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Division of
Biotechnology and
GRAS Notice Review

GRAS Notification
for
Pine Tree Phytosterols Esters

Volume 1 of 1

Submitted by:

Arboris LLC
1101 West Lathrop Avenue, Gate 16
Savannah, GA 31415

April 19, 2010

arboris®
pine tree extracts

April 19, 2010

Robert L. Martin, Ph.D.
Deputy Director
Division of Biotech and GRAS Notice Review, (HFS 255)
OFAS/CFSAN/FDA
University Station Building (Room 2045)
5100 Paint Branch Parkway
College Park, MD 20740

VIA: Federal Express

Re: GRAS Notification for Pine Tree Phytosterol Esters

Dear Dr. Martin:

Arboris LLC has determined that the use of Arboris® Sterol Ester is exempt from the premarket approval requirements of the Federal Food, Drug and Cosmetic Act because Arboris has determined that such use is GRAS. In accordance with proposed regulation, the following information is provided:

Proposed 21 CFR § 170.36 (c)(1)(I) The name and address of the notified:

Arboris LLC
1101 W. Lathrop Avenue
Gate 16
Savannah, GA 31415

Proposed 21 CFR § 170.36 (c)(1)(ii) The common or usual name of the notified substance:

Pine Tree Phytosterol Ester
Trade Name: Arboris® Sterol Ester

Proposed 21 CFR § 170.36 (c)(iii) The applicable conditions of use of the notified substance:

For the existing uses of phytosterols and phytosterol esters in foods to include: Margarine and vegetable-based spreads; yogurt and yogurt-like products; milk-based juice beverages; ice cream and non-standardized ice cream products; cream cheese and cream cheese-like products; snack bars; salad dressing; standardized and non-standardized bread products; baked foods; beverages; dairy analogs; cheese and cream; breakfast cereal; mayonnaise; pasta and noodles; sauces; salty snacks; processed soups; puddings; confections; vegetarian meat analogs; fruit/vegetable juice; vegetable oils; egg products, including egg whites and substitute egg products.

Sergio Maldonado, Technology Manager
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1101 West Lathrop Av., Savannah, GA 31415, USA.
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pine tree extracts

Proposed 21 CFR § 170.36 (c)(1)(iv) The basis for the GRAS determination:

This GRAS determination is based on scientific procedures.

Proposed 21 CFR § 170.36 (c)(1)(v) Availability of information:

The data and information that are the basis for the Arboris' GRAS determination are available for FDA review at Phoenix Regulatory Associates, Ltd. Any additional information may be obtained by contacting:

Dr. Clyde A. Takeguchi, Ph.D.
Phoenix Regulatory Associates, Ltd.
21525 Ridgetop Circle, Suite 240
Sterling, VA 20166
Phone: (703)-406-0906
Email: ctakeguchi@phoenixrising.com

Sincerely,

(b) (6)

Sergio Maldonado
Technology Manager
Arboris LLC

Enclosures: Original and two (2) copies

cc: Phoenix Regulatory Associates, Ltd. letter only

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Pine Tree Phytosterols and Phytosterol Esters

1. Introduction

Arboris, LLC (Arboris) submitted the relevant information on the identity, safety and use of its phytosterols on April 11, 2008 (GRN 250, incorporated by reference). On February 9, 2009, FDA stated in a letter that there were no additional questions to Arboris' conclusion that their phytosterol, Arboris® sterol AS-2®, is GRAS.

Since that time, the European Food Safety Authority (FSA), the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Food Standards Australia New Zealand (FSANZ) have concluded that phytosterols from all sources and their fatty acid esters are safe at the estimated dietary exposure levels.

Arboris has further concluded that its phytosterols and fatty acid esters of its phytosterols are substantially equivalent to other products currently in the marketplace and that there is general recognition by experts qualified in scientific experience that the use of phytosterols in food from plant and vegetable sources for the existing uses are safe based on scientific procedures. Therefore, the use of phytosterols and phytosterol esters manufactured by Arboris is safe for use in food.

2. Identity

The term "Phytosterols" is used as a collective term for sterols and stanols. The source of these phytosterols can be from pine tree, plant or vegetable oils and determines the relative amounts of individual phytosterols.

