APPLICATION FOR THE APPROVAL OF JUICES AND NECTARS WITH ADDED PHYTOSTEROLS

Regulation (EC) No 258/97 of the European Parliament and of the Council of 27th January 1997 concerning novel foods and novel food ingredients

Application of: Coca-Cola Services s.a.
Dr. Michael Knowles
Chaussée de Mons 1424
1070 Brussels, Belgium

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SUMMARY

Coca-Cola Services s.a. (Coca-Cola) seeks European Union (EU) Novel Food approval for juices, including tomato juice, and nectars (juice drinks with specified minimum juice levels) with added tall oil phytosterols. Juices and nectars are typical components of healthy diets and would provide convenient means of consuming additional phytosterols for consumers desiring to do so. Juices and nectars would provide individuals with milk protein allergies or who are lactose intolerant an important alternative to dairy products as a source of phytosterols. They also provide a choice that is lower in fat than other approved foods. The safety of tall oil phytosterols has previously been evaluated and approved by EU authorities. Because of the limited consumption of juices and nectars and established labelling requirements to guide consumer choice the addition of phytosterols to juices and nectars is unlikely to increase individual consumption of phytosterols above the accepted limit of 3 grams per day. Such products will provide a valuable addition to the range of foods available to help those consumers control cholesterol levels through dietary means.

INTRODUCTION

Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients Article 1(2) defines Novel Foods as:

> *–foods and food ingredients which have not hitherto been used for human consumption to a significant degree within the Community (before 15th May 1997) and which fall under the following categories:…*
>
> *(e) foods and food ingredients consisting of or isolated from plants…*

Whilst milk-based beverages of various descriptions containing phytosterols have recently been approved under Commission Decisions 333-336/2004 (CEC, 2004a-d) and are now marketed throughout the EU, other beverages have not. Under the strict labelling requirements of *Commission Regulation (EC) No 608/2004 concerning the labelling of foods and food ingredients with added phytosterols, phytosterol esters, phytostanols and/or phytostanol esters*

(CEC, 2004e), consumers are able to readily estimate intakes from dietary choices. We submit for approval the following categories of beverages:

- Juices and nectars within the scope of Council Directive 2001/112/EC and including tomato juice with added tall oil phytosterols up to a level of 1 g/250 ml with a recommended consumption per day of 2 servings of phytosterol / stanol fortified food, i.e., 2 g taking into account consumption of any other phytosterol / stanol fortified food.

Section 4 of the Commission Recommendation of 1997 outlines recommendations made by the Scientific Committee for Food (SCF) pertaining to the "Scientific Classification of Novel Foods for the Assessment of Wholesomeness" (SCF, 1997), which facilitates the safety and nutritional evaluation of a given novel food/food ingredient. Under Section 4, juices and nectars with added phytosterols would meet the definition of:

- Class 2.1: Complex Novel Food from non-genetically modified (GM) source – the source of the Novel Food has a history of food use in the EU.

Under this classification the recommendations for dossier composition are as follows:

I	Specification of the Novel Food
II	Effect of the production process applied to the Novel Food
III	History of the organism used as the source of the Novel Food
IV	Not required
V	Not required
VI	Not required
VII	Not required
VIII	Not required
IX	Anticipated intake/extent of use of the Novel Food
X	Information from previous human exposure to the Novel Food
XI	Nutritional information on the Novel Food
XII	Microbiological information on the Novel Food
XIII	Toxicological information on the Novel Food

I SPECIFICATIONS OF THE NOVEL FOOD

Based on the SCF guidelines, the following questions must be answered in the affirmative to ensure sufficient information pertaining to the specifications of the novel food:

- "Is appropriate analytical information available on potentially toxic inherent constituents, external contaminants and nutrients?"

- "Is the information representative of the novel food when produced on a commercial scale?"

- "Is there an appropriate specification (including species, taxonomy *etc*. for living organisms) to ensure that the novel food marketed is the same as that evaluated?"

I-1 Specification of the Added Phytosterols

The phytosterol ingredient is supplied by Cargill, Incorporated (The Health & Food Technologies Business Unit) 15407, McGinty Rd. W. MS110, Wayzata, MN 55391, USA (Cargill). Its specifications/levels of undesirable substances/production features/source is described by Cargill in its submission of August 2004 to the Finnish competent expert body with a view to support a notification under the procedure laid down in Regulation (EC) No 258/97, article 5. (Annex I)

I-2 Specifications of the Juices and Nectars With Added Phytosterols

Juices and nectars are produced from the relevant fruits and conform to the requirements of Council Directive 2001/112/EC and, the general specifications for the named fruit under the AIJN (Association of the Industry of Juices and Nectars from Fruits and Vegetables of the EU) Code of Practice. Phytosterols are added to the product as micro size particles verified by particle size analysis (method Horiba LA-910) to provide optimum mouth feel, appearance and suspension in the juice.

