidylserine and Cognitive Dysfunction and Dementia" (2003) Available at: http://www.cfsan.fda.gov/~dms/ds-ltr33.html

[3] Petition for Health Claim: Phosphatidylserine and Cognitive Dysfunction, Phosphatidylserine and Dementia (2002) Available at: http://www.fda.gov/ohrms/dockets/dailys/02/Sep02/091302/80027351.pdf

B. Trade Name:

The subject of this notification will be marketed as Sharp•PS™.

C. Chemical Abstract Registry Number:

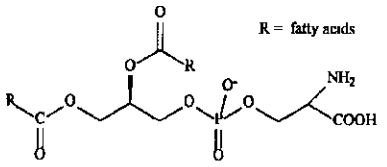
84776-79-4

D. Chemical Formula:

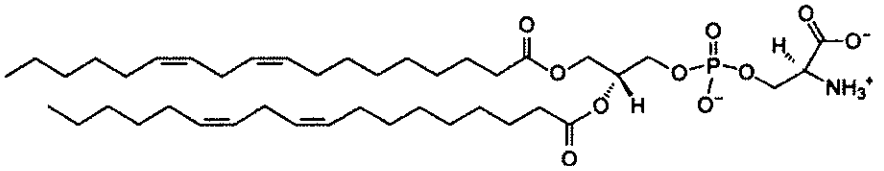
The empirical formula of the most abundant phosphatidylserine molecule in Sharp•PS™ (comprising two linoleic acids) is $C_{42}H_{73}O_{10}PNCa$

E. Structure:

Phosphatidylserine consists of a glycerophosphate skeleton conjugated with 2 fatty acids and L-serine *via* a phosphodiester linkage. The structural diagram below shows the general representation of glycerophosphate backbone with R as fatty acids. The counter ion for the phosphate moiety is Ca^{+}.



General structure of phosphatidylserine



Most abundant form (the counter ion for the phosphate moiety is Ca^{+})

F. Fatty Acid Profile:

The mean percentage of the fatty acids in Sharp•PS™ is presented in the following table

Fatty acid	Percentage*
Palmitic acid (C16·0)	14
Stearic acid (C18:0)	4
Oleic acid (C18·1)	15
Linoleic acid (C18·2)	62
Linolenic acid (C18.3)	5
Total	100
*As % of total fatty acids	

G. Molecular Weight

Based on the fatty acid profile given above, the average molecular weight of Sharp•PS™ is 819 Daltons.

H. Physical Characteristics

Sharp•PS™ is produced as an off-white to yellow-colored powder.

I. Typical Composition and Specifications

Typical compositional analysis and specifications of Sharp•PS™ are presented in the following Tables:

Typical compositional analysis of Sharp•PS™

Parameter	Typical values	Assay method
Phosphatidylserine	72%	HPTLC (AM-010)/^{31}P-NMR
Phosphatidic acid	10.6%	^{31}P-NMR
Lyso-phosphatidylserine	0.5%	^{31}P-NMR
Lyso-phosphatidic acid	0 3%	^{31}P-NMR
Phosphatidylethanolamine	1%	^{31}P-NMR
Other phospholipids	3.3%	^{31}P-NMR
Glycerides (Tri-, Di- and Mono-)	2.8%	AM-034
Sodium (Na^+)	277 ppm	AOAC 985.01
Calcium (Ca^{++})	2 5 %	AOAC 985 01
Chloride (Cl^-)	0 2 ppm	AOAC960.29
Free L-Serine	<0.1%	ACS 8th edition, page 491
Total phytosterols	0.028%	Capillary GC (According to Slover *et al*, Determination of tocopherols and sterols.)
Tocopherol	0.2 %	AOCS Ce 8-89
Ash	12.7%	AOAC 923.03
Heavy metals		
Lead (ppm)	<0.2	ICP
Arsenic (ppm)	<0 2	ICP
Cadmium (ppm)	<0.03	ICP

Typical compositional analysis of Sharp•PS™

Parameter	Typical values	Assay method
Mercury (ppm)	<0.2	ICP

Specifications of Sharp•PS™

Parameter	Specification	Assay method
Consistency	Powder	
Color	Off-white to light yellow	
Peroxide value	< 5 meq/kg	Modified AOCS official method Cd 8-53
Moisture	<2.0%	LOC using Precisa moisture analyzer with Halogen heat
Phosphatidylserine	60-80%	HPTLC (AM-010)/^{31}P-NMR
Ethanol residues	<1000 ppm	GC/MS Headspace
Microbiological assays		
Total plate count	< 1000 cfu/g	Israeli Standard SI 885 part 3 (1999)
Yeast and Mold	< 100 cfu/g	Israeli Standard SI 885 part 3 (1999)
Molds	< 100 cfu/g	Israeli Standard SI 885 part 3 (1999)
Coliform bacteria	Negative (cfu/g)	USP 61 (2000)
Staphylococcus aureus	Negative (cfu/g)	USP 61 (2000)
Salmonella	Negative (cfu/20 g)	Israeli Standard SI 885 part 3 (1999)
Shelf life	24 months	

cfu = colony forming units

J. Manufacturing process

High phosphatidylcholine enriched soybean lecithin, meeting Food Chemical Codex specifications, is used as a starting material in the manufacture of Sharp•PS™. Sharp•PS™ is produced through enzymatic transphosphatidylation of the enriched lecithin phospholipids with L-serine using a phospholipase enzyme, which catalyses the substitution of the choline head-group with serine to form phsophatidylserine. The enzyme used for transphosphatidylation is derived from a microorganism that is nonpathogenic and nontoxicogenic. The enzyme treatment does not alter the fatty acids attached to the molecule or its stereochemistry. Following the enzymatic reaction, the solid product is separated from the reaction mixture, purified and dried. Food grade antioxidants are added to the product in accordance with good manufacturing practices. Processing aids used such as acetic acid, sodium hydroxide, calcium chloride, and ethyl alcohol are of food grade quality as specified in Food Chemical Codex. Phosphatidylserine is manufactured in accordance with current good manufacturing practices (cGMP).

K. Intended Technical Effects

While there is no Reference Daily Intake, the nutritive contribution of phopshatidylserine is widely recognized. It is naturally occurring nutritive component in a variety of foods, but is found at high levels only in certain fish, poultry and meats (especially organ meats). The supplementation of phosphatidylserine through foods is to provide a nutrient for brain function. Although phosphatidylserine is present at certain levels in the diet, its supplementation to food is aimed at gaining certain health benefits. The level of phosphatidylserine required to achieve the health benefits was determined through intervention trials in which people consumed phosphatidylserine as a supplement to their diet (whether regular or vegetarian).

III. Summary of the Basis for the Notifier's Determination that Phosphatidylserine (Sharp•PS™) is GRAS

An independent panel of recognized experts, qualified by their scientific training and relevant national and international experience to evaluate the safety of food and food ingredients, was requested by Enzymotec to determine the Generally Recognized As Safe (GRAS) status of phosphatidylserine (Sharp•PS™) intended for use as a dietary nutrient. A comprehensive search of the scientific literature was also utilized for this review.

Based on a critical evaluation of the pertinent data and information summarized here, the Expert Panel members have individually and collectively determined by scientific procedures that addition of phosphatidylserine to milk, flavored milk, milk drinks, milk analogs (soy milk), milk-based meal replacement, yogurt, breakfast bars, breakfast cereals and fruit flavored drink, meeting the specification cited above and manufactured according to current Good Manufacturing Practice, is Generally Recognized As Safe (GRAS) under the conditions of intended use in selected foods, as specified herein.

In coming to its decision that phosphatidylserine is GRAS, the Expert Panel relied upon, the conclusions that neither phosphatidylserine nor any of its degradation products pose any toxicological hazards or safety concerns at the intended use levels, as well as published toxicology studies and other articles relating to the safety of the product. It is also their opinion that other qualified and competent scientists, reviewing the same publicly available toxicological and safety information, would reach the same conclusion.

IV. Basis for a Conclusion that Phosphatidylserine is GRAS for its Intended Use.

EXPERT PANEL STATEMENT

DETERMINATION OF THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF PHOSPHATIDYLSERINE AS A NUTRIENT

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DETERMINATION OF THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF PHOSPHATIDYLSERINE AS A NUTRIENT

1. INTRODUCTION

The undersigned, an independent panel of recognized experts (hereinafter referred to as the Expert Panel)[4], qualified by their scientific training and relevant national and international experience to evaluate the safety of food and food ingredients, was convened by EAS Consulting Group, LLC, at the request of Enzymotec, Israel, to determine the Generally Recognized As Safe (GRAS) status of phosphatidylserine (Sharp•PS™) as a nutrient [21 CFR§170.3(o)(20)][5] in milk, flavored milk, milk drinks (excluding milk fluid), milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, and fruit flavored drink at use levels of 100 mg phosphatidylserine *per* serving, and in breakfast cereals and milk fluid at 50 mg/serving. A comprehensive search of the scientific literature for safety and toxicity information on phosphatidylserine was conducted through January 2007 and made available to the Expert Panel. The Expert Panel independently and critically evaluated materials submitted by Enzymotec and other information deemed appropriate or necessary. Following an independent, critical evaluation, the Expert Panel conferred and unanimously agreed to the decision described herein.

1.1. Occurrence

Phosphatidylserine, a member of the class of phospholipids and structural component of cells, is commonly found in all biological membranes of plants, animals and other life forms (Hendler and Rorvik, 2001). The fatty acid composition of endogenous phopsphatidylserine depends on its localization and function in the cell. Approximately 30 g of phosphatidylserine is found in human body and about half of this amount (~13 g) is present in brain (Horrocks *et al.*, 1982). In brain, phosphatidylserine comprises 15% of the total phospholipid pool. Other organs containing phosphatidylserine include skeletal muscle (~3.3 g; 3.3%), liver (~2.4 g; 3.8%), lung (~0.2 g; 7.4%), and kidney (~0.3 g; 5.7%).

1.2. Chemistry and Biological Activity

Structurally, phosphatidylserine comprises three different parts: a glycerol backbone, a polar head group, and a hydrophobic moiety (Figure 1). The head group consists of the amino acid serine, which is attached to the 3-carbon backbone *via* a phosphate group; the two other hydroxy groups of the glycerol are each esterified with a fatty acid. The fatty acid moiety in position 2 is usually more unsaturated and has more carbon atoms than the fatty acid moiety in position 1. The term phosphatidylserine refers to a group of molecules due to the fact that the fatty acyl residues can vary considerably,

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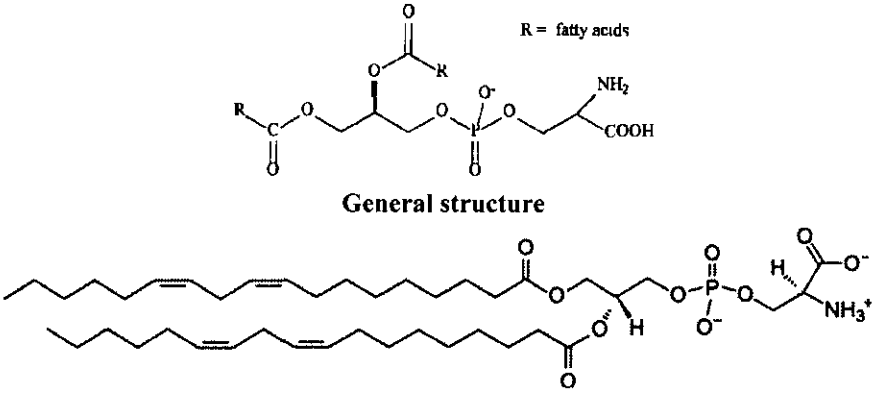
[4]Modeled after that described in section 201(s) of the Federal Food, Drug, and Cosmetic Act, As Amended See also attachments (curriculum vitae) documenting the expertise of the Panel members.

[5] "Nutrient supplements". Substances which are necessary for the body's nutritional and metabolic processes

depending on the natural source. Phosphatidylserine is amphiphilic in nature because of the negatively charged head group (hydrophilic) and the fat-soluble fatty acid tails (lipophilic) (Hendler and Rorvik, 2001). Phosphatidylserine cannot be synthesized by the human body *de novo*. It is produced only *via* exchange of the head group from phosphatidylcholine (PC) and/or phosphatidylethanolamine (PE), catalyzed by phosphatidylserine synthase-1 or -2. Thus, phosphatidylserine is formed from phosphatidylethanolamine by exchange of the ethanolamine head for L-serine.



General structure

Most abundant form (the counter ion for the phosphate moiety is Ca^{+})

Figure 1. Chemical structure of phosphatidylserine

Phosphatidylserine is primarily located in the internal layer of the cell membrane and performs a variety of structural and regulatory functions. It is involved in governing membrane fluidity and therefore in the regulation of biological cell activities. Aside from the regulation of many metabolic processes (such as activation of cell-membrane bound enzymes), phosphatidylserine is involved in neuronal signaling. Moreover, the sodium-potassium-stimulated enzyme ATPase is also activated by phosphatidylserine. Another enzyme activated by phosphatidylserine is tyrosine hydroxylase, which is involved in neurotransmitter synthesis thus influencing dopaminergic and adrenergic signal transduction in the brain. Phosphatidylserine facilitates the calcium uptake into the nerve cells that decreases in the aging brain. It is also involved in the processes of cell repair and removal. In addition to its role in brain glucose metabolism, it can stimulate synthesis of the neurotransmitter acetylcholine to improve receptor functioning and to restore nerve signal transduction.

1.3. Description, Manufacturing Process and Specifications

General descriptive parameters and properties of phosphatidylserine manufactured as Sharp•PS™ by Enzymotec are summarized in Table 1. Sharp•PS™ occurs as off-white to yellow-colored powder.