2.1. Phytosterol Esters

The phytosterol esters are manufactured with Arboris phytosterols and esterified or transesterified with food-grade fatty acids or from food-grade vegetable oils using methods commonly used in the food industry for fats and oils.

The Arboris ester has a purity of 96% for total phytosterols (90% ester and 6% free phytosterol). The current Food Chemicals Codex (FCC) specification for "vegetable oil phytosterol esters" is 95% for total phytosterols (86% ester and 9% free phytosterol) (FCC6).

Pine Tree Phytosterols and Phytosterol Esters (continued)
2. Identity (continued)

2.2. Food-Grade Specifications

Substance	(%)
Total free sterols and sterol ester	(b)(4)
Total sterol ester content	
Total sterols content calculated	
Total free sterols content	
Beta-Sitosterol	
Campesterol	
Campestanol	
Stigmasterol	
Sitostanol	
Other Sterols	

Appearance/Color	light yellow (liquid)
Creamy white (solid)	
Taste slightly vegetable oil	
Odor little to none	

Acid value mg KOH/g	(b)(4)
Moisture,	
Heavy metals	

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Pine Tree Phytosterols and Phytosterol Esters (continued)
2. Identity (continued)

3. Manufacture

Phytosterol esters are produced by the esterification of free phytosterols with vegetable oil derived fatty acids.

The phytosterols are directly esterified with vegetable fatty acids or by trans-esterification with an intermediate vegetable fatty acid ester. Trans-esterification is a more common process with typically higher purity and yields. The vegetable fatty acid is pre-esterified with a low molecular weight alcohol that can easily be removed from the end product. Typically methanol is used to produce the Fatty Acid Methyl Ester (FAME) but other alcohols can be used as well. The following steps for direct esterification or trans-esterification are the same.

The free phytosterols are heated in a reactor with fatty acid esters in the presence of catalyst. Reactor temperatures and pressures are selected to drive the reaction to completion and minimize any undesirable reactions. Typically these conditions are (b)(4) and deep vacuum. The reaction process esterifies the free sterols and liberates the alcohol that was used to pre-esterify the vegetable fatty acid.

The phytosterol esters are then separated from the reaction vessel and refined in series of processing steps which include: catalyst removal, residual free sterols separation, residual fatty acid separation, residual unreacted FAME separation, bleaching and deodorizing. The unit operations used to perform these process steps include filtration, distillation, raffination, solvent extraction, crystallization and steam stripping. The order of these can be varied or combined in a single operation.

Catalyst is removed from the product by filtration, raffination or liquid extraction.
Bleaching is performed to remove color bodies introduced with the raw materials or produced during the reaction. The bleaching compounds that can be used include activated carbon, active clays or bleaching earth. These are typically removed thorough filtration and are sometimes combined with the catalyst removal step. A filtration aid can be used to improve filtering.

Residual fatty acids and other low boiling point impurities are removed through distillation or evaporization. This operation is typically conducted at high temperatures and deep vacuum.

Residual free phytosterol removal is accomplished by crystallization. This step is not required if the residual free sterols are below the desired level.

Pine Tree Phytosterols and Phytosterol Esters (continued)
3. Manufacturing (continued)

Deodorization is typically performed to strip out any reaction products that may affect the odor or taste. Rancidity or other decomposition products are typically introduced with the vegetable fatty acid. A preservative, such as tocopherol or other antioxidants, is added after this step to reduce decomposition and inhibit the formation of rancidity products.

4. Conditions of Use

The various GRNs reviewed by FDA included the following uses: Margarine and vegetable-based spreads; yogurt and yogurt-like products; milk-based juice beverages; ice cream and non-standardized ice cream products; cream cheese and cream cheese-like products; snack bars; salad dressing; standardized and non-standardized bread products; baked foods; beverages; dairy analogs; cheese and cream; breakfast cereal; mayonnaise; pasta and noodles; sauces; salty snacks; processed soups; puddings; confections; vegetarian meat analogs; fruit/vegetable juice; vegetable oils; egg products, including egg whites and substitute egg products. (See Tables 1 and 2.)