Gas Chromatography with Flame Ionization Detection is used to quantify the total phytosterol concentration in the beverage. Emulsifiers, such as monoacylglycerols and diacylglycerols, if present, are saponified into sodium salts with sodium hydroxide in methanol. The fatty acid salts formed are then acidified to form free fatty acids. This step is necessary to minimize emulsion formation during liquid:liquid extraction. Chromatographic run time is also reduced. Sodium chloride is then added to the aqueous phase to drive the sterols into an organic solvent phase. Sterols are then derivitized with bis(trimethylsilyl)trifluoroacetamide + 1% trimethylchlorosilane to form trimethylsilane ethers. Epicoprostanol (5alpha-cholestan-3alpha-ol) or dihydrocholesterol (5alpha-cholestan-5alpha-ol) was used as an internal standard.

Analytical results from typical manufacturing lots of beverage with phytosterols are given in Table I to indicate that the manufacturing process produced a consistent product that met the specifications. The amount of plant sterols added to the fruit juice product when it was manufactured was 1 g/240 ml. Testing was done in-house at the time of production.

Table 1: Concentration of phytosterols (g/240 ml serving) ex. Production Batches

Samples	g / 240 mL
1	1.01
2	1.02
3	1.02
4	1.02
5	0.99
6	1.03
7	1.02
8	1.02
9	1.01
10	1.04
11	1.02
12	1.03
13	1.03
14	1.02
15	1.00
16	1.00
17	1.02
18	1.04

Stability testing of the phytosterol ingredient in orange juice beverage was conducted on a batch with measured 1.12 g total plant sterols after production. Phytosterol content was unaffected by the manufacturing process or storage up to 9 weeks.

Table 2:

Time	g/240 mL serving
Week 0	1.12
Week 3	1.11
Week 7	1.09
Week 9	1.11

II EFFECT OF THE PRODUCTION PROCESS APPLIED TO THE NOVEL FOOD

Based on the SCF guidelines, the following questions must be addressed to ensure sufficient information pertaining to the effect of the production process applied to the novel food:

- "Does the novel food undergo a production process?"
- "Is there a history of use of the production process for the food?"
- "Does the process result in a significant change in the composition or structure of the NF compared to its traditional counterpart?"

II-1 The Production of the Phytosterols

The phytosterol ingredient is supplied by Cargill, Incorporated (The Health & Food Technologies Business Unit) 15407, McGinty Rd. W. MS110, Wayzata, MN 55391, USA (Cargill). Its specifications/levels of undesirable substances/production features/source is as described by Cargill in its submission of August 2004 to the Finnish competent expert body with a view to support a notification under the procedure laid down in Regulation (EC) No 258/97, article 5. The content of this submission, and the opinion that the Finnish competent expert body will/has adopt(ed) is incorporated by this reference, per express authorisation of Cargill (see Annex I)."

II-2 The Production of The Juice and Nectar Products containing Phytosterols

Juices and nectars will be produced under standard EU Quality Control (QC) procedures HACCP in accordance with EU Hygiene legislation. The juices are produced in accordance with the Juice Directive (2001/112/EC) and all relevant requirements of Food Law. The juice + phytosterol product is manufactured by adding phytosterols to concentrated juice. The mixture is processed to completely disperse the phytosterols. The juice concentrate/phytosterol mixture is then blended with water and any added vitamins.

The juice and phytosterols 'juice-based-drink' will be packed in single serve (250 ml) and multi-serve containers, e.g. 0.5l PET bottles, containing 2 times 250ml individual servings. The recommended intake, for those whose sole source of phytosterol/stanols are fruit juices, will be 2 servings per day, morning and evening, with meals. This will be equivalent to a daily intake of 2g free phytosterols. One serving will be recommended for those who obtain 1-2 servings of phytostanol / sterol per day from other sources.

Table 3: Typical ingredient declaration for Orange Juice drink + phytosterols

Product Example	Ingredient List
Orange juice drink with plant sterols. (With added plant sterols)	Orange juice from concentrate (99.6%); plant sterols (0.4%)

III HISTORY OF THE ORGANISM USED AS THE SOURCE

Based on the SCF guidelines, the following questions must be addressed to ensure sufficient information pertaining to the history of the source organism:

- "Is the novel food obtained from a biological source (*i.e.*, a plant, animal or microorganism)?"