Table 1. General descriptive characteristics of phosphatidylserine formulations

Parameter	Description
Chemical name	1,2-diacyl-*sn*-glycero-3-phospho-L-serine
CAS Number	84776-79-4
Molecular weight	819 Daltons

Chemical formula	$C_{42}H_{73}O_{10}PNCa$
Physical state	Powder
Solubility	Chloroform· methanol 95:5
Stability	24 months
Color	Off-white to yellow
Odor	Light soy lecithin-like odor
Flavor	None
Storage	Below 25°C, in sealed containers, protected from light and moisture

1.3.1. Manufacturing Process

Phosphatidylserine (Sharp•PS™) is manufactured from high phosphatidylcholine enriched soybean lecithin (Figure 2). The phosphatidylcholine-enriched lecithin is enzymatically transphosphatidylated with L-serine using a phospholipase enzyme. The enzyme used for transphosphatidylation is derived from a microorganism that is nonpathogenic and nontoxicogenic. This enzymatic process catalyzes the substitution of the choline head-group with serine to form phsophatidylserine. The enzyme treatment does not alter the fatty acids attached to the molecule or its stereochemistry. Following the enzymatic reaction, the solid product is separated from the reaction mixture, purified and dried. Food grade antioxidants are added to the product in accordance with good manufacturing practices. Processing aids used such as acetic acid, sodium methoxide, calcium chloride, and ethyl alcohol are food grade quality as specified in Food Chemical Codex.

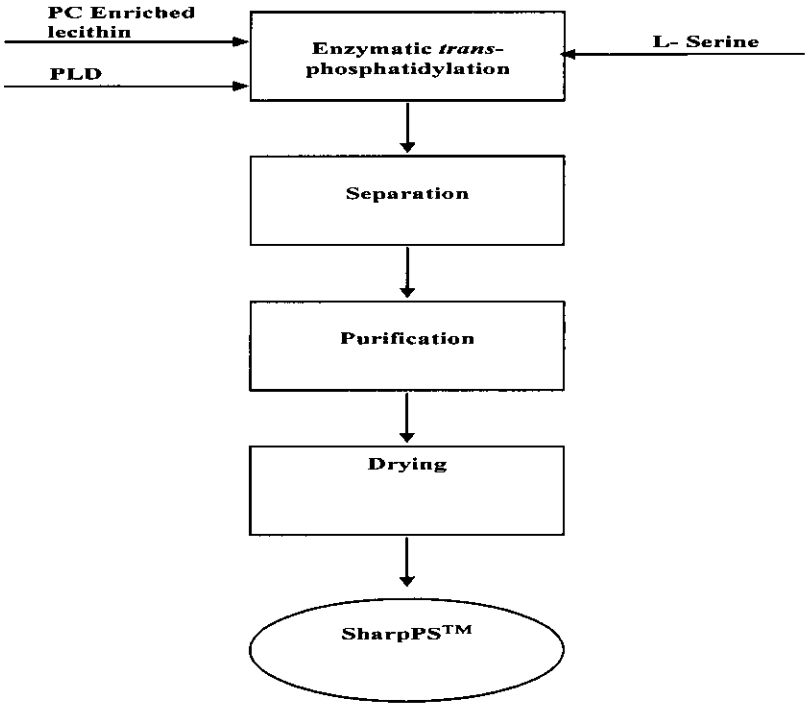


Figure 2. Manufacturing process of phosphatidylserine (Sharp•PS™)

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1.4. Identity and Specifications

Typical compositional analysis and specifications of Sharp•PS™ from Enzymotec are presented in Table 2 and 3, respectively. Analytical results of five lots from non-consecutive batches indicate that the Sharp•PS™ produced meets these specifications (Appendix I).

Table 2. Compositional analysis of Sharp•PS™

Parameter	Typical values/ Specifications	Assay method
Phosphatidylserine	72%	HPTLC (AM-010)/^{31}P-NMR
Phosphatidic acid	10.6%	^{31}P-NMR
Lyso-phosphatidylserine	0.5%	^{31}P-NMR
Lyso-phosphatidic acid	0 3%	^{31}P-NMR
Phosphatidylethanolamine	1%	^{31}P-NMR
Other phospholipids	3.3%	^{31}P-NMR
Glycerides (Tri-, Di- and Mono-)	2.8%	AM-034
Sodium	277 ppm	AOAC 985.01
Calcium	2.5 %	AOAC 985.01
Chloride	0.2 ppm	AOAC960 29
Free L-Serine	<0.1%	ACS 8th edition, page 491
Total phytosterols	0.028%	Capillary GC (According to Slover HT, et al, Determination of Tocopherols and sterols)
Tocopherol	0 2 %	AOCS Ce 8-89
Ash	12 7%	AOAC 923.03
Heavy metals		
Lead	<0.2 ppm	ICP
Arsenic	<0 2 ppm	ICP
Cadmium	<0 03 ppm	ICP
Mercury	<0 2 ppm	ICP

Table 3. Specifications of Sharp•PS™

Parameter	Specification	Assay method
Peroxide value	< 5 meq/kg	Modified AOCS official method Cd 8-53
Moisture	<2 0%	LOC using Precisa moisture analyzer with Halogen heat
Phosphatidylserine	60-80%	HPTLC (AM-010)/^{31}P-NMR
Ethanol residues	<1000 ppm	GC/MS Headspace
Microbiological assays		
Total plate count	< 1000 cfu/g	Israeli Standard SI 885 part 3 (1999)
Yeast and Mold	< 100 cfu/g	Israeli Standard SI 885 part 3 (1999)
Molds	< 100 cfu/g	Israeli Standard SI 885 part 3 (1999)
Coliform bacteria	Negative (cfu/g)	USP 61 (2000)

Table 3. Specifications of Sharp•PS™

Parameter	Specification	Assay method
Staphylococcus aureus	Negative (cfu/g)	USP 61 (2000)
Salmonella	Negative (cfu/20 g)	Israeli Standard SI 885 part 3 (1999)
Shelf life	24 months	

cfu = colony forming units

1.5. Fatty Acid Profile

Typical fatty acid profile of Sharp•PS™ is summarized in Table 4.

Table 4. Typical fatty acid profile of Sharp•PS ™

Fatty acid	Percentage*
Palmitic acid (C16:0)	14
Stearic acid (C18 0)	4
Oleic acid (C18 1)	15
Linoleic acid (C18:2)	62
Linolenic acid (C18·3)	5
Total	100

*Percent of total fatty acids

1.6. Technical Effects

Sharp•PS™ is intended for uses in food as a nutrient for individuals who wish to increase their daily intake of phosphatidylserine. While there is no Reference Daily Intake, the nutritive contribution of phosphatidylserine is well recognized. It is naturally present in a wide variety of foods with relatively higher amounts in specific foods such as fish, poultry and meats. Although phosphatidylserine is present at a certain level in the diet, its supplementation to food is aimed at gaining certain health benefits. The level of phosphatidylserine required to achieve the health benefits was determined through intervention trials in which people consumed phosphatidylserine to supplement their diet (whether regular or vegetarian). The supplementation of phosphatidylserine through foods is intended to assist in maintaining acuity and to aid in preventing age-related mental deterioration.

1.7. Current Uses

Phosphatidylserine is extensively marketed as a dietary supplement. FDA has concluded that "the use of phosphatidylserine as a dietary supplement is safe and lawful under 21 CFR§101.14 provided that bovine-derived sources, if used, are not derived from bovine tissues from cattle born, raised, or slaughtered in any country where BSE exists[6]."

In reply to two separate GRAS notices, FDA had no questions on the use of phosphatidylserine in different food categories under the conditions described in the

[6]Phosphatidylserine and Cognitive Dysfunction and Dementia (Qualified Health Claim: Final Decision Letter) http //www.cfsan.fda.gov/~dms/ds-ltr36.html

notifications. In one of the GRAS notifications from Degussa Food Ingredients GmbH (2006)[7], use of phosphatidylserine at levels of 20 mg/serving in yogurt, powdered milk, ready-to-drink soymilk, meal replacement, cereal bars, powdered beverage mixes, chewing gum, and breakfast cereals was considered as GRAS. In the 2nd GRAS notice submitted by Lipogen (2006)[8], use of phosphatidylserine in 28 different food products resulting in estimated mean and 90th percentile intake of approximately 140 and 240 mg/person/day, respectively was determined to be GRAS.

1.8. Intake from Natural Presence in Food

As mentioned earlier, phosphatidylserine is virtually present in all biological membranes of plants and animals. As such, phosphatidylserine is a typical constituent of the human diet. It is found in small amounts in foods such as meats, eggs, soy products, certain legumes, and milk. Bruni *et al.* (1989) reported an estimated daily intake of phosphatidylserine of about 75 mg/day. On the basis of a scientific analysis of phosphatidylserine exposure, Hamm (2004) determined an average intake of phosphatidylserine as 130 mg/day, with light eaters of meat and fish consuming about 100 mg and vegans consuming less than 50 mg/day. In a GRAS notification, Degussa (2006) determined estimated dietary intake of phosphatidylserine in the US population. Based on the analysis limited to the foods in which presence of phosphatidylserine has been reported, the estimated average and 90th percentile intake of phosphatidylserine for an adult from natural sources was determined as 98 and 184 mg/person/day, respectively. In another notification, Lipogen (2006) reported the background intake of phosphatidylserine from natural sources. In this report, it was estimated that consumers of meat ingest approximately 80 mg of naturally occurring phosphatidylserine *per* day. These reports show that dietary intake of phosphatidylserine, from its natural presence in diet, ranges from 75 to 184 mg/day.

1.9. Intended Use Levels and Food Categories

Enzymotec proposes to use Sharp•PS™ as a nutrient [21 CFR §170.3(o)(20)] at levels up to 100 mg phosphatidylserine/serving in milk, flavored milk, milk drinks (excluding milk fluid), milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, and fruit flavored drink, and at use levels of 50 mg phosphatidylserine/serving in breakfast cereals and milk fluid. Although some foods with standards of identity are included in the list of foods, at present the use of Sharp•PS™ is intended for foods without a standard of identity. Estimates of possible daily intake from the proposed use levels of Sharp•PS™ have been determined using CSFII 1994-96 (USDA, 1998) database (as determined by CanTox; see below) of the food product. Based on the maximum proposed use levels of Sharp•PS™, the resulting daily intake at the mean and 90th percentile level of phosphatidylserine is determined.

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[7] GRAS notice No GRN 000197 http //www.cfsan.fda.gov/~rdb/opa-g197.html
[8] GRAS notice No GRN 000186 http://www cfsan.fda.gov/~rdb/opa-g186.html

1.9.1. Estimated Daily Intake from the Intended Uses

Based on the exposure estimates prepared by CanTox Health Sciences International (Appendix II), approximately 60% of the total U.S. population was identified as consumers of phosphatidylserine (12,341 actual users identified). Although, infants are included in the intake determinations, phosphatidylserine is not intended to be used in products such as baby foods or infant formula that are specifically marketed for use by infants. Consumption of types of food categories intended for addition of phosphatidylserine by the total U.S. population resulted in estimated mean all-person and all-user intakes of phosphatidylserine of 24.61 mg/person/day (0.52 mg/kg body weight/day) and 44.75 mg/person/day (0.95 mg/kg body weight/day), respectively. The 90th percentile all-person and all-user intakes of phosphatidylserine from all intended food-uses by the total population were 70.00 mg/person/day (1.46 mg/kg body weight/day) and 98.73 mg/person/day (2.51 mg/kg body weight/day), respectively. For details of the consumption analysis, please see appendix II. The FDA commonly uses the estimated daily intake for the 90th percentile consumer of a food additive as a measure of high chronic dietary intake. Hence, for the safety determinations, the resulting 90th percentile intake of phosphatidylserine (98.73 mg/person/day) from its intended uses in the above described food categories is considered. A summary of the estimated daily intake of phosphatidylserine from the intended food categories is presented in Table. 5.

Table 5. Intake of phosphatidylserine (mg/person/day) based on USDA data

Population Group	Age Group (Years)	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
				Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Infant	0 to 2	52.5	1,880	16 23	6 23	46 25	27.39	17.43	60 49
Child	3 to 11	79.8	5,030	33 03	23.24	80.81	41.90	29.88	91.10
Female Teenager	12 to 19	54.1	380	25 37	11 62	70.00	45.80	33.20	89.15
Male Teenager	12 to 19	55.0	383	33.50	14 53	98.98	60.73	45 46	117.80
Female Adult	20 and Up	53.3	2,438	22.71	8.16	63 66	42 16	27.29	96.42
Male Adult	20 and Up	46.9	2,230	22.76	NA	66.40	49.62	33 20	105.00
Total Population	**All Ages**	59 9	12,341	24.61	9.96	70 00	44 75	30 30	98.73

NA = Not applicable

1.10. Summary of Consumption

The estimated daily intake of phosphatidylserine from Sharp•PS™ for the various food categories identified above was determined using CSFII 1994-96 database (USDA, 1998). From these determinations, the high users only 90th percentile consumption value of phosphatidylserine ingredients for food uses in different products [milk, flavored milk,

milk drinks, milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, breakfast cereals and fruit flavored drink] was considered as the estimated daily intake resulting from the intended use of Sharp•PS™. Based on these considerations, the intended uses of phosphatidylserine will result in daily 90th percentile exposure of 98.73 mg/person (2.51 mg/kg body weight/day). Phosphatidylserine is naturally present in food and its intake from diet ranges from 75 to 184 mg/day. Based on the available scientific information and as discussed below, the estimated daily intake, if ingested daily over a lifetime, is considered as safe.

2. Toxicology

The safety of phosphatidylserine is supported by multiple human clinical trials and a variety of animal as well as *in vitro* experimental studies further corroborate the human observations. Because of its physiological role and health benefits, there has been considerate effort to elucidate the biological role of phosphatidylserine in the human body. As a result, the literature is full of information on phosphatidylserine. Relevant biological and toxicological studies on phosphatidylserine are included in the following section in the order of their importance in support of the conclusions drawn in this determination.

2.1. Human Studies

In the published literature, there are over 35 clinical trials with oral administration of phosphatidylserine. Of these, 17 have been identified as double-blind trials. The majority of the studies with phosphatidylserine involved geriatric individuals diagnosed with some form of dementia or cognitive dysfunction. The objective of these studies was to examine the effect of phosphatidylserine in reducing the symptoms of dementia and cognitive dysfunction. Although the primary end point of these investigations was to study the efficacy of phophatidylserine, clinical observations also included any adverse effects. A summary of clinical trial design, doses and adverse effects noted in these investigations with oral phophatidylserine treatment is given in Table 6.