The estimates of dietary exposure for all proposed uses from the GRN submissions were 5.5 to 7.3g/p/d at the mean and 10.6 to 12.9 g/p/d at the 90th percentile.
(See Tables 2 and 3.)

Arboris believes that its phytosterol products will be used as an alternative source of phytosterols and phytosterol esters currently used as ingredients in commercial food products.

Pine Tree Phytosterols and Phytosterol Esters (continued)
4. Conditions of Use (continued)

Table 1: GRAS Notification for Sterols

GRN No.	Novartis 39	ADM 61	ADM 176	Teriaka 112	Michael Fd 181
ID	Tall oil phytosterols	Plant sterols and plant sterol esters	Plant sterols and plant sterol esters	phytosterols	Plant phytosterols
Mfg	Tall oil soap, by product of paper pulping process, organic solvent extraction, crystallized from alcohol	Phytosterols from vegetable oils are esterified with vegetable oil fatty acids	Phytosterols from vegetable oils and tall oil	Phytosterols, vegetable fat mixture, vegetable oil mixture, or anhydrous milk fat mixture. Phytosterols from veg oils or tall oil	Phytosterols from vegetable oils and tall oil (< 5%)
Use	In vegetable oil spread	In vegetable oil spreads, salad dressing, health drinks, health bars, and yogurt-type products	In margarines and vegetable oil spreads, salad dressing, beverages, snack bars, dairy analogs, cheese and cream, baked foods, breakfast cereal, mayonnaise, pasta and noodles, sauces, salty snacks, processed soups, puddings, yogurt, confections, vegetarian meat analogs, fruit/veg juice, vegetable oils	In margarine and vegetable-based spreads, yogurt and yogurt-like products; milk-based juice beverages, ice cream and non-standardized ice cream produces, cream cheese and cream cheese-like products, snack bars, salad dressing, standardized and non-standardized bread products	Egg products, including egg whites and egg substitutes
Level	Up to 12% free phytosterols	EDI 5.5 g/p/day @ mean, 10.6 g @ 90th percentile	EDI 3.9 g/p/day @ 90th percentile	EDI 1.6g/p/day @ mean 3.6 g/p/day 90th percentile	Up to 20 mg plant sterol/g egg product; 1100 mg phytosterol/serving
GRAS Panel	yes	yes	yes	no	yes

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Pine Tree Phytosterols and Phytosterol Esters (continued)
4. Conditions of Use (continued)

Table 2: GRAS Notification for Sterol Esters

GRN No.	Cargill 48	P&G 53	HeartBlend 177	Enzymotec 206
ID	vegetable oil phytosterol esters	Phytosterol esters	Plant sterol esters	Phytosterol esters and diglycerides
Mfg	Soy sterols are esterified with vegetable oil fatty acids from soy canola, sunflower or other veg oils. After esterification, adsorbants are used to remove trace components, vacuum stripped and filtered.	Cargill	ADM	Enzymatic and chemical transesterification of vegetable fats/oils with vegetable phytosterols
Use	In vegetable oil spreads, salad dressing, bars, yogurt.	In vegetable oil at a level up to 13.3% for home use, and salad dressings	In ground roasted coffee	In baked goods and baking mixes; fats and oils; frozen dairy desserts and mixes; gelatins, puddings, and fillings; grain products and pastas; gravies and sauces; hard candy; milk; milk products; soft candy; soups and soup mixes; and snack foods at a level of 0.65 g/ esters/RACC
Level	3 g plant sterol or stanols, or 5 g plant sterol or stanol esters/person/ day	Additional consumption of 0.75 g/ person/day to 2.1 g/person/day @ 90th percentile	1 g plant sterol esters/8 fl oz serving 1.4 g/person/day mean, 2.5 g/person/day 90th percentile	7.3 g/p/d @ mean, 12.9 g/p/d @ 90th percentile
GRAS Panel	yes	yes	yes	yes

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Pine Tree Phytosterols and Phytosterol Esters (continued)

5. Safety and Effectiveness

5.1 Regulatory Status

FDA

FDA has not made its own determination on the GRAS status of phytosterols, but has listed its responses to several GRAS notices on phytosterols (GRN 00039, 00061, 00112, 00176, and 00181) and phytosterol esters (GRN 00048, 00053, 00177, and 00206) obtained from vegetables, plants, and pine trees. (See Tables 1 and 2.)