III-1 Source of the phytosterols

The source phytosterols (Cargill) are derived from tall oil soap. Annex 2 of Commission Decisions 2004/333, 2004/334, 2004/335 and 2004/336 (CEC, 2004a-d) states "Phytosterols/phytostanols are sterols and stanols that are extracted from plants and may be presented as free sterols and stanols or esterified with food grade fatty acids".

They are free from unacceptable levels of contaminants as shown in Annex I.

IV

Not Required

V

Not Required

VI

Not Required

VII

Not Required

VIII

Not Required

IX ANTICIPATED INTAKE/EXTENT OF USE OF NOVEL FOOD

Based on the SCF guidelines, the following questions must be addressed to ensure sufficient information pertaining to the effect of the production process applied to the novel food:

- "Is there information on the anticipated uses of the novel food based on its properties?"
- "Is there information to show anticipated intakes for groups predicted to be at risk?"
- "Will introduction of the novel food be restricted geographically?"
- "Will the novel food replace other foods in the diet?"
- "Are any of the replaced foods significant nutritional sources?"
- "Does the probable level of substitution have a nutritional significance for any population groups?"

The anticipated food uses, juices and beverages, are novel only to the extent that they will contain up to 0.4% added phytosterols. As a consequence of the low level of added phytosterols, the juices and nectars will not differ appreciably in nutrient content from usual juices and nectars.

Current juice and nectar consumers are expected to substitute phytosterol containing juices and nectars for their usually consumed juices and nectars so there should be no net negative impact on overall nutrient consumption. See also Section X.

For consumers who drink little or no juices or nectars, a net nutritional benefit might be expected due to increased consumption.

Indeed it might be expected that there will be a net nutritional benefit due to increased consumption of fruit juices e.g. increased consumption of potassium, folate and vitamin C, and have increased cardiovascular benefits, amongst others.

IX-1 The Intakes of Phytosterols from Juices and Nectars

Both the *SCF General view 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 of 26 September 2002* (SCF, 2002a) and the *SCF Opinion on Applications for Approval of a Variety of Plant Sterol-Enriched Foods* (expressed on 5 March 2003) (SCF, 2003a) have reviewed the effects of overall intake of phytosterols/phytostanols.

Their conclusions led to the implementation of *Commission Regulation (EC) No 608/2004 concerning the labelling of foods and food ingredients with added phytosterols, phytosterol esters, phytostanols and/or phytostanol esters* (CEC, 2004e). In essence Article 2 of this regulation lays down the following criteria:

For labelling purposes, phytosterol, phytosterol ester, phytostanol and phytostanol ester shall be designated respectively by the terms "plant sterol", "plant sterol ester", "plant stanol" or "plant stanol ester" or their plural form, as appropriate.

Without prejudice to the other requirements of Community or national law concerning the labelling of foodstuffs, the labelling of foods or food ingredients with added phytosterols, phytosterol esters, phytostanols or phytostanol esters shall contain the following:

1. *in the same field of vision as the name under which the product is sold there shall appear, easily visible and legible, the words: "with added plant sterols/plant stanols";*

2. *the amount of added phytosterols, phytosterol esters, phytostanols or phytostanol esters content (expressed in % or as g of free plant sterols/plant stanols per 100 g or 100 ml of the food) shall be stated on the list of ingredients;*

3. *there shall be a statement that the product is intended exclusively for people who want to lower their blood cholesterol level;*

4. *there shall be a statement that patients on cholesterol lowering medication should only consume the product under medical supervision;*

5. *there shall be an easily visible and legible statement that the product may not be nutritionally appropriate for pregnant and breastfeeding women and children under the age of five years;*

6. *advice shall be included that the product is to be used as part of a balanced and varied diet, including regular consumption of fruit and vegetables to help maintain carotenoid levels;*

7. *in the same field of vision as the particular required under point 3 above, there shall be a statement that the consumption of more than 3 g/day of added plant sterols/plant stanols should be avoided;*

8. *there shall be a definition of a portion of the food or food ingredient concerned (preferably in g or ml) with a statement of the plant sterol/plant stanol amount that each portion contains.*

Individual consumption of phytosterols above the accepted limit of 3 grams per day, due to the fortification of juices, is unlikely because of the labelling requirements discussed above, current consumption patterns and individual dietary responsibility and increased cost of phytosterol – fortified juices.

Fruit juice consumption in the UK (Henderson, 2002, 2003)

Current consumption of fruit juice by British adults (consumers and non-consumers) is on average 340g (or mls) per week in men and 327g per week in women. This averages out as a daily intake of just under 50 g per day, or 150g/day at the 97, 5 percentile.