Table 6. Reported adverse effects of phosphatidylserine in clinical trials

Reference; study design	PS Source	Number Subjects	Dose (mg/day); Duration	Adverse Effects Reported
Allegro *et al*, 1987	BC-PS	30	300, 60 days	No symptoms of adverse reactions were observed
Amaducci *et al*, 1988; DB-PC	BC-PS	142	200, 90 days	No change noted in pre- and post-dose clinical exams, clinical chemistries, and blood counts; no adverse events
Caffarra *et al*, 1987	BC-PS	30	300, 60 days	None reported
Cenacchi *et al.*, 1987, DB-PC	BC-PS	130	300, 60 days	No treatment related clinically significant adverse effects.
Cenacchi *et al*, 1993; DB-PC	BC-PS	425	300; 180 days	Dizziness, vomiting and dyspepsia reported in a few patients. No adverse effects of phosphatidylserine. No pharmacological interactions

Crook *et al.*, 1991, DB-PC	BC-PS	149	300; 12 wks.	Well tolerated; no adverse events
Crook *et al*, 1992; DB-PC	BC-PS	51	300; 12 wks.	Well tolerated, no adverse events
Crook, 1998	S-PS	50	300; 12 wks	No adverse effects noted
Delwaide *et al*, 1986, DB-PC	BC-PS	35	300; 6 wks	No significant side effects noted
Engel *et al*, 1992; DB	BC-PS	33	300; 8 wks	None reported
Fahey and Pearl, 1998, DB	S-PS	11	800; 2 wks.	None reported
Funfgeld *et al*, 1989; DB-PC	NA	62	300; NA	None reported
Granata & Michele, 1987	BC-PS	35	300; 60 days	None reported
Gindin *et al*, 1993; DB-PC	S-PS	57	300 mg, 3 mos.	No adverse effects noted
Heiss *et al*, 1994	BC-PS	18	400; 6 mos	None reported
Hershkowitz *et al*, 1989, DB	BC-PS	24	300, 6 mos.	None reported
Jorissen *et al.*, 2001; DB-PC	S-PS	81	300 or 600, 12 wks	None reported
Maggioni *et al*, 1990; DB	BC-PS	10	300, 30 days	None reported
Monteleone *et al*, 1992	BC-PS	9	800; 10 days	None reported; BP unchanged
Palmieri *et al*, 1987, DB-PC	BC-PS	87	300, 60 days	No change noted in pre- and post-dose clinical and neurological exams, clinical chemistries, and EEG
Puca *et al*, 1987	BC-PS	27	300; 60 days	No change in pre- and post-dose blood biochemistry parameters
Rabboni *et al*, 1990	BC-PS	30	400; 60 days	No reported changes in liver and kidney function blood biochemistry or blood counts
Ransmayr *et al*, 1987; DB-PC	BC-PS	39	300, 60 days	Few patients with epigastric pain associated with oil or gelatin caps
Schreiber *et al*, 2000	S-PS	18	300, 12 wks	No changes noted in serum electrolytes, glucose, thyroid function, and differential blood counts, no adverse effects noted
Sinforiani *et al*, 1987	BC-PS	34	300; 60 days	No remarkable side effects
Villardita *et al.*, 1987, DB-PC	BC-PS	170	300; 90 days	None reported

PS = phosphatidylserine; DB-PC = double-blind placebo-controlled; BC-PS = Bovine cortex derived phosphatidylserine; S-PS = soy derived phosphatidylserine; wks = weeks, mos = months

In the clinical trials with phosphatidylserine, over 1500 subjects participated and the treatment lasted for periods of up to 6 months. The doses used in these trials ranged from 200 to 800 mg/day. The results of these studies show that oral administration of phosphatidylserine at doses of up to 600 mg/day for up to 3 months were without any significant adverse effects. In the largest double-blind, placebo-controlled trial (Cenacchi

et al., 1993), of the 494 participants' only one subject dropped out because of an adverse effect, as compared to seven drop-outs from the placebo group.

Hendler and Rorvik (2001) reported occasional gastrointestinal side effects (nausea and indigestion) following phosphatidylserine ingestion. These effects were attributed to the oily nature of the ingested phosphatidylserine and vehicle used. These symptoms can be minimized by consuming phosphatidylserine with food. In a review article, Pepping (1999) reported that phosphatidylserine is well-tolerated at a dosage of 300 mg/day or less. The only adverse effects that are reported are stomach upset in some individuals at doses higher than 300-400 mg/day and sleeplessness at doses ≥600 mg taken before bedtime. There are no reported drug, nutritional supplement, food or herb interactions with phosphatidylserine.

In the majority of the clinical trials described in Table 5, phosphatidylserine derived from bovine cortex was used. In five trials, the source of phosphatidylserine was soy. As discussed below the source of phosphatidylserine is unlikely to affect its safety. In the studies with soy-derived phosphatidylserine, 218 subjects participated and the majority of the subjects received a daily dose of 300 mg phosphatidylserine for about 3 months. In these studies, no adverse effects of phosphatidylserine administration were reported. In one of these studies, Jorissen *et al* (2002) investigated the safety of soy-derived phosphatidylserine in the elderly. In this study, 120 male and female elderly subjects with age-associated memory impairment received one of three treatments: placebo, 300 or 600 mg phosphatidylserine daily. At baseline, and after 6 and 12 weeks of treatment, standard biochemical and hematological safety parameters, blood pressure, heart rate and adverse events were assessed. No significant treatment-related differences were found in any of the outcome variables between the treatment groups. The investigators concluded that phosphatidylserine is safe for older persons at a dosage of 600 mg *per* day.

2.2. Source of Phosphatidylserine and Safety

Historically, phosphatidylserine is derived from animal sources such as bovine cortex. In recent years because of potential contamination concerns from bovine spongiform encephalopathy (BSE) prions, this has been supplanted by vegetable sources. The safety database contains studies with both bovine and plant derived phosphatidylserine. Hence, it is important to compare the composition of these two forms of phosphatidylserine for an understanding of the applicability of the various studies in safety assessment. Soy-derived phosphatidylserine mainly contains polyunsaturated fatty acids, while bovine cortex derived phosphatidylserine (BCPS) primarily contains saturated and monounsaturated fatty acids, as well as some docosahexaenoic acid (Hendler and Rorvik, 2001).

The phosphatidylserine molecule from soy has approximately 7% α-linolenic acid (omega-3) and 47% linoleic acid (omega-6), while the phosphatidylserine molecule derived from bovine brain cortex has been reported to range from 8-30% docasahexaenoic acid (omega-3) and 2% arachidonic acid (omega-6). Typically, soy-derived phosphatidylserine contains 40-60% linoleic acid (18:2), 15% palmitic acid

(16:0), and approximately 5% of each of the following: stearic acid (18:0), oleic acid (18:1) and α-linolenic acid (18:3). The omega-3 fatty acids in BCPS include α-linolenic acid (18:3), eicosapentaenoic acid (EPA) (20:5) docosapentaenoic acid (22:5), and docosahexaenoic acid (22:6). The omega-6 fatty acids in phosphatidylserine include linoleic acid (18:2), linolenic acid (18:3), dihomo-γ-linolenic acid (20:3), arachidonic acid (20:4), adrenic acid (22:4) and docosapentaenoic acid (22:5).

Although, fatty acid composition between bovine cortex-derived and soy-derived phosphatidylserine differs, as discussed below, these differences are unlikely to affect the safety profile. Following ingestion, phosphatidylserine of any origin is modified in the gastrointestinal mucosa. In the human body, ingested phosphatidylserine, particularly its fatty acid composition, from different sources is modified depending on the body need. Secondly, depending on the target tissue requirements, the fatty acid profile of phosphatidylserine is modified to meet the need of the tissue/organ. These facts demonstrate that the fatty acid composition of phosphatidylserine and thus the source is unlikely to play a role in its safety.

2.3. Absorption, Metabolism and Excretion

Following dietary ingestion of phosphatidylserine, pancreatic digestive enzymes cleave specific fatty acids. The lysophospholipids thus formed are absorbed by the mucosal cells of the intestine and could be reacylated into phosphatidylserine. The fatty acids released can be further used for triglyceride synthesis (Tso, 1994). Because of the high activity of decarboxylases in the mucosal cells, the majority of the phosphatidylserine is converted into other phospholipids. Phosphatidylserine is decarboxylated mainly to phosphatidylethanolamine (Wise *et al.,* 1965). The reacylated phosphatidylserine, phosphatidylethanolamine and other phospholipids enter the lymph and circulation, and are redistributed. Available evidence indicates that only part of the ingested phosphatidylserine reaches systemic circulation as part of the phospholipid pool. The exact fatty acid profile of the phosphatidylserine that is ingested is unlikely to limit its final disposition in the nerve cells, and *in situ,* the most active form of phosphatidylserine in membranes is the lyso form, which lacks a tail in the 2-position. Unlike phosphatidylcholine, phosphatidylserine does not tend to accumulate in the body (Toffano *et al.,* 1987). Approximately 60% of the ingested phosphatidylserine is excreted in feces, while 10% is eliminated in urine. The major metabolite recovered was lysophosphatidylcholine and to a lesser extent lysophosphatidylserine (Toffano *et al*, 1987).

Pharmacokinetic studies of phosphatidylserine in rats and mice show good bioavailability. Following intravenous administration of 20 mg/kg of phosphatidyl L-[U-^{14}C]-serine to mice, blood levels of radioactivity declined in biphasic manner. A rapid increase in brain radioactivity was noted. At 20 minutes after the injection, the amount of radioactivity peaked in the brain and was 0.25% of the dose. The amount of radioactivity in liver was 36% of the dose and reached a peak also after 20 minutes (Mazzari *et al.,* 1982). Following a bolus intravenous injection of radio-labeled phosphatidylserine (2 mg/kg) to rats, plasma concentration showed a biphasic decline with half-lives of 0.85 and 40 min (Palatini *et al.,* 1991). The initial decline was found to be due to the

irreversible uptake of phosphatidylserine liposomes by the mononuclear phagocyte system, as demonstrated by the almost exclusive accumulation of phosphatidylserine in liver and spleen. The slow decline phase reflects the elimination of that fraction of phosphatidylserine, which has been incorporated into high density plasma lipoproteins. Comparative analysis of the biotransformation products found in tissues following either [^{3}H]-glycerol- or [^{14}C]-serine-phosphatidylserine injection show that parenterally administered phosphatidylserine follows two pathways: decarboxylation to phosphatidylethanolamine and extensive hydrolytic degradation with release of the individual components of the molecule.

2.4. Subchronic Studies

Results from repeat-dose safety studies in rats and dogs show that oral administration of phosphatidylserine at doses up to 1000 mg/kg/day for up to 6 months was without any significant adverse effects.

2.4.1. Rat Study

In a repeat-dose study, groups of Sprague-Dawley rats (20/sex/group) were administered daily with 0 (vehicle control), 10, 100, and 1000 mg/kg BCPS *via* gavage for 26 weeks (Heywood *et al.,* 1987). Compared to controls, BCPS administration did not significantly affect survival, weight gain and, feed, or water consumption. In some of the animals receiving 1000 mg/kg/day, post-dose salivation was noted. No significant hematological changes attributable to BCPS treatment were noted. In male and female rats receiving the highest dose of BCPS, a slight increase in alkaline phosphatase levels was observed. At week 13, in males receiving the highest dose of BCPS, serum albumin levels were slightly lowered, potassium levels were elevated and serum sodium values were decreased. In males and females receiving the highest dose, lower urine pH values were recorded. Terminal necropsy did not reveal any adverse macroscopic or microscopic treatment related findings. In the absence of dose-related effects, minimal changes, and lack of histological changes, the adverse effects noted in this study were considered minor. The results of this study show that the no-observed-adverse-effect level (NOAEL) is lower than 1000 mg/kg/day but is closer to this dose.

2.4.2. Dog Studies

Groups of pure-bred beagle dogs (5/sex/group) were administered BCPS at dosage levels of 0 (vehicle control; corn oil), 10, 100, and 1000 mg/kg/day *via* gavage for 26 weeks (Heywood *et al* , 1987). No deaths were recorded in any of the groups during the treatment. During the first eight weeks of the study, animals in the high-dose group consumed less feed. Following week 9, animals were given moistened feed and the intake was matched with the control group. Compared to controls, animals receiving the highest dose showed a decrease in body weight gain. In dogs receiving 1000 mg/kg/day dose, the blood glucose and cholesterol levels were significantly decreased. No treatment related macroscopic findings or changes in organ weights were noted. Histological examinations of tissues did not reveal any treatment related changes. Similar to the 26-week rat study, the adverse effects noted were minor and the results show that NOAEL is lower than 1000 mg/kg/day but is closer to this dose.

In another repeat-dose study, groups of pure-bred beagle dogs (4/sex/group) were administered BCPS at dosage levels of 0 (vehicle control), 5, 10, and 15 mg/kg/day *via* intramuscular injection for 13 weeks (Heywood *et al.,* 1987). BCPS administration did not affect body weight gain. In animals receiving 10 and 15 mg/kg/day dose, pain reaction during the dosing procedure and subcutaneous hardening of injection site was noted. Hematological examinations revealed elevations in erythrocyte sedimentation rates and total white blood cell counts in animal receiving highest dose of BCPS. Morphological examinations at termination did not reveal any changes, except for injection site changes in all groups.

2.5. Teratogenicity/Reproduction Studies

In a teratogenicity study, BCPS was administered *via* oral gavage to pregnant Sprague-Dawley rats at daily doses of 0, 10, 100, and 200 mg/kg/day from Days 6 to 15 of gestation (Heywood *et al.,* 1987). Based on the results summarized for this study, the highest dose described in methods section should be 1000 mg/kg/day, instead of 200 mg/kg/day. On day-20, animals were killed, litter values determined, and fetuses were examined for skeletal and visceral malformations. The only sign of toxicity noted in rats receiving 1000 mg BCPS/kg/day was a slight increase in salivation. BCPS treatment did not affect mean weight gain during gestation. At terminal autopsy, no treatment-related macroscopic changes were noted. BCPS treatment did not affect litter values as assessed by litter size, post-implantation loss, litter and mean fetal weights, and the embryonic and fetal development.