The GRAS panels for earlier notices have concluded that phytosterols meeting food-grade specifications are GRAS by scientific procedures for their intended use and FDA did not question their conclusion.

On September 8, 2000, FDA issued an interim final rule (FDA 2000) allowing the use of health claims on the association between plant sterol/stanol esters and the reduced risk of coronary heart disease. To be eligible for using the health claim, a food product must contain at least 0.65g of plant sterol esters per reference amount customarily consumed (RACC) in spreads and salad dressing, or at least 1.7g of plant stanol esters per RACC in spreads, salad dressings, snack bars, and dietary supplements in softgel form.

On February 14, 2003, FDA issued a letter regarding enforcement discretion with respect to expanded use of the health claims to all the forms and sources of phytosterols (FDA 2003). This letter expands the health claims to free forms of phytosterols from several sources and allows a wider range of uses.

The European Union

The Scientific Committee on Food (SCF) previously determined that the use of phytosterols is safe provided that the sterol-containing foodstuffs are not consumed in amounts resulting in total phytosterol intakes exceeding 3g/day (SCF, 2002; 2003a, b and c). In principle, this can be applied also to the phytosterol and phytosterol ester mixtures.

However, the mixtures can only be accepted if the composition complies with the phytosterol/phytostanol profile accepted by the SCF (SCF, 2003b). The SCF reemphasized that appropriate risk management measures should be developed to minimize the likelihood of a daily intake exceeding 3g phytosterols/phytostanols, in particular from the cumulative intakes of different types of products (SCF, 2002; 2003a, b and c). The Commission of the European Communities (Commission) issued a regulation on the labeling of food and food ingredients containing phytosterols (EC 2004).

Based on the SCF's decisions, the Commission issued Commission Decisions and Notifications for the use of phytosterols in yellow fat spreads, milk-based beverages, fermented milk and cheese type products, milk based fruit drinks, soy drinks, salad dressings, rye bread, and spicy sauces (EC 2010).

Pine Tree Phytosterols and Phytosterol Esters (continued)
5. Safety and Effectiveness (continued)

Joint FAO/WHO Expert Committee on Food Additives (JECFA)

New specifications for phytosterols, phytostanols and their esters were prepared at the 69th JECFA (JECFA 2008a), and published in FAO JECFA Monographs 5 (JECFA 2008b). JECFA issued an ADI of 0-40mg/kg bw, expressed as the sum of phytosterols and phytostanols in their free form. Based on available data, JECFA concluded that dietary exposure to phytosterols and phytostanols would typically be within the ADI.

Food Standards Australia New Zealand (FSANZ)

FSANZ, the food safety regulatory agency for Australia and New Zealand, reevaluated the safety of phytosterol-fortified foods on the basis of JECFA's ADI, and found that there was no justification for establishing an ADI (FSANZ 2009, FSANZ 2010a).

FSANZ also issued a report on February 19, 2010 on the equivalence of plant stanols, sterols, and their fatty acid esters (FSANZ 2010b). FSANZ was requested to assess the substantial equivalence of all types of phytosterols (phytosterols, phytostanols, and their fatty acid esters) from all sources (including plant and tall oil sources) meeting JECFA specifications. FSANZ concluded that all the phytosterols are bioequivalent in terms of their food safety properties and that existing estimates of dietary intake are not expected to change.

Pine Tree Phytosterols and Phytosterol Esters (continued)
5. Safety and Effectiveness (continued)

5.2 Safety and Toxicity of Phytosterols and Phytosterol esters

It is clear from current literature review on phytosterols that no difference exists between vegetable or plant oil derived sterols and tall oil or pine tree oil derived sterols concerning toxicity or safety aspects (Ostlund, 2007; Rozner and Garti, 2006, FSANZ 2010a, FSANZ 2010b). FSANZ concluded that the source and form (free or esterified) of the phytosterol is not an important factor in obtaining a lowering of cholesterol if the phytosterols are suitably dispersed in the food matrix.