However, in a weekly period, less than half adult consumers (43% of men and 47% women) drink fruit juice. The average of consumers is approximately 100g per day (797g and 697g per week by men and women respectively.), or approximately 300g/day at the 97, 5 percentile. It is, therefore, highly unlikely that any individual will consume more than 3 grams per day of plant sterol in juice, which would be approximately 750 grams per day.

Table 4: Total quantities (grams) of fruit juices consumed per day by age of respondent (consumers only)

Consumers aged (years)	Mean (grams)	% Consumers
Men, 19-24	113.1	33
Men, 25-34	90.3	41
Men, 35-49	133.9	42
Men, 50-64	114	48
All Men	113.9	43
Women, 19-24	100.1	50
Women, 25-34	89.3	50
Women, 35-49	98.6	44
Women, 50-64	109.4	47
All Women	99.6	47

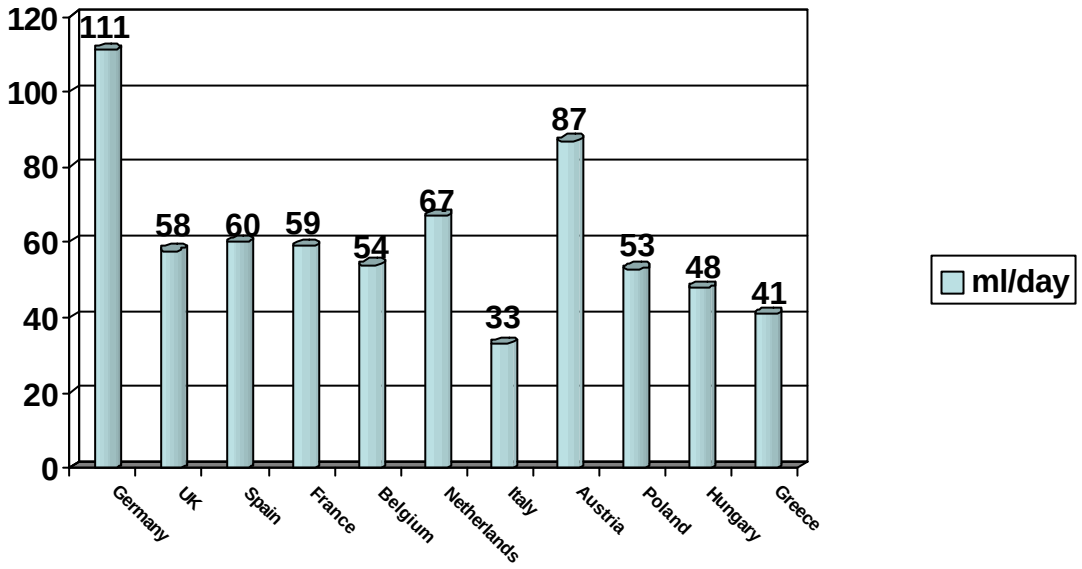
Source: Henderson and Gregory, 2002. 'The National Diet & Nutrition Survey: adults aged 19 to 64 years'. Volume 1, A survey carried out in Great Britain on behalf of the Food Standards Agency and the Departments of Health by the Social Survey Division of the Office for National Statistics and Medical Research Council Human Nutrition Research

Juice Consumption outside the UK

Apart from Germany, which has a higher than European average consumption, approximately half of it are nectars (high percentage juice-drinks), the average consumption of commercial juices and nectars is similar to the UK.

Table 5:

2002 Canadean Per Cap Summary – Commercial Juice/Nectars



Source: Canadean Report Global Juice & Nectars 2003 – West & East Europe

Therefore it is reasonable to assume that the arguments made by Unilever and others regarding the actual purchase and consumption of phytosterol-fortified foods, would be the same for juices/ juice drinks (Lea, 2002).

Fat consumption and the value of marketing fruit juice containing phytosterols.

Fruit juice is fat free and therefore contributes no fat to the British diet. It provides approximately 1% of the energy. Juices and nectars would thus offer individuals a lower fat alternative to existing approved phytosterol food uses.

The average amount of fat spreads (butter, soft and PUFA margarine, and other low fat and very low fat spreads) used by men is 103g per week and by women 65g per week (14.7g and 9.3g per day respectively). Amongst consumers, 13% men and 12% women consume PUFA low fat spread (11.7g and 7.6g per day respectively) and 23% men and 19% women consume PUFA reduced fat spread (11.6g and 7.1g per day respectively). Average daily consumption of

other low fat and reduced fat spreads is similar. Fat spreads provide 4% of the energy, 12% of fat and 11% saturated fat in the UK adult diet.