In another teratogenicity study, BCPS was administered *via* oral gavage to pregnant New Zealand white rabbits at daily doses of 0, 50, 150, and 450 mg/kg/day from Days 6 to 18 of pregnancy (Heywood *et al.,* 1987). At the highest dose level, BCPS administration resulted in a decrease in body weight gain during the first four days of dosing. On day-29 of pregnancy, animals were killed, litters were examined macroscopically, and fetuses were examined for skeletal and visceral abnormalities. The mean fetal weights at the highest dose were slightly lower but did not reach statistical significance. BCPS administration did not affect embryonic and fetal development.

In summary, results of teratogenicity studies in rats at doses up to 200 mg/kg/day and in rabbits at doses up to 450 mg/kg/day show that oral administration of phosphatidylserine did not affect embryonic and fetal development.

2.6. Genotoxicity

The mutagenic potential of BCPS was investigated in a human lymphocytes chromosomal damage assay, mouse-lymphoma cell mutation test, cultured human epithelial cell DNA repair assay and in an *in vivo* mouse micronucleus assay (Heywood *et al.,* 1987). Cultures of human lymphocytes were exposed to BCPS at concentrations of 0, 17, 83 and 166 μg/ml with and without metabolic activation. Compared to the control, no significant increase in chromosomal damage was noted in either the presence or absence of metabolic activation. In the *in vitro* mouse lymphoma L5178Y mammalian cell test system, which detects mutations from the heterozygous condition for the thymidine kinase locus (TK+/-) to the thymidine kinase deficient genotype (TK-/-),

exposure to BCPS did not reveal any significant increases in the number of mutant colonies or mutation frequency either in the presence or absence of metabolic activation. In the DNA repair assay with autoradiographic techniques, cultured human epitheloid cells did not reveal any evidence of DNA repair synthesis in the HELA S3 cells either in the presence or absence of metabolic activation.

In the micronucleus test, BCPS was administered *via* oral gavage to mice at total dosages of 30, 150 and 300 mg/kg in two equal doses separated by 24-hours. The positive control group was treated with mytomycin C. At six hours after the second dose, mice were killed and bone marrow smears were examined for the presence of micronuclei in 1000 polychromatic erythrocytes per mouse and for the ratio of normochromatic and polychromatic erythrocytes. The results of the study did not reveal any evidence of mutagenic potential or bone marrow toxicity.

Under the conditions of the above *in vitro* and *in vivo* studies BCPC is devoid of any genotoxic or clastogenic activity.

2.7. Acute and Short-term Studies

The acute oral and subcutaneous LD_{50} of BCPS in Sprague-Dawley rats by standard methods was reported as greater than 5 g/kg body weight. The intravenous LD_{50} of BCPS in rats was reported as 236 mg/kg body weight (Heywood *et al*, 1987). In a series of studies conducted in rats and mice to evaluate the maximum tolerated dose of phosphatidylserine derived from soy, single doses up to 2000 mg/kg body weight were well tolerated in both the species (Degussa, 2006).

In a repeat-dose short-term study, groups of 10 male and 10 female Sprague-Dawley rats were administered BCPS at dose levels of 0 (vehicle control), 5, 20, and 80 mg/kg/day *via* intravenous route for four weeks (Heywood *et al.*, 1987). In all BCPS treated groups except females at 5 mg/kg dose, reddening and swelling of paws and around the muscle region was noted. At the highest dose level, a decrease in body weight and food consumption was noted. In animals receiving the highest dose (80 mg/kg/day), a significant decrease in red blood cell counts, hemoglobin, packed cell volume and increases in neutrophil, lymphocyte counts and alkaline phosphatases were noted. Increases in the weights of spleen (in male and female rats receiving 80 mg/kg/day; and in males receiving 20 mg/kg/day), adrenal (in males and females receiving 80 mg/kg/day) and kidney (in male rats receiving 20 and 80 mg/kg/day) were noted. Injection site thrombosis was noted in some rats in all groups (Heywood *et al*, 1987).

In another four week repeat-dose study, groups of pure-bred beagle dogs (3/sex/group) were administered BCPS at dosage levels of 0 (vehicle control), 5, 15, and 40 mg/kg/day *via* intravenous route for 28 days (Heywood *et al.*, 1987). No mortality was noted in any group. In animals receiving 15 and 40 mg/kg/day dose, generalized tremors of body muscles were noted. In male animals receiving the highest dose of BCPS, a significant reduction in weight gain, increases in white blood cell count and total serum protein were noted. BCPS treatment did not affect organ weights. Histological examinations of liver revealed centrilobular and periportal sinusoidal aggregations of

polymorphonuclear leucocytes in one animal receiving 15 mg/kg/day and four animals receiving 40 mg/kg/day of BCPS.

In summary, the acute oral LD_{50} of phosphatidylserine in rats was greater than 5 g/kg body weight. Short-term intravenous administration studies in rats and dogs indicate that phosphatidyserine causes adverse effects. However, as discussed above these effects resulting from intravenous administration of phosphatidylserine were not observed in long-term studies following oral ingestion.

3. SUMMARY

Phosphatidylserine, a structural component of cells, is found in all biological membranes of plants, animals and other life forms. The human body contains about 30 g of phosphatidylserine, about half (~13 g) of which is found in brain. Phosphatidylserine plays a vital role in several metabolic processes such as activation of cell-membrane bound enzymes and is involved in neuronal signaling. Enzymotec proposes to use a standardized soy lecithin derived phosphatidylserine (Sharp•PS™) as a nutrient at levels up to 100 mg phosphatidylserine/serving in milk, flavored milk, milk drinks (excluding milk fluid), milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, and fruit flavored drink and at use levels up to 50 mg phosphatidylserine/serving in breakfast cereals and milk fluid. The intended use of Sharp•PS™ will result in an estimated daily mean and 90^{th} percentile intake for "users only" of 44.75 mg/person (0.95 mg/kg body weight/day) and 98.73 mg/person (2.51 mg/kg body weight/day), respectively. Phosphatidylserine has been the subject of two GRAS Notices submitted to FDA for use as a nutrient. In each case, FDA responded that they had no questions on the proposed use and did not object to the respective GRAS determination. In one of these notices, the use of phosphatidylserine was determined as GRAS at estimated daily intake levels of 240 mg/person/day.

Several clinical studies (> 35) with over 1500 participants revealed that oral administration of phosphatidylserine at doses of 200 to 600 mg/day is without any adverse effect. In the majority of these studies, phosphatidylserine was derived from bovine cortex. Available scientific evidence indicates that phosphatidylserine derived from soy lecithin is toxicologically equivalent to phosphatidylserine naturally found in diet or derived from bovine cortex. Once inside the body, orally ingested phosphatidylserine is hydrolyzed in the intestine prior to its absorption. The absorbed phosphatidylserine is transported and rapidly converted into other endogenous constituents. In repeat-dose safety studies in rats and dogs, oral administration of phosphatidylserine at doses up to 1000 mg/kg/day for up to 6 months was without any significant toxicity. The adverse effects noted in animal safety studies at 1000 mg/kg/day were considered minor as these changes were small in magnitude, not supported by any histological damage, and lacked any dose-response correlation. In teratogenicity studies in rats and rabbits, phosphatidylserine did not affect embryonic and fetal development. Multiple genotoxicity studies show that phosphatidylserine did not reveal any genotoxic or clastogenic activity. The acute oral LD_{50} of phosphatidylserine in rats was reported as greater than 5 g/kg body weight.

4. RISK ASSESSMENT

There is sufficient qualitative and quantitative scientific evidence, including human and animal data, to determine safety-in-use or acceptable daily intake (ADI) for phosphatidylserine. The safety data on phosphatidylserine includes over 35 human clinical trials, repeat-dose (6 month) studies in rats and dogs, teratogenicity/reproductive toxicity studies in rats and rabbits, and *in vitro* and *in vivo* genotoxicity studies. Generally, ADIs are derived from a no-observed-adverse-effect level determined from animal studies with considerations of uncertainty factors to account for variabilities and uncertainties. The animal studies did not show significant toxicity at doses up to 1000 mg/kg/day. Several human clinical trials (>35) and historical use supports the safety of phosphatidylserine at even higher use levels than can be determined by available animal studies. The discussion presented in this dossier supports a safe level of 300 mg/day.

The clinical evidence of phosphatidylserine safety is supported by:

- Phosphatidylserine is commonly found in daily-consumed foods such as meat, fish, legume, etc.
- Phosphatidylserine is an endogenous substance found in human body.
- The bioavailability of the ingested phosphatidylserine is limited due to extensive hydrolysis in the intestine prior to absorption, and that the absorbed phosphatidylserine is transported and rapidly converted into other endogenous constituents.
- In multiple (>35) human clinical studies, safety of phosphatidylserine was confirmed at doses of 300 mg/day.
- The majority of the clinical studies of phosphatidylserine included susceptible groups (elderly).
- There is no evidence that consumption of phosphatidylserine either in foods or as a dietary supplement has a cumulative effect that would affect its safety.
- A variety of animal and *in vitro* studies corroborate the human clinical safety data.

Phosphatidylserine has been marketed as a dietary supplement for over 10 years without any adverse effects (except gastrointestinal side effects such as nausea and indigestion). The typical recommended doses of phosphatidylserine as a dietary supplement are 100 mg three times a day (300 mg/day). Additionally, recently FDA has agreed to exercise enforcement discretion with a Health Claim Petition [9] on phosphatidylserine. The petitioner in this submission demonstrated that soy-derived phosphatidylserine is safe at levels up to 500 mg/day[10]. In a notice submitted to the FDA, use of phosphatidylserine was determined as GRAS at an estimated 90th percentile intake of 240 mg/person/day.

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[9] "Letter Regarding Dietary Supplement Health Claim for Phosphatidylserine and Cognitive Dysfunction and Dementia" (2003) Available at: http://www.cfsan.fda.gov/~dms/ds-ltr33 html

[10] Petition for Health Claim. Phosphatidylserine and Cognitive Dysfunction, Phosphatidylserine and Dementia (2002) Available at http://www.fda.gov/ohrms/dockets/dailys/02/Sep02/091302/80027351.pdf

The intended use of Sharp•PS™ will result in a daily estimated 90th percentile intake for "users only" of 98.73 mg phosphatidylserine/person (2.51 mg/kg body weight/day). The 90th percentile intake of phosphatidylserine is approximately 3-fold lower than the safe levels (300 mg/day) determined on the basis of available safety studies.

On the basis of scientific procedures[11], and history of exposure from natural sources, the consumption of phosphatidylserine as an added food ingredient is considered safe at levels up to 300 mg/day. The intended uses are compatible with current regulations, *i.e.,* phosphatidylserine is used in milk, flavored milk, milk drinks, milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, breakfast cereals, and fruit flavored drink, and is produced according to current good manufacturing practices (cGMP).

[11] 21 CFR §170.3 Definitions. (h) Scientific procedures include those human, animal, analytical, and other scientific studies, whether published or unpublished, appropriate to establish the safety of a substance.

5. CONCLUSION

Based on a critical evaluation of the publicly available data summarized above, the Expert Panel members whose signatures appear below, have individually and collectively concluded that phosphatidylserine, meeting the specifications cited above, and when used as a nutrient [21 CFR 170.3(o)(20)] at maximum use levels of up to 100 mg phosphatidylserine/serving in milk, flavored milk, milk drinks (excluding milk fluid), milk imitation (soy milk), milk-based meal replacement, yogurt, breakfast bars, and fruit flavored drink and at use levels of 50 mg phosphatidylserine/serving in breakfast cereals and milk fluid is safe.

It is also our opinion that other qualified and competent scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion. Therefore, we have also concluded that phosphatidylserine, when used as described, is GRAS based on scientific procedures

Signatures

Stanley M. Tarka, Jr. Ph D. Date

Sidney Green, Ph.D., FATS Date

Madhusudan G. Soni, Ph.D., FACN Date

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7. APPENDIX I

Analytical data from five manufacturing lots

Typical composition and Specifications of Sharp®PS™ from five different lots

Component	Typical level	Lot PL-106	Lot PL-116	Lot PL-118	Lot PL-119	Lot PL-136
Phosphatidylserine (%w/w)	72%	76.5	76.8	68.2	67 1	70.4
Phosphatidic acid (%w/w)	10 6%	11.3	10.1	10.2	10 6	10.9
Lyso-phosphatidylserine (%w/w)	0 5%	0.0	0.6	0.8	0.6	0 6
Lyso-phosphatidic acid (%w/w)	0.3%	0 3	0.2	0.2	0 1	0 3
Phosphatidylethanolamine (%w/w)	1%	0.0	0.7	1.6	1 9	0 6
Other phospholipids (PC, PI, APE) (%w/w)	3 3%	1.9	2 7	5.9	4.3	1 6
Glycerides (Tri-, Di- and Mono-) (%w/w)	2.8	3.2	2.2	2.8	3.7	2.1
Moisture (%w/w)	<2	0.7	0 7	0.9	<0.5	0.8
Sodium (ppm)	277	193	255	326	334	279
Calcium (%w/w)	2 5	2 64	2.49	2.32	2.39	2 54
Chloride (ppm)	0 2	0.2	0.1	0 3	0.1	0.2
Free L-Serine (%w/w)	<0 1	<0.1	<0 1	<0 1	<0 1	<0.1
Total phytosterols (%w/w)	0 028	0.031	0.011	0 025	0 046	0.025
Tocopherol (%w/w)	0 2	0 14	0.19	0 17	0.27	0.21
Ash (%w/w)	12 7	13.0	13.0	12.3	12.2	13.1
Peroxide value (meq/Kg)	<5 0	0 5	<0 5	<0 5	<0.8	0.5

Heavy metal analysis from five manufacturing lots

	Lot PL-106	Lot PL-116	Lot PL-118	Lot PL-119	Lot PL-136
Lead (ppm)	<0.2	<0 2	<0.2	<0.2	<0 2
Arsenic (ppm)	<0.2	< 0 2	<0.2	< 0.2	< 0.2
Cadmium (ppm)	<0.03	<0 03	<0.03	<0.03	<0.03
Mercury (ppm)	<0.2	<0.2	<0 2	<0.2	<0 2