JECFA assessed the chemical and technical aspects of phytosterols obtained from all sources, phytostanols from phytosterols, and the esters of these phytosterols and phytostanols (JECFA 2008b). They concluded that the purification process for food-grade products resulted in a stable product, and the esters were also stable, fat-type material with comparable properties to edible fats and oils and the analysis of total phytosterol/phytostanol content can be analyzed separately, if required. They suggested that the product specification for the esters include a minimum value for esterification and a limit value for the free stanol/sterol content.

In their risk assessment report on the equivalence of plant sterols, stanols and their fatty acid esters, FSANZ concluded that there was no new evidence that would change its previous conclusions on the safety of pytosterols based on a review of toxicity data, clinical studies, and published literature (FSANZ 2009, 2010a, FSANZ 2010b).

FSANZ stated that less than 5% of dietary plant phytosterols entered the circulation, while 80% of structurally related cholesterol in the diet enters the circulation. Further, that the major portion ingested by man is excreted unchanged in the feces, and the absorbed phytosterols are metabolized in the liver and excreted through the bile (FSANZ 2009).

FSANZ had previously concluded that the consumption of phytosterols raised no safety concern and a reference health standard was not needed (FSANZ 2009) However, it decided to re-evaluate its conclusion because of the JECFA ADI of 40mg/kg bow for phytosterols based on several short-term studies in rats (FSANZ 2009). They concluded that the apparent treatment-related effects are explained by the background incidence of historical control data relevant for the strain of rats used, and reconfirmed that a reference health standard was not needed (FSANZ 2009, FSANZ 2010a).

Pine Tree Phytosterols and Phytosterol Esters (continued)
5. Safety and Effectiveness (continued)

Based on the absence of new evidence that would indicate that phytosterols are toxic at high doses in animals and the lack of human adverse effects, FSANZ concluded that the previous conclusions on safety has not changed. Further, these foods containing phytosterols occupy a niche market and generally there seem to be very few consumers whose phytosterol intake would exceed 3g/day (FSANZ 2009, FSANZ 2010a, FSANZ 2010b).

Additional findings also have corroborated that consumption of phytosterols does not result in changes in vitamin levels in serum that could be considered nutritionally significant. They reported that the serum concentrations of carotenoids and tocopherol remain within the normal range and that an increase in the dietary intake of carotenoids mediates the effects of plant sterols on serum carotenoids. Thus, the earlier concerns regarding the reduction of serum levels of some fat-soluble vitamins and precursors have been lowered (FSANZ 2009, FSANZ 2010a, FSANZ 2010b).

After an extensive review and analysis of epidemiological studies to assess plant sterol concentrations with increased risk of cardiovascular disease, FSANZ concluded that plant sterols do not increase risk of cardiovascular disease other than in the group of individuals with a rare genetic (autosomal recessive) disorder of lipid absorption that results in a progressive accumulation of plant sterols in plasma and tissues that can lead to premature atherosclerosis and early cardiovascular death (FSANZ 2010a, FSANZ 2010b).

5.3 Conclusions on Safety

Arboris believes that there is general recognition that the use of Arboris phytosterols and phytosterol esters as another source of phytosterol and phytosterol esters is safe based on the following:

- GRAS Panels convened for eight GRAS Notifications submitted to FDA have concluded that the use of phytosterols and the phytosterol esters are safe for the proposed uses and FDA did not question their conclusion.

Pine Tree Phytosterols and Phytosterol Esters (continued)
5. Safety and Effectiveness (continued)

- FDA issued an interim final rule allowing the use of health claims on the association between plant sterol/stanol esters and the reduced risk of coronary heart disease. FDA concluded that the petitioner of the health claim has satisfied the requirement to demonstrate that the use of these sterol/stanol esters at the levels necessary to justify a claim is safe. FDA has also issued a letter stating that it would consider enforcement discretion for foods containing free and esterified phytosterols from tall oil and vegetable oil sources for the uses listed in the eight GRAS Notifications.