All fats provide 35.8% of men's food energy and 34.9% of women's. These means meet the recommendations of 35% energy for women and very nearly meet them for men. However, on an individual basis, only 43% men and 50% women consume 35% energy or less from fat. Mean saturated fat intakes are above the recommendations of 11% food energy, standing at 13.4% for men and 13.2% for women. Looking at individuals, only 12% men and 17% women consume 10% energy or less from saturated fat and only 31% men and 35% women consume 12% or less.

The UK Guideline Daily Amounts (GDAs) for fat are 95g and 70g per day for men and women respectively. GDAs for saturated fat are 30g and 20g. Amongst men, mean daily intake of total fat is 86.5g, with 71% consuming less than 100g, and of saturated fat is 32.5g, with 46% consuming less than 30g. Amongst women, mean daily intake of fat is 61.4g with 69% consuming less than 70g, and of saturates is 23.3g with 40% consuming less than 20g.

Value of marketing fruit juice containing phytosterols.

Those with raised blood cholesterol, who would be advised to use phytosterol, should be aiming for lower fat intakes, especially lower saturated fat intakes. In general phytosterol/stanol fat spreads replace other fat spreads and there use would not be expected to result in an increase in fat intake. However, one way to contribute to the dietary fat reduction would be to reduce use of fat spreads on a daily basis. Using a low fat or fat free vehicle as the daily provider of phytosterols is a practical alternative to fat spreads.

A large number of people with raised cholesterol levels are overweight. Fat is the most energy dense nutrient so reduced intake should aid weight loss. Those on a calorie controlled diet are also likely to eat small amounts of bread and therefore do not need the full amount of fat spread (e.g. 24g) required to provide the recommended daily dose of phytosterols. Obtaining half the amount of phytosterols from fat spread (12g per day) and the other half from fruit juice makes a practical alternative.

Those who are restricting their total fat intake may not want to use any of their 'fat allowance' on phytosterol containing fat spreads, preferring to eat more of other fat containing foods (meat, cheese, vegetable oil-based salad dressings etc).

Some people do not use fat spreads regularly. If they have raised blood cholesterol, it would not be advisable for them to start using them, so fruit juice with phytosterols provides an alternative

Some individuals consume large quantities of fat spreads. Ideally, those with high cholesterol should reduce the amounts and switch to low saturated fat varieties, which could be those

fortified with phytosterols/stanols. However, in the short-term better compliance may be obtained from the simple advice to consume fruit juice with phytosterols.

In the UK, over a weekly period, 43% men and 47% women consumed fruit juice, each man and woman consuming a daily average of 114g and 100g respectively (Henderson, 2002). Fruit juice is consumed daily by many, so substituting this with fruit juice containing phytosterols is an easy way obtaining half the effective dose. On the other hand, more than half the adult population do not drink fruit juice regularly. However to obtain the effective dose of at least 2g/day consumers will be advised to drink 2 x 250 ml/day of the orange juice drink. If fortification of juice with phytosterols encourages non-consumers to start drinking it, that will have an overall health benefit. It will also contribute one of the five recommended portions of fruits and vegetables a day.

Unilever consumer carelines (Lea, 2002) have indicated that consumers would like additional products. Fruit juice provides an alternative which fits into the low fat healthy diet recommended for those with high blood cholesterol levels.

Potential consumption of other sources of phytosterols.

Unilever SEAC, in their submission to the FSA (Lea, 2002) have shown a need for alternative carriers to fat spreads for phytosterols. They pointed out that most consumers use 15-18g spread per day, providing 1.2-1.4g phytosterol. This is just over half the daily dose, of 3 g plant sterols / day.

The UK NDNS Survey (Henderson, 2002) shows that 32% men and 40% women consumed yoghurt during a weekly period, with an average intake of 404g, or about three 125- 150g cartons per week.

75% of the adult population consume semi-skimmed milk, but their mean daily intake is under 200mls per day (188g by men and 155g for women) and the median weekly intake is 1102g for men and 929g for women, indicating that well over half do not consume enough to get 1g phytosterol per day (250ml). Only 12% men and 13% women consume ‘other milks’, which would include flavoured milks. Their mean consumption is 492g and 409g, or about 2 x 200-250ml cartons per week.

Fruit juice can provide the additional phytosterol required for those who consume the average amount of spread, as described above. Or juice may be an alternative for those who do not like yoghurts or milk, or who do not consume sufficient amounts of either (e.g. small amounts in tea and coffee only).