Ethanol residues from three manufacturing lots

	Lot PL-78	Lot PL-93	Lot PL-136
Residual ethanol (ppm)	<100	<100	161

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8. APPENDIX II

ESTIMATED DAILY INTAKE OF PHOSPHATIDYLSERINE BY THE U.S. POPULATION FROM PROPOSED FOOD-USES

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(Attached separately)

CANTOX
HEALTH SCIENCES INTERNATIONAL

ESTIMATED DAILY INTAKE OF PHOSPHATIDYLSERINE BY THE U.S. POPULATION FROM PROPOSED FOOD-USES

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ESTIMATED DAILY INTAKE OF PHOSPHATIDYLSERINE BY THE U.S. POPULATION FROM PROPOSED FOOD-USES

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Table B-7 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by the Total Population (All Ages) Within the United States 50 mg/Serving (1994-1996, 1998 USDA CSFII Data) B-7

ESTIMATED DAILY INTAKE OF PHOSPHATIDYLSERINE BY THE U.S. POPULATION FROM PROPOSED FOOD-USES

1.0 INTRODUCTION

Cantox Health Sciences International (Cantox) has completed an assessment of the consumption of phosphatidylserine by the U.S. population in breakfast cereals (instant and regular hot cereals and ready-to-eat cereals), dairy product analogs (imitation milk and soy milk), grain products and pastas (nutritional bars (breakfast, granola, protein)), milk and milk products (flavored milk and milk drinks, fluid, milk, fluid (regular, filled, buttermilk, and dry reconstituted), milk-based meal replacements, and yogurt), and processed fruits and fruit juices (fruit flavored drinks)

Estimates for the intake of phosphatidylserine were based on the proposed food-uses and use-levels in conjunction with food consumption data included in the United States Department of Agriculture's (USDA) 1994-1996 Continuing Survey of Food Intakes by Individuals (CSFII 1994-1996) and the 1998 Supplemental Children's Survey (CSFII 1998) (USDA, 2000) Calculations for the mean and 90th percentile all-person and all-user intakes, and percent consuming were performed for each of the individual food-uses of phosphatidylserine Similar calculations were used to determine the estimated total intake of phosphatidylserine from all proposed food-uses combined. In both cases, the per person and per kilogram body weight intakes were reported for the following population groups:

infants, ages 0 to 2,
children, ages 3 to 11,
female teenagers, ages 12 to 19;
male teenagers, ages 12 to 19;
female adults, ages 20 and up,
male adults, ages 20 and up, and
total population (all population and gender groups combined)

2.0 FOOD CONSUMPTION SURVEY DATA

2.1 Survey Description

Nationwide dietary intake data for the years 2001-2002 are now available for public use, however, only Day 1 interview data are included in the present release. It is well established that the length of a dietary survey affects the estimated consumption of individual users and that short-term surveys, such as the typical 1-day dietary survey, overestimate consumption over longer time periods (Anderson, 1988) Because two 24-hour dietary recalls administered on 2 non-consecutive days (Day 1 and Day 2) are available from the CSFII 1994-1996, 1998 surveys, these data were used to generate estimates for the current intake analysis

USDA CSFII 1994-1996 provides food consumption data on persons of all ages, whereas, CSFII 1998 is limited to children from birth through 9 years of age Combined, these surveys provide the most appropriate data for evaluating food-use and food-consumption patterns in the United States, containing 4 years of data on individuals selected *via* stratified, multistage area probability sampling of American households within all 50 states.

CSFII 1994-1996, 1998 survey data were collected from individuals and households *via* 24-hour dietary recalls administered on 2 non-consecutive days (Day 1 and Day 2) throughout all 4 seasons of the year. Data were collected in-person, a minimum of 3 days apart, on different days of the week, to achieve the desired degree of statistical independence. CSFII 1994-1996 contains 2-day dietary food consumption data for more than 15,000 individuals of all ages, and 1-day data for 16,103 individuals. CSFII 1998 contributes data from an additional 5,559 children, birth through 9 years of age, to data reported for 4,253 children of the same ages within CSFII 1994-1996 The overall CSFII 1994-1996, 1998 response rate for individuals selected for participation in the survey was 81 5 and 77 5% for Day 1 and Day 2, respectively.

In addition to collecting information on the types and quantities of foods being consumed, CSFII 1994-1996, 1998 collected physiological and demographic information from individual participants in the survey, such as sex, age, self-reported height and weight, and other variables useful in characterizing consumption The inclusion of this information allows for further assessment of food intake based on consumption by specific population groups of interest within the total population USDA sample weights were developed and incorporated with CSFII 1994-1996, 1998 to compensate for the potential under-representation of intakes from specific population groups as a result of sample variability due to survey design, differential non-response rates, or other factors, such as deficiencies in the sampling frame (USDA, 2000)

2.2 Statistical Methods

Consumption data from individual dietary records, detailing food items ingested by each survey participant on each of the 2 survey days, were collated by computer and used to generate

estimates for the intake of phosphatidylserine from all proposed food-uses by the U.S. population. Estimates for the daily intake of phosphatidylserine from all proposed food-uses represent projected 2-day averages for each individual from Day 1 and Day 2 of CSFII 1994-96, 1998 data. These average amounts comprised the distribution from which mean and percentile intake estimates were produced Mean and percentile estimates were generated using ratio estimation and non-parametric techniques, respectively, incorporating USDA survey weights in order to provide representative intakes for the entire U S. population All-person intake refers to the estimated intake of phosphatidylserine averaged over all individuals surveyed, regardless of whether they consumed food products containing phosphatidylserine, and therefore includes "zero" consumers (those who reported no intake of phosphatidylserine during the 2 survey days). All-user intake refers to the estimated intake of phosphatidylserine by those individuals consuming food products containing phosphatidylserine, hence the 'all-user' designation. Individuals were considered users if they consumed 1 or more food products of the proposed phosphatidylserine on either Day 1 or Day 2 of the survey

2.3 Statistical Reliability

Mean or percentile intake estimates based on small sample sizes or with high variability relative to the mean [assessed using the coefficient of variation (CV)] may be less statistically reliable than estimates based on adequate sample sizes or low variability relative to the mean (LSRO, 1995) Data presented herein for the estimated daily intake of phosphatidylserine follow the guidelines proposed by the Human Nutrition Information Service/National Center for Health Statistics Analytic Working Group for evaluating the reliability of statistical estimates adopted in the "Third Report on Nutrition Monitoring in the United States", whereby an estimated mean may be unreliable if the CV is equal to or greater than 30% (LSRO, 1995). The CV is the ratio of the estimated standard error of the mean to the estimated mean, expressed as a percentage (LSRO, 1995). Therefore, for the estimated intakes of phosphatidylserine presented herein, values were considered statistically unreliable if the CV was equal to or greater than 30%. These values were not considered when assessing the relative contribution of specific food-uses to total phosphatidylserine consumption and are marked with an asterisk

3.0 FOOD USAGE DATA

The individual proposed food-uses and use-levels for phosphatidylserine employed in the current intake analysis are summarized in Table 3-1. Food codes representative of each proposed food-use were chosen from the CSFII 1994-1996, 1998 (USDA, 2000) and grouped in food-use categories according to Title 21, Section §170.3 of the *Code of Federal Regulations* (CFR, 2006a). Product-specific adjustment factors were developed based on data provided in the standard recipe file for the CSFII 1994-1996, 1998 survey (USDA, 2000) All food codes included in the current intake assessment are listed in Appendix C

Table 3-1 Summary of the Individual Proposed Food-Uses and Use-Levels for Phosphatidylserine in the United States

Food Category	Proposed Food-Use	Use-Level (mg/RACC)	RACC* (g or mL)	Use-Level (%)
Breakfast Cereals	Instant and Regular Hot Cereals	50	240	0 0208
	Ready-to-Eat Cereals	50	15 to 55	0 333 to 0 0909
Dairy Product Analogs	Imitation Milk	100	240	0 042
	Soy Milk	100	240	0 042
Grain Products and Pastas	Nutritional Bars (Breakfast, Granola, Protein)	100	40	0 250
Milk Products	Flavored Milk and Milk Drinks, Fluid	100	240	0.042
	Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	50	240	0.0208
	Milk-Based Meal Replacements	100	240	0 042
	Yogurt	100	225	0 044
Processed Fruits and Fruit Juices	Fruit Flavored Drinks	100	240	0 042

* RACC – Reference Amounts Customarily Consumed Per Eating Occasion (21 CFR §101 12) (CFR, 2006b) When a range of values is reported for a proposed food-use, particular foods within that food-use may differ with respect to their RACC

4.0 FOOD SURVEY RESULTS

Estimates for the total daily intakes of phosphatidylserine from all proposed food-uses are provided in Tables 4.1-1 and 4 1-2 Estimates for the daily intake of phosphatidylserine from individual food-uses in the U S. are summarized in Tables A-1 to A-7 and B-1 to B-7 of Appendices A and B, respectively. Tables A-1 to A-7 provide estimates for the daily intake of phosphatidylserine per person (g/day), whereas Tables B-1 to B-7 provide estimates for the daily intake of phosphatidylserine on a per kilogram body weight basis (g/kg body weight/day).

4.1 Estimated Daily Intake of Phosphatidylserine from All Proposed Food-Uses

The estimated total intake of phosphatidylserine from all proposed food-uses in the U.S. by population group is summarized in Table 4 1-1 Table 4 1-2 presents this data on a per kilogram body weight basis

Approximately 59 9% of the total U.S. population was identified as consumers of phosphatidylserine (12,341 actual users identified) Consumption of these types of foods by the total U S population resulted in estimated mean all-person and all-user intakes of phosphatidylserine of 24 61 mg/person/day (0 52 mg/kg body weight/day) and 44.75 mg/person/day (0 95 mg/kg body weight/day), respectively (Tables 4.1-1 and 4 1-2). The 90th percentile all-person and all-user intakes of phosphatidylserine from all proposed food-uses by the total

population were 70.00 mg/person/day (1.46 mg/kg body weight/day) and 98.73 mg/person/day (2 15 mg/kg body weight/day), respectively The 50th percentile or median reports the value in the middle of the distribution. The median is less sensitive to extreme values than the mean and is useful if the overall distribution is highly skewed In this assessment there are a low number of individuals reported for each food group causing the values of the 50th percentile to be low, as presented in Tables 4.1-1 and 4.1-2, therefore, for the purpose of this report, the 50th percentile will not be discussed further.

On an individual population basis, the greatest mean all-person and all-user intakes of phosphatidylserine on an absolute basis were determined in male teenagers, at 33 50 mg/ person/day (0 56 g/kg body weight/day), and 60.73 mg/person/day (1 01 mg/kg body weight/day), respectively Children encompassed the greatest percentage of users of any population group at 79 8% Infants had the lowest intakes of phosphatidylserine on an absolute basis, with all-person and all-user mean intakes of 16 23 and 27 39 mg/person/day, respectively On a body weight basis, mean all-person intake of phosphatidylserine was highest in children, at 1.36 mg/kg body weight/day, and the mean all-user intake was highest in infants, at 2 21 mg/kg body weight/day. The lowest mean all-person and all-user intakes on a per kilogram body weight basis were observed in male adults (0 28 and 0.61 mg/kg body weight/day) (Table 4 2-2)

Table 4.1-1 Summary of the Estimated Daily Intake of Phosphatidylserine from All Proposed Food Categories in the U.S. by Population Group (1994-1996, 1998 USDA CSFII Data)

Population Group	Age Group (Years)	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
				Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Infant	0 to 2	52 5	1,880	16 23	6 23	46 25	27 39	17 43	60.49
Child	3 to 11	79 8	5,030	33 03	23 24	80 81	41 90	29 88	91.10
Female Teenager	12 to 19	54 1	380	25 37	11 62	70 00	45 80	33 20	89 15
Male Teenager	12 to 19	55 0	383	33 50	14 53	98 98	60 73	45 46	117.80
Female Adult	20 and Up	53 3	2,438	22 71	8 16	63 66	42 16	27 29	96 42
Male Adult	20 and Up	46 9	2,230	22 76	na	66 40	49 62	33 20	105.00
Total Population	All Ages	59 9	12,341	24.61	9 96	70 00	44 75	30 30	98 73

Table 4.1-2 Summary of the Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from All Proposed Food Categories in the U.S. by Population Group (1994-1996, 1998 USDA CSFII Data)

Population Group	Age Group (Years)	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
				Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Infant	0 to 2	52 5	1,880	1 32	0 55	3 80	2 21	1 35	4 86
Child	3 to 11	79 8	5,030	1 36	0 88	3 34	1 72	1 23	3 64
Female Teenager	12 to 19	54 1	380	0 47	0 22	1 35	0 83	0 60	1 67
Male Teenager	12 to 19	55 0	383	0 56	0 24	1 66	1 01	0 72	2 18
Female Adult	20 and Up	53 3	2,438	0 35	0 12	0 99	0 65	0 43	1 47
Male Adult	20 and Up	46 9	2,230	0 28	na	0 83	0 61	0 40	1 31
Total Population	All Ages	59 9	12,341	0 52	0 15	1 46	0 95	0 56	2 15

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When heavy consumers (90th percentile) were assessed, all-person and all-user intakes of phosphatidylserine from all proposed food-uses on an absolute basis also were determined to be greatest in male teenagers (98.98 and 117.80 mg/person/day, respectively) The lowest 90th percentile all-person and all-users intakes of phosphatidylserine on an absolute basis were in infants (46.25 and 60 49 mg/person/day, respectively) (Table 4 1-1) On a body weight basis, infants were determined to have the greatest all-person 90th percentile intakes (3 80 mg/kg body weight/day) and the greatest all-user 90th percentile intakes of phosphatidylserine (4 86 mg/kg body weight/day) (Table 4 1-2). The lowest all-person and all-user 90th percentile intakes of phosphatidylserine on a body weight basis were observed in male adults (0 83 and 1.31 mg/kg body weight/day, respectively).