- The European Union Scientific Committee on Food, determined that the use of phytosterols is safe for the proposed uses. However, there was still a concern of: 1) total phytosterol intakes exceeding 3g/day, 2) consumption of phytosterol-containing foods by people with inborn error of phytosterol metabolism (phytosterolaemia), and 3) consumption of phytosterol-containing foods by patients on cholesterol-lowering medication because of the potential β-carotene-lowering effect.

  The SCF recommended that appropriate risk management measures should be developed to minimize the likelihood of exceeding the 3g/d daily intake of phytosterols, recommended that the small number of people with phytosterolaemia should be made aware of foods containing high levels of phytosterols, and that consumers using cholesterol-lowering medication be notified about the potential β-carotene-lowering effect by phytosterols in the diet.

  Based on the SCF's decisions, the Commission of the European Communities issued a regulation allowing phytosterols to be added to foods and food ingredients to a maximum of 3g/day and continues to issue Notifications for such uses.

- Since the submission of GRN 0250, JECFA and FSANZ have concluded that phytosterols from all sources and their fatty acid esters are safe at the estimated dietary exposure levels.

- The recent literature that is referenced and discussed in the FSANZ reports do not raise any additional safety concerns and resolves the outstanding safety concerns that were listed by the SCF: on daily intake exceeding 3g/day, decrease of fat-soluble vitamin levels in the serum as a result of phytosterol consumption, and increased risk of cardiovascular disease in individuals with a rare genetic disorder of lipid absorption.

Pine Tree Phytosterols and Phytosterol Esters (continued)
5. Safety and Effectiveness (continued)

- These phytosterols and phytosterol esters obtained by Arboris from pine trees are substantially equivalent to other pine-tree derived phytosterols. Arboris believes that its products will provide an additional source of free and esterified phytosterol esters for the existing uses listed in earlier GRAS submissions and will not change the cumulative dietary intake of phytosterols.

  Arboris concludes that there is general recognition by experts qualified in scientific experience that the use of phytosterols in food from plant and vegetable sources at the existing and proposed uses are safe based on scientific procedures.

  Therefore, the use of Arboris' phytosterols and phytosterol esters in food is safe.

6. References

Arboris® Sterol AS-2® Specifications, March 12, 2008.

Arboris Sterol Esters Specifications, March 12, 2008.

EC 2004, 2004/608/EC: Commission Regulation No 608/2004 of March 31, 2004 concerning the labeling of foods and food ingredients with added phytosterols, phytosterol esters, phytostanols and/or phytostanol esters, OJ L 97, 1.4.2004, p. 44.

EC 2010, Notifications pursuant to Article 5 of Regulation (EC) No 258/97 of the European Parliament and of the Council (April 2007) with regard to genetically modified foods and food ingredients which do no longer fall under the scope of Regulation (EC) No 258/97 (former category b of Article 1(2) see register pursuant to Article 28 of Regulation (EC) 1829/2003 as from April 18, 2005.

FCC 6, United States Pharmacopeia (USP). "Vegetable oil phytosterol esters," Food Chemicals Codex. 6th ed. Rockville, MD: USP; 1007, 2007.

FCC 6, Vegetable oil phytosterol esters, Food Chemicals Codex Sixth Edition, page 1007, United States Pharmacopoeia. 2008

FDA 2000, Food Labeling: Health Claims; Plant Sterol/Stanol Esters and Coronary Heart Disease, Federal Register 65:54686-54739.

FSANZ (2009) Application A1019. Exclusive use of phytosterol esters in reduced-fat cheese products, SD1 Risk Assessment, FANZ Canbarra. Available at http://www.foodstandards.gov.au/foodstandards/applications/applicationa1019phyt4161.cfm

FSANZ (2010a) Application A1019. Exclusive use of phytosterol esters in reduced-fat cheese products, Approval report, FANZ Canbarra. Available at http://www.foodstandards.gov.au/foodstandards/applications/applicationa1019phyt4161.cfm

FSANZ (2010b) Application A1024. Equivalence of plant stanols, sterols & their fatty acid esters FANZ Canbarra. Available at http://www.foodstandards.gov.au/foodstandards/applications/applicationa1024equi4316.cfm

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Pine Tree Phytosterols and Phytosterol Esters (continued)
6. References (continued)

Joint FAO/WHO Expert Committee on Food Additives (JECFA 2008a), Sixty-ninth meeting, Rome, Italy, June 17 - 26 2008, JECFA/69/SC, July 4, 2008.