In addition, phytosterol-fortified juices offer an alternative to those consumers who have an intolerance to milk and milk-based products. Many individuals are either allergic to milk protein or are lactose intolerant and avoid dairy products. Milk allergen frequency in Europe is estimated at 2% of children (Strobel, 1997). Five percent of adults may demonstrate clinical

symptoms. While frequency of milk allergy is relatively low severe morbidity and even fatalities are possible (Bahna, 2002). Lactose intolerance is more common ranging from 4% in Denmark to 81% in the Mad population in Russia (Sahi, 2001). The frequency of lactose intolerance is genetically linked with incidence up to 100% in some populations from Africa and the Asia (Sahi, 1994).

Potential for over consumption or consumption by children

In the UK, over a one week period 46% boys and 51% girls aged 4 to 18 years consumed fruit juice (Gregory, 2000). Mean intakes were 821g and 750g, just over 100ml per day. Unilever's post launch monitoring suggested that within any household, only one person was using spread containing phytosterol since the amounts purchased per household across their 5 main European markets were similar regardless of the number of people in the household. Consumer purchase data also showed that those individuals purchasing phytosterol/stanol products also purchased the equivalent unfortified product. It seems likely these patterns would be similar with any other food or drink containing phytosterol.

Existing consumption patterns suggest that children are no more likely to over consume fruit juices than to over consume milk and yogurt. (Gregory, 2000)

Further the higher price of phytosterol-fortified products is a deterrent to over-consumption. The price, and the above purchasing patterns, makes the regular consumption by children unlikely.

There is no evidence from toxicology studies or clinical studies in children of phytosterols that incidental consumption by children would have an adverse effect.

X INFORMATION FROM PREVIOUS HUMAN EXPOSURE

Based on the SCF guidelines, the following questions must be answered in the affirmative to ensure sufficient information pertaining to previous human exposure to the novel food:

- "Is there information from previous direct, indirect, intended or unintended human exposure to the novel food or its source which is relevant to the EU situation with respect to production, preparation, population, lifestyles and intakes?"

- "Is there information to demonstrate that exposure to the novel food is unlikely to give rise to mitochondrial, toxicological and/or allergenicity problems?"

X-1 A Review of Existing Intakes

Intakes of phytosterols/phytostanols have been reviewed on a number of occasions for each approval that has been granted. Notably *the SCF Opinion on Applications for Approval of a*

Variety of Plant Sterol-Enriched Foods (expressed on 5 March 2003) (SCF, 2003a) reviewed the overall intakes of phytosterols/phytostanols.

Phytosterol/phytostanol may now be added to the following foods in the EU: They are on the market to varying degrees but no comprehensive intake data is available.

- yellow fat spreads (Commission Decisions 2004/333;2004/334;2004/336) (CEC 2004a,b,d)
- fermented milk type products (Commission Decisions 2004/333; (CEC, 2004a)
- milk type products (Commission Decisions 2004/333;2004/334;2004/335 (CEC, 2004a-c)
- soya drinks (Commission Decisions 2004/333) (CEC, 2004a)
- cheese type products (Commission Decisions 2004/333;2004/336) (CEC, 2004a,d)
- yoghurt type products (Commission Decisions 2004/334;2004/335;2004/336) (CEC, 2004b-d)
- spicy sauces (Commission Decisions 2004/334) (CEC, 2004b)
- milk based fruit drinks (Commission Decisions 2004/336; (CEC, 2004d)

Phytostanol spreads have been marketed in Finland since 1996 and phytosterol and phytostanol spreads have been marketed in the US since 1999. Phytosterol spreads are approved and marketed in Japan and Australia as well. An orange juice + phytosterol product – Minute Maid Heart Wise (Figure I) – has been on the market throughout the USA since 2003, containing 1 g/ 240 ml (8 oz) serving, of phytosterols: two servings a day are recommended. No intake data is currently available.

Figure I: US phytosterol fortified orange juice: labelling information to aid consumer use and general dietary advice (from the Mayo Clinic)

XI NUTRITIONAL INFORMATION ON THE NOVEL FOOD

Based on the SCF guidelines, the following question must be answered in the affirmative to ensure sufficient nutritional information pertaining to the novel food:

- "Is there information to show that the novel food is nutritionally equivalent to existing foods that it might replace in the diet?"

The anticipated food uses, juices and nectars, are novel only to the extent that they will contain up to 0.4% added phytosterols. As a consequence of the low level of added phytosterols, the juices and nectars will not differ appreciably in nutrient content from usual juices and nectars. Consumers are expected to substitute phytosterol containing juices and nectars for their usually

consumed juices and nectars and therefore there should be no net impact on overall nutrient consumption.

The SCF General view 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 of 26 September 2002 (SCF, 2002a) reviewed the overall nutritional impact of phytosterols/phytostanols.