4.1.1 All-Person Intakes

Estimates for the mean and 90th percentile daily intakes of phosphatidylserine from each individual food category are summarized in Tables A-1 to A-7 and B-1 to B-7 on a mg/day and mg/kg body weight/day basis, respectively Tables A-7 and B-7 summarize the estimates for the mean all-person intakes of phosphatidylserine by the total population (all ages) from each of the individual food-uses on a mg/person/day and mg/kg body weight/day basis, respectively. The total U.S. population was identified as being significant consumers of ready-to-eat cereals (43.7% users) and milk products (13 6% users)

Consumption of ready-to-eat cereals made the most significant contribution to the mean and 90th percentile all-person intakes of the proposed phosphatidylserine, at 9 89 mg/person/day (0 22 mg/kg body weight/day) and 33.20 mg/person/day (0.68 mg/kg body weight/day) On a body weight basis, the highest mean and 90th percentile all-person intakes were 0 22 mg/kg body weight/day and 0 68 mg/kg body weight/day, for ready-to-eat cereals, respectively. Meal replacements, fruit flavoured drinks and dairy product analogs had a negligible impact on the all-person intakes of phosphatidylserine

Of the individual population groups, the consumption of ready-to-eat cereals made the most significant contribution to the mean all-person intakes of phosphatidylserine (Tables A-1 to A-6 and Tables B-1 to B-6) The consumption of ready-to-eat cereals also made a significant contribution to the 90th percentile intakes of phosphatidylserine in each population group The highest mean all-person intakes of phosphatidylserine, on an absolute basis, were reported in male teenagers consuming ready-to-eat cereals, at 16.71 mg/person/day (0.28 mg/kg body weight/day), and the highest 90th percentile all-person intakes also were reported in male teenagers consuming ready-to-eat cereals, at 49.90 mg/person/day (0.86 mg/kg body weight/day) On a body weight basis, consumption of ready-to-eat cereals in children led to the highest mean and 90th percentile all-person intakes (0 67 and 1.69 mg/kg body weight/day, respectively) of phosphatidylserine The lowest mean all-person intakes of phosphatidylserine across the various individual population groups were identified consistently for meal replacements or dairy product analogs.

4.1.2 All-User Intakes

Tables A-7 and B-7 also summarize the estimates for the mean all-user intakes of phosphatidylserine by the total population (all ages) from each of the individual food-uses on a mg/person/day and mg/kg body weight/day basis, respectively. When the number of users of each individual food-use is taken into account, consumers of ready-to-eat cereals were identified as having the greatest contribution to the mean and 90th percentile all-user intakes of phosphatidylserine at 26.61 and 49 80 mg/person/day (0 59 and 1.23 mg/kg body weight/day), respectively. Of the other food categories with a significant number of users of phosphatidylserine in the total population, consumption of yogurt, fluid milk products, and nutritional bars also made significant contributions to the estimates for the mean (49.96, 23 81, and 67 89 mg/person/day, respectively) and 90th percentile (94.33, 54 96 and 113 40 mg/person/day, respectively) The lowest all-user mean and 90th percentile percent user adjusted intakes of phosphatidylserine were observed for dairy product analogs, at 65 29 and 153.31 mg/person/day (1 99 and 4 42 mg/kg body weight/day), respectively.

On an individual population group basis, the consumption of ready-to-eat cereals made the most significant contribution to the all-user intakes of phosphatidylserine (Tables A-1 to A-6 and Tables B-1 to B-6) On an absolute basis children consuming ready-to-eat were determined to have the highest reliable mean and 90th percentile all-user intakes of phosphatidylserine of 477 62 and 604 80 mg/person/day, respectively On a per kilogram body weight basis, infants consuming dairy product analogs experienced the highest reliable mean and 90th percentile all-user intakes of phosphatidylserine of 10.66 and 19 52 mg/kg body weight/day, respectively

5.0 CONCLUSIONS

Consumption data and information pertaining to the individual food-uses of phosphatidylserine were used to estimate the all-person and all-user intakes of phosphatidylserine for specific demographic groups and for the total U.S. population This type of intake methodology is generally considered to be 'worst case' as a result of several conservative assumptions made in the consumption estimates. For example, it is well established that the length of a dietary survey affects the estimated consumption of individual users Short-term surveys, such as the typical 2- or 3-day dietary surveys, overestimate the consumption of food products that are consumed relatively infrequently

In summary, on an all-user basis, the mean intake of phosphatidylserine by the total U S population from all proposed food-uses was estimated to be 44.75 mg/person/day or 0 95 mg/kg body weight/day. The heavy consumer (90th percentile) all-user intake of phosphatidylserine by the total U.S. population from all proposed food-uses was estimated to be 98 73 mg/person/day or 2.15 mg/kg body weight/day.

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APPENDIX A

Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Different Population Groups Within the United States

Table A-1 Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Infants Aged 0 to 2 Years Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	12 0	429	1.70	na	6 29	11 67	9 63	23 01
Ready-to-eat Cereals	39 8	1,424	6.41	na	20 13	14 33	11 62	29 05
Dairy Product Analogs								
Soy and Imitation Milk Products	0 3	9	0.40*	na	na	143 86	135.06	257.25
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	3 2	115	1 96	na	na	51 34	46 25	92 50
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	0 9	31	0 51	na	na	57 87	52 42	157 50
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	5 3	190	1 29	na	na	21 90	12 74	55 74
Milk-Based Meal Replacements	0 1	4	0 06*	na	na	48 83*	29.30*	117 42*
Yogurt	9 0	322	3 88	na	3 37	38 36	28 05	62 35
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	< 0 1	1	0 02*	na	na	37 80*	na	37 80*

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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Table A-2 Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Children Aged 3 to 11 Years Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	13 2	830	1 68	na	6 08	14 87	12 22	26 10
Ready-to-eat Cereals	65 3	4,116	16 52	12 45	41 09	25 99	22 41	47 45
Dairy Product Analogs								
Soy and Imitation Milk Products	0 2	15	0 15*	na	na	99 91	77 18	154 35
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	5 8	363	3 73	na	na	58.05	46 25	105 00
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	4 3	272	3 64	na	na	62.16	52 50	105 00
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	13 6	858	3.94	na	12 74	25 32	19 11	50 96
Milk-Based Meal Replacements	0 2	14	0 16	na	na	62 20	52 08	117 18
Yogurt	9 5	597	2 90	na	na	36 69	27 44	54 89
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 4	27	0 31	na	na	80 44	na	126 00

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

Table A-3 Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	5 8	41	0.94	na	na	15.61	12 79	25 17
Ready-to-eat Cereals	40 7	286	10 96	na	33 20	26 05	23 24	47 27
Dairy Product Analogs								
Soy and Imitation Milk Products	0 1	1	0 04*	na	na	51 45*	51 45*	51 45*
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	5 1	36	3.43	na	na	58 37	53 75	81 25
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	4 6	32	2.97	na	na	71 80	52 50	131 04
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	13 5	95	3.76	na	12 74	25 74	22 30	63 70
Milk-Based Meal Replacements	0 3	2	0 24*	na	na	100 82	100 82	130 20
Yogurt	3 6	25	1 64	na	na	45 56	40 43	74 84
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 3	2	1 40*	na	na	477 62*	na	604 80*

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3).

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Table A-4 Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	6 0	42	1 03	na	na	19 60	16.22	38 01
Ready-to-eat Cereals	42 7	297	16 71	na	49 90	38 78	31.13	69 72
Dairy Product Analogs								
Soy and Imitation Milk Products	0 1	1	0 12*	na	na	76 97	76 97	76 97
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	4.9	34	3 24	na	na	67 19	53 75	107 50
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	5 7	40	4 95	na	na	77 52	52 50	157 50
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	12 9	90	4 81	na	12 74	37 78	25.48	92 37
Milk-Based Meal Replacements	0 1	1	0 26*	na	na	155 61	155 61	155 61
Yogurt	2 6	18	1 62	na	na	54 40	40 43	106 04
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 4	3	0 77*	na	na	186.69	na	239 40

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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Table A-5 Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Female Adults Aged 20 and Over Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	12 8	586	1 66	na	6 29	14 30	12 17	25.27
Ready-to-eat Cereals	31 9	1,458	7 30	na	25 45	22 73	18 69	41 09
Dairy Product Analogs								
Soy and Imitation Milk Products	0 2	10	0 10*	na	na	45 43	51 45	77 18
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	2 9	134	2.21	na	na	64 20	46 25	107 50
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	1 1	50	0 81	na	na	73 72	52 50	110 04
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	19 2	876	4 09	na	15 86	20 52	15 91	44 41
Milk-Based Meal Replacements	0 9	40	0 86	na	na	88 11	71 61	136 71
Yogurt	7 8	357	4 37	na	na	52 66	49.90	99 79
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	1 1	52	1 29	na	na	115 23	na	252.00

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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Table A-6 Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Male Adults Aged 20 and Over Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	11 8	561	1 87	na	na	18 89	13 21	36 50
Ready-to-eat Cereals	29 9	1,422	9 16	na	34 24	31 41	25 45	58 10
Dairy Product Analogs								
Soy and Imitation Milk Products	0 1	6	0 08*	na	na	62 44*	34 30*	154 31*
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	2 6	123	2 73	na	na	86 10	70 88	162 50
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	0 8	36	0 64	na	na	85 95	52 50	204.96
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	14 8	702	3 86	na	12 74	25 70	19 11	57 30
Milk-Based Meal Replacements	0 5	24	0 42	na	na	107 35	103 74	195.72
Yogurt	4 0	190	2 58	na	na	57 63	49 90	107 80
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 6	129	1 12	na	na	141 57	na	252 00

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3).

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Table A-7 Estimated Daily Intake of Phosphatidylserine from Individual Proposed Food-Uses by Total Population (All Ages) Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg)			All-Users Consumption (mg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	12 1	2,489	1 66	na	3 97	15 88	12 58	27.55
Ready-to-eat Cereals	43 7	9,003	9 89	na	33 20	26 61	22 20	49 80
Dairy Product Analogs								
Soy and Imitation Milk Products	0 2	42	0.11	na	na	65.29	51 45	154 31
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	3 9	805	2 71	na	na	67 89	53 75	113 40
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	2 2	461	1 49	na	na	70 92	52 50	110 04
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	13 6	2,811	3 89	na	12 74	23 81	19 03	50 96
Milk-Based Meal Replacements	0 4	85	0 51	na	na	92 11	71 61	143 22
Yogurt	7 3	1,509	3 23	na	na	49 96	49 90	94 33
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 6	129	1 12	na	na	141 57	na	252 00

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

APPENDIX B

Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by Different Population Groups Within the United States

Table B-1 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by Infants Aged 0 to 2 Years Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	12 1	2,489	0.14	na	0 57	0 96	0 79	1 99
Ready-to-eat Cereals	43 7	9,003	0 50	na	1 57	1 12	0 88	2.26
Dairy Product Analogs								
Soy and Imitation Milk Products	0 2	42	0 03*	na	na	10 66	8 89	19 52
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	3 9	805	0 16	na	na	4 03	3 40	7 02
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	2 2	461	0 04	na	na	4 45	3 30	13 33
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	13 6	2,811	0 10	na	na	1 71	1 16	3 71
Milk-Based Meal Replacements	0 4	85	< 0 01*	na	na	4.14*	3 08*	9 94*
Yogurt	7 3	1,509	0 34	na	0 55	3 24	2 63	5 93
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 6	129	< 0 01*	na	na	2 52*	2 52*	2 52*

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

Table B-2 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by Children Aged 3 to 11 Years Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	13 2	830	0 08	na	0 25	0 67	0 56	1 18
Ready-to-eat Cereals	65 3	4,116	0 67	0 50	1 69	1 05	0 85	1 99
Dairy Product Analogs								
Soy and Imitation Milk Products	0 2	15	0 01*	na	na	4 06	2 83	5 66
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	5 8	363	0 16	na	na	2 34	1 91	4 21
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	4 3	272	0 14	na	na	2 46	2 17	4 13
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	13 6	858	0 16	na	0 54	1 01	0 76	2 10
Milk-Based Meal Replacements	0 2	14	0 01	na	na	2 09	1 68	4 52
Yogurt	9 5	597	0 14	na	na	1 67	1 37	2 84
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 4	27	0 01	na	na	3 06	2 46	9 70

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

Table B-3 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by Female Teenagers Aged 12 to 19 Years Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	5 8	41	0.02	na	na	0 29	0 24	0 50
Ready-to-eat Cereals	40 7	286	0.21	na	0 61	0 48	0 41	0 87
Dairy Product Analogs								
Soy and Imitation Milk Products	0 1	1	< 0 01*	na	na	1 08*	1.08*	1.08*
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	5 1	36	0.06	na	na	1 04	1 03	1 67
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	4 6	32	0 05	na	na	1 30	1 04	2 40
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	13 5	95	0 07	na	0 24	0 46	0 35	1 08
Milk-Based Meal Replacements	0 3	2	< 0 01*	na	na	1 55	1 55	1 85
Yogurt	3 6	25	0 03	na	na	0 81	0 81	1 32
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0.3	2	0 02*	na	na	8 16*	10 40*	10 40*

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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Table B-4 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by Male Teenagers Aged 12 to 19 Years Within the United States 50mg/Serving (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	6 0	42	0 02	na	na	0 33	0 28	0 63
Ready-to-eat Cereals	42 7	297	0 28	na	0 86	0 65	0 54	1 26
Dairy Product Analogs								
Soy and Imitation Milk Products	0 1	1	< 0 01*	na	na	1 25*	1 25*	1 25*
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	4 9	34	0 06	na	na	1 25	1 08	2 53
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	5 7	40	0 08	na	na	1 25	1 07	2 17
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	12 9	90	0 08	na	0 18	0 63	0 40	1 35
Milk-Based Meal Replacements	0 1	1	< 0 01*	na	na	2 36*	2 36*	2 36*
Yogurt	2 6	18	0 03	na	na	0 88	0 78	1 17
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 4	3	0 01*	na	na	1 71	1 85	2 07