JECFA, 2008b. Phytosterols, phytostanols and their esters. Chemical and Technical Assessment, 1-13. Available at http://www.fao.org/ag/agn/agns/jecfa/cta/69/Phytosterols_CTA_69.pdf

Kritchevsky, D., "Safety of Phytosterols Esters as Functional Food Components," in Phytosterols as Functional Food Components and Nutraceuticals, P.C. Dutta, ed., Marcel Dekker, Inc., NY, 2004.

Nimal Ratnayake, W.M. and Vavasour, E.J., "Potential Health Risks Associated with Large Intakes of Plant Sterols," in Phytosterols as Functional Food Components and Nutraceuticals, P.C. Dutta, ed., Marcel Dekker, Inc., NY, 2004.

Nissinen, M.J., Gylling, H., Miettinen, T.A., "Effects of plant stanol esters supplied in a fat free milieu by pastilles on cholesterol metabolism in colectomized human subjects," Nutr Metab Cardiovas Dis, 2006, 16: 426 – 435.

Normen, L., Frohlich, J., and Trautwein, E., "Role of Plant Sterols in Cholesterol Lowering," in Phytosterols as Functional Food Components and Nutraceuticals, P.C. Dutta, ed., Marcel Dekker, Inc., NY, 2004.

Ostlund, Jr., R.E., Spilburg, C.A., Stenson, W.F., "Sitostanol administered in lecithin micelles potently reduces cholesterol absorption in humans," Am J Clin Nutr 1999, 70:826–31. – Ostlund Jr, R.E., "Phytosterols, cholesterol absorption and healthy diets," Lipids, 2007, 42:41 45.

Plat, J., Brufau, G., Dasselaax, M., Mensink, R.P., "A stanol yogurt drink alone or combined with a low-dose otc statin lowers non-HDLc, but also lowers TGs and elevates HDLc in metabolic syndrome patients," Wednesday, June 21, 2006: Poster Session. P14 Nutritional Approaches.

Rozner, S., Garti, N., "The activity and absorption relationship of cholesterol and phytosterols. Colloids and Surfaces A: Physicochem," Eng. Aspects, 2006, 282–283: 435–456.

Rudkowskaa, I., Roynettea, C.E., Nakhasib, D.K., Jonesa, P.J.H., "Phytosterols mixed with medium-chain triglycerides and high-oleic canola oil decrease plasma lipids in overweight men," Metabolism, 2006, 55: 391– 395.

Pine Tree Phytosterols and Phytosterol Esters (continued)
6. References (continued)

SCF (Scientific Committee on Food) 2000, Opinion of the Scientific Committee on Food on a request for the Safety Assessment of the Use of Phytosterol Esters in Yellow Fat Spreads, April 6, 2000.

SCF 2002a, General view of the Scientific Committee on Food on the long-term effects of the intake of elevated levels of phytosterols from multiple dietary sources, with particular attention to the effects on ß-carotene, September 26, 2002.

SCF 2002b, Opinion of the Scientific Committee on Food on a report on Post Launch Monitoring of "yellow fat spreads with added phytosterol esters," September 26, 2002.

SCF 2003a, Opinion of the Scientific Committee on Food on Applications for Approval of Variety of Plant Sterol-enriched Foods, March 5, 2003.

SCF 2003b, Opinion of the Scientific Committee on Food on an Application from ADM for Approval of Plant Sterol-enriched Foods, April 4, 2003.

SCF 2003c, Opinion of the Scientific Committee on Food on an Application from MultiBene for Approval of Plant-sterol enriched foods, April 4, 2003.

VitaCaps Certificate of Analysis for 5 batches of Vitasterol S-80 esterified non GMO, October 2009 through January 2010.

SUBMISSION END