Juices and nectars are low fat foods that provide a variety of nutrients including vitamin C, folate, potassium and thiamin. They contain significantly less fat than spreads, dressings and cheese and most milks and yoghurts. For many consumers needing to reduce/control cholesterol levels, dietary choices include low/reduced fat foods. Juice + phytosterols offer an important dietary choice for such consumers who wish to use dietary means to control their cholesterol levels. In addition *the SCF Opinion on Applications for Approval of a Variety of Plant Sterol-Enriched Foods (expressed on 5 March 2003)* (SCF, 2003a) has also briefly reviewed the clinical trials conducted.

Table 6: Typical Minute Maid orange juice + phytosterols

Orange juice	
Nutritional Values	
	For 100ml
Proteins	-
Fat	-
Carbohydrates	11.2 g
Energy	43.1 kcal 180,2 kJ
Sodium	-
Potassium	164 mg
Acidifiers	-
Vitamins: average content	
Beta Carotene	70 µg
B1 (thiamin)	73 µg
B2 (Riboflavin)	20 µg
B3 / PP (niacin)	0.24 mg
B5 (pantotenic acid)	0.15 µg
B6 (pyridoxin)	27 µg
B8 (biotin)	0.8 µg
B9 (folic acid)	33 µg
Vit. C (ascorbic acid)	42 mg
Phytosterols	0.46 g

Both the above opinions review the cholesterol reducing effects of phytosterols/phytostanols.

Their conclusions led to the implementation of Commission Regulation (EC) No 608/2004 concerning the labelling of foods and food ingredients with added phytosterols, phytosterol esters, phytostanols and/or phytostanol esters (CEC, 2004e).

In addition a recent study showed that phytosterols are just as effective when added to orange juice, especially in reducing LDL – cholesterol. The study, undertaken by Professor Sridevi Devaraj and her team at the University of California, Davis Medical Center, Sacramento, is published in 8 March 2004, issue of 'Arteriosclerosis, Thrombosis and Vascular Biology' (Ref.). In this study, which was double-blinded, placebo-controlled and randomized, the researchers enrolled 72 healthy volunteers aged 20 – 73 with normal to mildly elevated cholesterol levels. The volunteers ate their normal diet but drank a glass (240 ml) of orange juice with their normal breakfast and dinner. Half the group had phytosterol-containing juice (containing 1.15g of phytosterol); the other half had the same juice without phytosterols. Volunteers who drank the fortified juice for a period of 8 weeks had a 7.2 % decrease in total cholesterol and a 12.4 % decrease in LDL cholesterol compared to baseline and to the group that received the regular orange juice. These decreases in total cholesterol and LDL-cholesterol, as compared to baseline and placebo, were statistically significant. The effectiveness of consuming phytosterols this way was demonstrated without the use of special diets. The only requirement is to consume the effective dose in this very convenient way with normal meals.

Some producers of plant sterol or stanol ester containing products have questioned the efficacy of non-esterified plant sterols in low or no fat foods. Several recent studies have confirmed that non-esterified phytosterols reduce blood cholesterol levels in people with normal to elevated cholesterol levels consuming usual diets or reduced fat diets. The relevant studies were reviewed in a letter from Cargill, Inc., to the US FDA in May 2004 (Cargill, 2004)(Annex II). One recent study, conducted by Jones et al (2003), reported that 1.8 g of unesterified phytosterols incorporated into low or non-fat beverages did not lower blood cholesterol levels compared to a non-fat control beverage. These researchers concluded that the cholesterol-lowering potential of phytosterols may depend on their previous dispersion into a fat matrix and on the physical nature of the food, although they provided little information on their preparation process or beverage composition. The study's experimental design raises concerns e.g. only 15 subjects and study duration time (3 weeks) not long enough to allow for stabilisation of changes of lipid levels when non-fat and low-fat beverages were administered with controlled diets, and would tend to invalidate Jone's conclusions based on the reported findings. Clearly, the results of the Jones study cannot be generalized to other low fat or fat-free foods and beverages.