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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Table B-5 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by Female Adults Aged 20 and Over Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	12 8	586	0 03	na	0 09	0 22	0 18	0 44
Ready-to-eat Cereals	31 9	1,458	0 11	na	0 39	0 35	0 28	0 65
Dairy Product Analogs								
Soy and Imitation Milk Products	0 2	10	< 0 01*	na	na	0 76*	0.61*	1 36*
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	2 9	134	0 04	na	na	1 02	0 75	2 04
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	1 1	50	0 01	na	na	1 10	0 89	1 97
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	19 2	876	0 06	na	0 24	0 32	0 24	0 67
Milk-Based Meal Replacements	0 9	40	0 01	na	na	1 27	1 18	1 95
Yogurt	7 8	357	0 07	na	na	0 82	0 72	1 46
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	1 1	52	0 02	na	na	1 62	1 28	3 00

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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Table B-6 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by Male Adults Aged 20 and Over Within the United States (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	11.8	561	0 02	na	na	0 24	0 19	0.46
Ready-to-eat Cereals	29 9	1,422	0 11	na	0 41	0 39	0 32	0 73
Dairy Product Analogs								
Soy and Imitation Milk Products	0 1	6	< 0 01*	na	na	1 08*	0 44*	2 42*
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	2 6	123	0 03	na	na	1 03	0 86	1 87
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	0 8	36	0 01	na	na	1 04	0 72	2 01
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	14 8	702	0 05	na	0 15	0 31	0 22	0 66
Milk-Based Meal Replacements	0 5	24	0 01	na	na	1 31	1 31	1 84
Yogurt	4 0	190	0 03	na	na	0 70	0 58	1 33
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 6	129	0 02	na	na	1 95	1 35	3 65

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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Table B-7 Estimated Daily Per Kilogram Body Weight Intake of Phosphatidylserine from Individual Proposed Food-Uses by the Total Population (All Ages) Within the United States 50 mg/Serving (1994-1996, 1998 USDA CSFII Data)

Food-Use Category	% Users	Actual # of Total Users	All-Person Consumption (mg/kg)			All-Users Consumption (mg/kg)		
			Mean	50th Percentile	90th Percentile	Mean	50th Percentile	90th Percentile
Cereal and Cereal Products								
Instant and Regular Hot Cereals	12 1	2,489	0 04	na	0 07	0 34	0 23	0 72
Ready-to-eat Cereals	43 7	9,003	0 22	na	0 68	0 59	0 41	1 23
Dairy Product Analogs								
Soy and Imitation Milk Products	0 2	42	< 0 01*	na	na	1 99	1 03	4 42
Grain Products and Pastas								
Nutritional Bars (Breakfast, Granola, Protein)	3 9	805	0 06	na	na	1 46	1 08	2.96
Milk and Milk Products								
Flavored Milk and Milk Drinks, Fluid	2 2	461	0 04	na	na	1 71	1 30	2 96
Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)	13 6	2,811	0 07	na	0 21	0 45	0 29	1 00
Milk-Based Meal Replacements	0 4	85	0 01	na	na	1 39	1 27	2 02
Yogurt	7 3	1,509	0 07	na	na	1 11	0 78	2.13
Processed Fruits and Fruit Juices								
Fruit Flavored Drinks	0 6	129	0 02	na	na	1 98	1 39	3 17

*Indicates an intake estimate that may not be statistically reliable, as the CV of the mean is equal to or greater than 30% (see Section 2 3)

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APPENDIX C

Representative CSFII 1994-1996, 1998 Food Codes for All Proposed Food-Uses of Phosphatidylserine in the United States

Representative CSFII 1994-1996, 1998 Food Codes for All Proposed Food-Uses of Phosphatidylserine in the United States

Breakfast Cereals

Instant and Regular Hot Cereals

[Phosphatidylserine] = 0 0208 %

56200300	Cereal, cooked, NFS
56200350	Cereal, cooked, instant, NS as to grain
56200990	Grits, cooked, corn or hominy, NS as to regular, quick or instant, NS as to fat added in cooking
56201000	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, fat not added in cooking
56201010	Grits, cooked, corn or hominy, regular, fat not added in cooking
56201020	Grits, cooked, corn or hominy, regular, fat added in cooking
56201030	Grits, cooked, corn or hominy, regular, NS as to fat added in cooking
56201040	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, fat added in cooking
56201060	Grits, cooked, corn or hominy, with cheese, NS as to regular, quick, or instant, NS as to fat added
56201061	Grits, cooked, corn or hominy, with cheese, NS as to regular, quick, or instant, fat not added in cooking
56201062	Grits, cooked, corn or hominy, with cheese, NS as to regular, quick, or instant, fat added in cooking
56201070	Grits, cooked, corn or hominy, with cheese, regular, NS as to fat added in cooking
56201071	Grits, cooked, corn or hominy, with cheese, regular, fat not added in cooking
56201072	Grits, cooked, corn or hominy, with cheese, regular, fat added in cooking
56201080	Grits, cooked, corn or hominy, with cheese, quick, NS as to fat added in cooking
56201081	Grits, cooked, corn or hominy, with cheese, quick, fat not added in cooking
56201082	Grits, cooked, corn or hominy, with cheese, quick, fat added in cooking
56201090	Grits, cooked, corn or hominy, with cheese, instant, NS as to fat added in cooking
56201091	Grits, cooked, corn or hominy, with cheese, instant, fat not added in cooking
56201092	Grits, cooked, corn or hominy, with cheese, instant, fat added in cooking
56201110	Grits, cooked, corn or hominy, quick, fat not added in cooking
56201120	Grits, cooked, corn or hominy, quick, fat added in cooking
56201130	Grits, cooked, corn or hominy, quick, NS as to fat added in cooking
56201210	Grits, cooked, corn or hominy, instant, fat not added in cooking
56201220	Grits, cooked, corn or hominy, instant, fat added in cooking
56201230	Grits, cooked, corn or hominy, instant, NS as to fat added in cooking
56201240	Grits, cooked, flavored, corn or hominy, instant, fat not added in cooking
56201250	Grits, cooked, flavored, corn or hominy, instant, fat added in cooking
56201260	Grits, cooked, flavored, corn or hominy, instant, NS as to fat added in cooking
56201300	Grits, cooked, corn or hominy, NS as to regular, quick, or instant, NS as to fat added in cooking, made with water
56201510	Cornmeal mush, made with water
56201520	Cornmeal mush, fried
56201530	Cornmeal mush, made with milk
56201540	Cornmeal, made with evaporated milk and sugar, Puerto Rican Style (Harina de maize con leche)
56201560	Cornmeal sticks, boiled
56201600	Cornmeal, lime-treated, cooked (Masa harina)
56201700	Cornstarch with milk, eaten as a cereal (2 tbsp cornstarch in 2-1/2 cups milk)
56201990	Millet, cooked, NS as to fat added in cooking
56202000	Millet, cooked, fat not added in cooking

56202100	Millet, cooked, fat added in cooking
56202500	Muesli, prepared, instant
56202960	Oatmeal, cooked, NS as to regular, quick or instant, NS as to fat added in cooking
56202970	Oatmeal, cooked, quick (1 or 3 minutes), NS as to fat added in cooking
56202980	Oatmeal, cooked, regular, NS as to fat added in cooking
56203000	Oatmeal, cooked, NS as to regular, quick or instant, fat not added in cooking
56203010	Oatmeal, cooked, regular, fat not added in cooking
56203020	Oatmeal, cooked, quick (1 or 3 minutes), fat not added in cooking
56203030	Oatmeal, cooked, instant, fat not added in cooking
56203040	Oatmeal, cooked, NS as to regular, quick, or instant, fat added in cooking
56203050	Oatmeal, cooked, regular, fat added in cooking
56203060	Oatmeal, cooked, quick (1 or 3 minutes), fat added in cooking
56203070	Oatmeal, cooked, instant, fat added in cooking
56203080	Oatmeal, cooked, instant, NS as to fat added in cooking
56203090	Oatmeal, fortified, cooked, instant, fat not added in cooking
56203100	Oatmeal, fortified, cooked, instant, fat added in cooking
56203110	Oatmeal with maple flavor, cooked
56203120	Oatmeal, with oat bran, fortified, cooked, instant, fat not added in cooking
56203140	Total Oatmeal, cooked, quick, fat not added in cooking
56203200	Oatmeal with fruit, cooked
56203210	Oatmeal, NS as to regular, quick, or instant, made with milk, fat not added in cooking
56203220	Oatmeal, NS as to regular, quick, or instant, made with milk, fat added in cooking
56203230	Oatmeal, NS as to regular, quick, or instant, made with milk, NS as to fat added in cooking
56203540	Oatmeal, made with evaporated milk and sugar, Puerto Rican style
56203600	Oatmeal, multigrain, cooked, NS as to fat added in cooking
56203610	Oatmeal, multigrain, cooked, fat not added in cooking
56203620	Oatmeal, multigrain, cooked, fat added in cooking
56206970	Wheat, cream of, cooked, quick, NS as to fat added in cooking
56206980	Wheat, cream of, cooked, regular, NS as to fat added in cooking
56206990	Wheat, cream of, cooked, NS as to regular, quick, or instant, NS as to fat added in cooking
56207000	Wheat, cream of, cooked, NS as to regular, quick, or instant, fat not added in cooking
56207010	Wheat, cream of, cooked, regular, fat not added in cooking
56207020	Wheat, cream of, cooked, quick, fat not added in cooking
56207030	Wheat, cream of, cooked, instant, fat not added in cooking
56207040	Wheat, cream of, cooked, made with milk
56207050	Wheat, cream of, cooked, made with milk and sugar, Puerto Rican style
56207060	Wheat, cream of, cooked, instant, fat added in cooking
56207070	Wheat, cream of, cooked, instant, NS as to fat added in cooking
56207080	Wheat, cream of, cooked, NS as to regular, quick, or instant, fat added in cooking
56207100	Wheat, rolled, cooked, fat not added in cooking
56207110	Bulgur, cooked or canned, fat not added in cooking
56207120	Bulgur, cooked or canned, fat added in cooking
56207130	Bulgur, cooked or canned, NS as to fat added in cooking
56207140	Wheat, rolled, cooked, NS as to fat added in cooking
56207150	Couscous, plain, cooked, fat not added in cooking
56207160	Couscous, plain, cooked, NS as to fat added in cooking
56207180	Couscous, plain, cooked, fat added in cooking
56207190	Whole wheat cereal, cooked, NS as to fat added in cooking
56207200	Whole wheat cereal, cooked, fat not added in cooking
56207210	Whole wheat cereal, cooked, fat added in cooking
56207220	Wheat, cream of, cooked, regular, fat added in cooking
56207230	Wheat, cream of, cooked, quick, fat added in cooking
56207290	Wheat hearts, cooked, NS as to fat added in cooking
56207300	Whole wheat cereal, wheat and barley, cooked, fat not added in cooking

56207310	Wheat hearts, cooked, fat not added in cooking
56207330	Whole wheat cereal, wheat and barley, cooked, fat added in cooking
56207340	Whole wheat cereal, wheat and barley, cooked, NS as to fat added in cooking
56207350	Wheat cereal, chocolate flavored, cooked, made with milk
56207360	Wheat cereal, chocolate flavored, cooked, fat not added in cooking
56207370	Wheat cereal, chocolate flavored, cooked, NS as to fat added in cooking
56208000	Multigrain cereal, cooked, fat not added in cooking
56208010	Multigrain cereal, cooked, fat added in cooking
56208020	Multigrain cereal, cooked, NS as to fat added in cooking
56208500	Oat bran cereal, cooked, fat not added in cooking
56208510	Oat bran cereal, cooked, fat added in cooking
56208520	Oat bran cereal, cooked, NS as to fat added in cooking
56208530	Oat bran cereal, cooked, made with milk, fat not added in cooking
56208540	Oat bran cereal, cooked, made with milk, fat added in cooking
56208550	Oat bran cereal, cooked, made with milk, NS as to fat added in cooking
56209000	Rye, cream of, cooked
56210000	Nestum cereal

Ready-to-Eat Cereals
[Phosphatidylserine] = 0 333 to 0 0909 %

57137000	Corn Puffs
57301500	Kashi, Puffed
57306100	Malt-O-Meal Puffed Rice
57306120	Malt-O-Meal Puffed Wheat
57307500	Millet, puffed
57340000	Rice, puffed
57416000	Wheat, puffed, plain
57416010	Wheat, puffed, presweetened with sugar
57000000	Cereal, NFS
57000050	Kashi cereal, NS as to ready to eat or cooked
57000100	Oat cereal, NFS
57100100	Cereal, ready-to-eat, NFS
57101000	All-Bran
57101020	All-Bran with Extra Fiber
57101500	Almond Delight
57102000	Alpen
57103000	Alpha-Bits
57103020	Alpha-bits with marshmallows
57103050	Amaranth Flakes
57103100	Apple Cinnamon Cheerios
57103400	Apple Cinnamon Oh's Cereal
57103450	Apple Cinnamon Rice Krispies
57104000	Apple Jacks
57106000	Banana Frosted Flakes
57106200	Batman
57106250	Berry Berry Kix
57106300	Bigg Mixx
57106500	Bill and Ted's Excellent Adventure
57106530	Blueberry Morning, Post
57107000	Booberry
57109000	Body Buddies, natural fruit flavor
57110000	All-Bran Bran Buds, Kellogg's (formerly Bran Buds)
57111000	Bran Chex
57111300	Bran News
57111500	Bran Muffin Crisp

57112500	Breakfast with Barbie
57113000	Buc Wheats
57113300	Bunuelitos
57114000	C-3PO's
57116100	Cabbage Patch
57117000	Cap'n Crunch
57117500	Cap'n Crunch's Christmas Crunch
57118000	Cap'n Crunch's Choco Crunch
57119000	Cap'n Crunch's Crunch Berries
57119500	Cap'n Crunch's Deep Sea Crunch
57120000	Cap'n Crunch's Peanut Butter Crunch
57123000	Cheerios
57124000	Chex cereal, NFS
57124200	Chocolate flavored frosted puffed corn cereal
57124500	Cinnamon Grahams, General Mills
57125000	Cinnamon Toast Crunch
57125900	Honey Nut Clusters (formerly called Clusters)
57126000	Cocoa Krispies
57126500	Cocoa Blasts, Quaker
57127000	Cocoa Pebbles
57128000	Cocoa Puffs
57128880	Common Sense Oat Bran, plain
57128900	Common Sense Oat Bran, with raisins
57130000	Cookie-Crisp
57131000	Crunchy Corn Bran, Quaker
57132000	Corn Chex
57134000	Corn flakes, NFS
57134090	Corn flakes, low sodium
57135000	Corn flakes, Kellogg
57138000	Total Corn Flakes
57139000	Count Chocula
57141000	Cracker Jack
57144000	Crisp Crunch
57148000	Crispix
57148500	Crispy Brown Rice Cereal
57151000	Crispy Rice
57152000	Crispy Wheats'n Raisins
57152100	Croonchy Stars
57201200	Dairy Crisp w/strawberries
57201700	Dino Pebbles
57202100	Donkey Kong
57203100	Donkey Kong Jr
57204100	Donutz Cereal
57205100	Donutz Cereal, Chocolate
57205250	Double Chex
57205260	Double Dip Crunch, Kellogg's
57205300	E T Cereal
57206700	Fiber One
57206800	Fiber 7 Flakes, Health Valley
57212100	French Toast Crunch, General Mills
57213800	Frosted Bran, Kellogg's
57213850	Frosted Cheerios
57214100	Frosted Wheat Bites
57215000	Frosty O's
57216000	Frosted rice, NFS
57217000	Frosted Rice Krinkles

57218000	Frosted Rice Krispies
57219000	Fruit & Fibre (fiber), NFS
57220000	Fruit & Fibre (fiber) with apples and cinnamon
57221000	Fruit & Fibre (fiber) with dates, raisins, and walnuts
57221500	Fruit & Fibre (fiber) tropical fruit w/oat clusters
57221600	Fruit & Fibre (fiber) with peaches, raisins, almonds and oat clusters
57221700	Fruit Rings, NFS
57221800	Fruit Whirls
57222500	Fruit Wheats
57224000	Golden Grahams
57225000	Golden Harvest Proteinola
57231000	Grape-Nut Flakes
57231500	Gremlins
57232000	Halfsies
57232100	Healthy Choice Almond Crunch with raisins, Kellogg's
57232120	Healthy Choice Multi-Grain Flakes, Kellogg's
57235500	Heartwise, plain
57235600	Heartwise, with fruit nuggets
57237000	Honey Bran
57237100	Honey Bunches of Oats
57237300	Honey Bunches of Oats with Almonds, Post
57238000	Honeycomb, plain
57239000	Honeycomb, strawberry
57239100	Honey Crunch Corn Flakes, Kellogg's
57240000	Honey Graham Chex
57241000	Honey Nut Cheerios
57243000	Honey Smacks
57243600	Hot Wheels
57243900	Jetsons
57301100	Kaboom
57301700	Kenmei Rice Bran
57302100	King Vitaman
57303100	Kix
57304100	Life (plain and cinnamon)
57305100	Lucky Charms
57305150	Frosted oat cereal with marshmallows
57305170	Malt-O-Meal Coco-Roos
57305200	Malt-O-Meal Crispy Rice
57305500	Malt-O-Meal Honey and Nut Toasty O's
57306500	Malt-O-Meal Golden Puffs (formerly Sugar Puffs)
57306700	Malt-O-Meal Toasted Oat Cereal
57306800	Malt-O-meal Tootie Fruities
57307100	Fruity Marshmallow Krispies (formerly called Marshmallow Krispies)
57307550	Mini Buns Cereal (cinnamon)
57308000	Morning Funnies
57308300	Multi Bran Chex
57308400	Multi Grain Cheerios
57308410	Multi-Grain Cheerios Plus
57311600	Nintendo
57311790	Nut and Honey crunch biscuits
57311800	Nut and Honey Crunch (flakes)
57311900	Nutrific Oatmeal Flakes
57313000	Nutri-Grain Corn
57313900	Nutri-Grain Raisin Bran
57315000	Nutri-Grain Golden Wheat (formerly Nutri-Grain Wheat)
57316100	Nutri-Grain Almond Raisin

57316300	Oat Bran Flakes, Health Valley
57316350	Oat Bran Options
57316700	Oh's, Crunchy Nut
57316710	Oh's, Honey Graham
57316750	Oh's, Fruitangy, Quaker
57316800	O J 's
57317000	Oat flakes, fortified
57317200	Oat Flakes, Post
57322500	Oreo O's cereal, Post
57323000	Sweet Crunch, Quaker (formerly called Popeye)
57323050	Sweet Puffs, Quaker
57323200	Pop Tarts Crunch Cereal
57325000	Product 19
57327450	Quaker Oat Bran Cereal
57328000	Quisp
57328500	Rainbow Brite
57335530	Razzle Dazzle Rice Krispies
57335550	Reese's Peanut Butter Puffs cereal
57336000	Rice Chex
57337000	Rice Flakes, NFS
57339000	Rice Krispies
57339500	Rice Krispies Treats Cereal (Kellogg's)
57340200	Ripple Crisp Golden Corn
57340210	Ripple Crisp Honey Bran, General Mills
57340900	S W Graham
57342000	Slimer! & Ghostbusters
57342500	S'mores Crunch
57343000	Smurf Magic Berries
57344000	Special K
57344050	Spider-Man, Ralston
57344100	Sprinkle Spangles
57345000	Strawberry Krispies
57346500	Toasted Oatmeal, Honey Nut (Quaker)
57347000	Corn Pops
57347500	Strawberry Squares Mini-Wheats, Kellogg's (formerly Strawberry Squares)
57348000	Frosted corn flakes, NFS
57349000	Frosted Flakes, Kellogg
57349010	Cocoa Frosted Flakes, Kellogg's
57350000	Frosted Flakes, Ralston Purina
57352000	Sugar-Sparkled Flakes
57353000	Sugar-Sparkled Rice Krinkles
57354000	Sun Flakes
57355000	Golden Crisp (Formerly called Super Golden Crisp)
57401100	Toasted oat cereal
57402000	Team
57402250	Teddy Grahams Breakfast Bears
57402500	Teenage Mutant Ninja Turtles
57402600	Temptations, French Vanilla Almond, Kellogg's
57402610	Temptations, Honey Roasted Pecan, Kellogg's
57402750	Tiny Toon Adventures
57403100	Toasties, Post
57404100	Malt-O-Meal Toasty O's
57406100	Total
57406200	Triples
57408100	Uncle Sam's Hi Fiber Cereal
57409100	Waffle Crisp, Post

57410000	Weetabix Whole Wheat Cereal
57415000	Wheat'n Raisin Chex
57418000	Wheaties
57418200	Wheaties, Honey Frosted (formerly Wheaties Honey Gold)
57103500	Apple Cinnamon Squares Mini-Wheats, Kellogg's (formerly Apple Cinnamon Squares)
57105000	Apple Raisin Crisp
57106100	Basic 4
57207000	Bran Flakes, NFS (formerly 40% Bran Flakes, NFS)
57208000	Complete Wheat Bran Flakes, Kellogg's (formerly 40% Bran Flakes)
57210100	40+ Bran Flakes
57214000	Frosted Mini-Wheats
57229000	Granola, lowfat, Kellogg's
57229500	Granola with Raisins, lowfat, Kellogg's
57232110	Healthy Choice Multi-Grain Squares, Kellogg's
57241200	Honey Nut Shredded Wheat, Post
57244000	Just Right
57245000	Just Right Fruit and Nut (formerly Just Right with raisins, dates, and nuts)
57308180	Mueslix Crispy Blend (formerly Mueslix Five Grain Muesli Cereal)
57308200	Mueslix golden crunch cereal
57308210	Muesli with apples and almonds, Ralston Purina
57308220	Strawberry muesli with pecans and raisins, Ralston
57312100	Nutri-Grain Biscuits, Whole Grain Shredded Wheat Cereal
57316410	Apple Cinnamon Oatmeal Crisp (formerly Oatmeal Crisp with Apples)
57316450	Oatmeal Crisp with Almonds
57316500	Oatmeal Raisin Crisp
57327500	Quaker Oatmeal Squares (formerly Quaker Oat Squares)
57329000	Raisin bran, NFS
57330000	Raisin Bran, Kellogg
57330500	Raisin Bran, Nutri System
57331000	Raisin Bran, Post
57332050	Raisin Bran, Total
57332100	Raisin Nut Bran
57332300	Super Raisin Bran, New Morning
57334000	Raisin Life
57335000	Raisins, Rice and Rye
57335500	Raisin Squares Mini-Wheats, Kellogg's (formerly Raisin Squares)
57341000	Shredded Wheat'N Bran
57417000	Shredded Wheat, 100%
57417500	Shredded Wheat with Oat Bran

Dairy Product Analogs

Imitation milk and soy milk
[Phosphatidylserine] = 0 042 %

11310000	Milk, imitation, fluid, soy based
11320000	Milk, soy, ready-to-drink, not baby

Grain Products and Pastas

Nutritional Bars (Breakfast, Granola, Protein)
[Phosphatidylserine] = 0 250 %

41435010	High protein bar, soy base
41435110	High protein bar, candy-like, soy and milk base
41435200	High protein bar, cookie type, soy and milk base

53540000	Breakfast bar, nfs
53540100	Breakfast bar, cake-like
53540200	Breakfast bar, cereal crust with fruit filling, lowfat
53540250	Breakfast bar, cereal crust with fruit filling, fat free
53540500	Breakfast bar, date, with yogurt coating
53541100	Breakfast bar, diet meal type
53544450	PowerBar (fortified high energy bar)
53541200	Meal replacement bar (incl slim fast bar)
53542100	Granola bar w/ oats, sugar, raisins, coconut
53542200	Granola bar, oats, fruit, nuts, lowfat
53542210	Granola bar, nonfat
53543100	Granola bar w/ peanuts, oats, sugar, wheat germ
53544100	Granola bar, w/ nougat
53544200	Granola bar, chocolate-coated
53544210	Granola bar, w/ coconut, chocolate-coated
53544220	Granola bar w/ nuts, chocolate-coated
53544250	Granola bar, coated w/ nonchocolate coating
53544300	Granola bar, high fiber, yogurt coating, not choc
53544400	Granola bars, w/ rice cereal

Milk Products

Flavored Milk and Milk Drinks, Fluid
[Phosphatidylserine] = 0 042 %

11511000	Milk, chocolate, nfs
11513000	Cocoa & sugar mixture, milk added, ns type milk
11513400	Chocolate syrup milk added, ns as to type of milk
11514300	Cocoa w/ nf dry milk, lo cal sweetener, water added
11514500	Cocoa w/ whey, lo cal sweetnr, fortifd, water added
11515100	Cocoa & sugar w/ milk, fortified, Puerto Rican
11515400	Cocoa w/ nfdm, low calorie, hi calcium, water added
11516000	Cocoa, whey, lo cal sweetner mix, lowfat milk added
11518000	Milk bev w/ nf dry mlk, lo cal sweet, water, choc
11518050	Milk bev w/nf dry milk, lo cal sweet, water, not choc
11518100	Milk bev w/nfd milk, lo cal sweet, hi calcium, choc
11519000	Milk beverage, not chocolate, w/ whole milk
11519050	Milk, not chocolate, whole milk based
11519100	Milk beverage, beads, whole milk added
11551050	Milk fruit drink (incl licuado)
11551100	Milk fruit drink, Puerto Rican style (champola de frutas)
11552200	Milk-based fruit drink (incl orange julius)
11553000	Fruit smoothie drink, w/ fruit and dairy products
11553100	Fruit smoothie drink, nfs
11560000	Choc-flavored drink, whey-& milk-based (incl yoo-hoo)
11560020	Milk drink, whey & milk-base, not choc (incl yoo-hoo)
11560100	Flav milk drink, skim milk & cream-based, not choc
11560110	Chocolate flav milk drink, skim milk & cream-based

Milk, Fluid (Regular, Filled, Buttermilk, and Dry reconstituted)
[Phosphatidylserine] = 0 0208 %

11100000	Milk, nfs
11112000	Milk, cow's, fluid, not whole, ns as to % fat

11113000 Milk, cow's, fluid, skim or nonfat

Milk-Based Meal Replacements
[Phosphatidylserine] = 0 042 %

11611000 Instant breakfast, fluid, canned
11612000 Instant breakfast, powder, milk added
11613000 Instant bfast, pwdr, swt w/ lo cal swt, milk added
11621000 Diet beverage, liquid, canned
11622000 Diet beverage powder, milk added
11622010 Diet beverage, pwdr, reconst w/skim (incl carnation)
11623000 Meal supplement / replacement, prepared, rtd
11631000 High calorie bev, canned or powdered, reconstituted
11641000 Meal replacement, milk based, high protein, liquid
11651010 Meal replacement, cambridge, reconst, all flavors

Yogurt
[Phosphatidylserine] = 0 044 %

11410000 Yogurt, ns as to type of milk/flavor
11411100 Yogurt, plain, whole milk
11411200 Yogurt, plain, lowfat milk
11411300 Yogurt, plain, nonfat milk
11420000 Yogurt, vanilla, lemon, coffee, ns as to milk type
11421000 Yogurt, vanilla, lemon, coffee, whole milk
11422000 Yogurt, vanilla, lemon, coffee, lowfat milk
11423000 Yogurt, vanilla, lemon, coffee, nonfat milk
11424000 Yogurt, vanilla, lemon, coffee, nonfat milk, low cal sweet
11425000 Yogurt, chocolate, ns as to type of milk
11426000 Yogurt, chocolate, whole milk
11427000 Yogurt, chocolate, nonfat milk
11430000 Yogurt, fruit variety, ns as to milk type
11431000 Yogurt, fruit variety, whole milk
11432000 Yogurt, fruit variety, lowfat milk
11433000 Yogurt, fruit variety, nonfat milk
11433500 Yogurt, fruited, nonfat milk, low cal sweetener
11444000 Yogurt, fruit & nuts, ns as to type of milk
11445000 Yogurt, fruit & nuts, lowfat milk

Processed Fruits and Fruit Juices

Fruit Flavored Drinks
[Phosphatidylserine] = 0 042 %

92741000 Fruit-flavored drink, non-carb, from low cal powder

SUBMISSION END