Six recently published human studies have evaluated the effect of non-esterified phytosterols in low fat or fat-free beverages on serum lipids or cholesterol absorption. Five of these studies reported positive results with the addition of free phytosterols to products such as orange juice, low fat milk, lemonade, a low fat yogurt drink, and a Crystal Lite drink (Devaraj et al, 2004; Poteau et al, 2003; Spilburg et al, 2003; Volpe et al, 2001; Ostlund et al, 1999). Jones et al (2003) was the only study that did not observe a beneficial effect on serum lipids with

phytosterol-supplemented fat-free and low fat beverages. With the exception of Ostlund et al (1999), who used less than 2 g, these studies utilized a phytosterol dose in the 2 g range. Overall, the data show a consistent, statistically and clinically significant cholesterol lowering effect of free, non-esterified plant stanols and sterols in a variety of formulations that include low fat and fat-free food matrices. The effect was observed as to both total and LDL cholesterol, in hypercholesterolemics and normocholesterolemics. Free unesterified phytosterols lowered blood cholesterol levels in those consuming their usual diet, as well as those on a low fat diet. These findings are consistent with those observed with phytosterol esters.

A recently completed but not yet published study using 42% orange juice reduced calorie drink has shown similar efficacy.

Studies by Plat J, Mensink, Hallikainen MA, Uusitupa MIJ, Gylling H, Miettinen TA, Weststrate JA, Meijer GW found no significant differences between tall oil derived phytosterols and vegetable oil derived phytosterols. The magnitude of the cholesterol reduction within the studies differed slightly; however, the direction of the slight differences was not consistent. We do not believe that there is a meaningful difference in efficacy between tall oil and vegetable oil derived phytosterols with respect to blood cholesterol reduction.

XII MICROBIOLOGICAL INFORMATION

Based on the SCF guidelines, the following question must be addressed to ensure sufficient microbiological information on the novel food:

• “Is the presence of any microorganisms or their metabolites due to the novelty of the product/process?”

XII-1 The Source Phytosterols

No microorganism or their metabolites are present in the ingredient or would be contributed to the final products by the phytosterol novel ingredient. (see Annex I)

XII-2 The Juice and Nectar Products

The juices and nectars will be produced according to existing EU processing and quality control procedures including HACCP in accordance EU hygiene legislation and all other relevant food law.

XIII TOXICOLOGICAL ASSESSMENT OF THE NOVEL FOOD

Based on the SCF guidelines, the following questions must be addressed to ensure sufficient toxicological information pertaining to the novel food:

- "Is there a traditional counterpart to the novel food that can be used as a baseline to facilitate the toxicological assessment?"
- "Is there information from a range of toxicological studies appropriate to the novel food to show that the novel food is safe under anticipated conditions of preparation and use?"
- "Is there information which suggests that the novel food might pose an allergenic risk to humans?"

To date the safety of phytosterols/phytostanols has been reviewed on 6 occasions as follows:

General view on the long-term effects of the intake of elevated levels of phytosterols from multiple dietary sources, with particular attention to the effects on â-carotene (expressed on 26 September 2002) (SCF, 2002a)

Opinion on a report on Post Launch Monitoring of "yellow fat spreads with added phytosterol esters" (expressed on 26 September 2002) (SCF, 2002b)

Opinion on a request for the safety assessment of the use of Phytosterol Esters in Yellow Fat Spreads (6 April 2000) (SCF, 2000)

Opinion on Applications for Approval of a Variety of Plant Sterol-Enriched Foods (expressed on 5 March 2003) (SCF, 2003a)

Opinion on an application from MultiBene for approval of plant-sterol enriched foods (expressed on 4 April 2003) (SCF, 2004)

Opinion on an application from ADM for approval of plant sterol-enriched foods (expressed on 4 April 2003) (SCF, 2003b)

Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to a Novel Food application from Forbes Medi-Tech for approval of plant sterol-containing milk-based beverages (Request N° EFSA-Q-2003-075) (Scientific Panel on Dietetic Products, Nutrition and Allergies, 2004)

The phytosterol ingredient to be supplied by Cargill has been reviewed by the Finnish authorities and granted 'substantial equivalence' (Annex I).

The overall assessment therefore is that the safety of phytosterol-containing foods is acceptable subject to appropriate labelling, dietary advice on carotenoid intakes from the diet and observing a maximum 3 g/day intake.

CONCLUSIONS

The acceptability of adding tall oil phytosterols to foods in the EU has previously been established. The consumption of juices and nectars, and established EU labelling requirements and purchasing patterns (Unilever submission) make it unlikely that addition of phytosterols to juices and nectars will increase individual consumption of phytosterols above the accepted limit of 3 grams per day. Therefore, approval of the addition of tall oil phytosterols to juices and nectars will offer consumers important dietary alternatives for consuming phytosterols.

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ANNEX I

- Finnish opinion (English translation) - CONFIDENTIAL

- original submission in 2 parts

    A) CARGILL - EU Substantial Equivalence Notification

    B) CARGILL - EU Appendix 1 – Substantial Equivalence Notification

ANNEX II

Letter from Cargill, Inc., to the US FDA in May 2004