EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions
C2 - Management of scientific committees; scientific co-operation and networks

Scientific Committee on Food

SCF/CS/NF/DOS/24 ADD 2 Final
15 April 2003

Opinion of the Scientific Committee on Food on an application from MultiBene for approval of plant-sterol enriched foods

(expressed on 4 April 2003)

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Opinion of the Scientific Committee on Food
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1. TERMS OF REFERENCE

With reference to the initial assessment carried out by the authorities of Finland, taking into account the relevant comments/objections presented by Member States and pursuant to Article 11 of Regulation (EC) N° 258/97, the Committee is asked to assess the safety, from the point of view of consumer health, of phytosterols and phytosterol esters as requested by MultiBene.

2. BACKGROUND

Within the framework of Regulation (EC) N° 258/97 on novel foods and novel food ingredients, a request by the company MultiBene for authorisation to place phytosterols and phytosterol esters as novel food ingredients on the market in the Community has been received (1).

According to the application, the phytosterol-enriched MultiBene ingredient is intended to be added to dairy products, bakery products, processed meat products, edible fats, condiment (spice) sauces and soft drinks. The sources of the MultiBene ingredient are tall oil, wood-based oil and vegetable oil, and the phytosterols occurring either in free form or as fatty acid esters (1).

The major concerns and suggestions raised by the Member States were as follows:

- potential contamination of tall oil-derived sterols by constituents and impurities of crude tall oil from the wood processing industry;
- a concern, in general, on the use of tall oil as a source for sterol preparations;
- potential risk associated with the possible unknown cumulative effect of the intake of phytosterols from different enriched products;
- lack of long-term studies on the effects of phytosterols in children, during pregnancy and lactation;
- the very high estimated consumption for high consumers;
- phytosterol-related decrease in the absorption of fat-soluble vitamins and carotenoids;
- lack of data on phytosterolaemia;
- a need for appropriate labelling, particularly because the application is for an ingredient;

- potential hormonal effects;

- need for an adequate monitoring of the distribution of the enriched products to the consumers.

Most of the above concerns apply to phytosterols in general and had been addressed by the Committee in its previous opinions (13, 14 16).

The Committee expressed an opinion in April 2000 on the safety assessment of the use of phytosterol esters in yellow fat spreads (13). The Committee concluded that the use of phytosterol esters (including 30-65% β-sitosterol, 10-40% campesterol, 6-30% stigmasterol and a total of 5% other phytosterols, based on total sterol w/w content) in yellow fat spreads at a maximum level corresponding to 8% free phytosterols is safe for human use.

The Committee has very recently expressed an opinion on three other applications for products based on phytosterols and phytosterol esters (16). These included submissions by "Oy Karl Fazer AB" (plant sterol-enriched bakery products, grain-based snack products and gum arabicum pills), "Pouttu Ltd" (meat products which are plant sterol-enriched frankfurters, sausages and cold cuts) and "Teriaka Ltd" (plant sterol-enriched fat ingredient Diminicol planned to be added to yoghurts, fresh cheese, margarine and fruit-milk drinks). The early recommendation of the Committee for the phytosterol profile of phytosterol esters of fatty acids (13) was updated and extended to unesterified phytosterols/phytostanols resulting in the following phytosterol/phytostanol profile acceptable in general (16): up to 80% β-sitosterol, 15% β-sitostanol, 40% campesterol, 5% campestanol, 30% stigmasterol, 3% brassicasterol and 3% other phytosterols.

The Committee has also been asked to look into the effect of "overconsumption" and has recently expressed a "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 β-carotene" (14). It was concluded that "the available data do not provide a basis for setting a numerical upper level of total daily intake of phytosterols. In consideration of the dosages found to be effective for cholesterol-lowering, without evidence of additional benefits at higher intakes and the possibility that high intakes might induce undesirable effects, it is prudent to avoid plant sterols intakes exceeding a range of 1-3 g/day. Since a number of foods appear as potential candidates to be enriched with plant sterols, additional management measures may be needed to avoid excessive intakes" (14).

Furthermore, in the first application concerning plant sterols in yellow fat spreads, it was the opinion of the Committee (13) that the applicant should perform a post-marketing surveillance study to obtain data on consumption and further investigation of possible health effects, among others the effects on plasma β-carotene levels. The results of this task have been recently assessed by the Committee in its opinion on a report on post-launch monitoring of "yellow fat spreads with added phytosterol esters" (15).

In its recent opinions the Committee noted again that the consequences of persistently decreased blood concentrations of β-carotene on human health are largely unknown and that situations where vitamin A requirements are greater than normal as in pregnancy, lactation or infancy may be of concern (14). It also reiterated the particular circumstances of phytosterolemic patients and of people under cholesterol-lowering medication, and that additional management measures may be needed to avoid excessive intakes because a number

of foods appear as potential candidates to be enriched with plant sterols (14). In particular the Commission was encouraged (16) to initiate a programme monitoring the total intake of phytosterol-enriched products, in particular who the consumers are and how often and which amounts of these products are consumed.

3. EVALUATION OF THE NOVEL FOOD INGREDIENT

3.1 Specifications on the origin and composition of the novel food

According to EC recommendations on the Assessment of Novel Foods (12) the novel food ingredient was classified by the initial assessment body under Class 1.1 (Pure Chemicals or simple mixtures from non-GM sources, the sources of the Novel Foods (NFs) having a history of food use in the Community). It falls into the categorisation of the EC NFs and NFs ingredients Regulation 258/97 (9) as "food and food ingredients consisting of or isolated from plants …"

The main components of MultiBene-ingredient are tall oil- and/or vegetable oil-derived plant sterols. The product is described as a mixture of crystalline, only physically processed plant sterols and/or their esterified forms and mineral salts. Mineral salt composition can vary depending on food application (1).

The different salts of potassium, magnesium and calcium are as carbonate, citrate, chloride, gluconate, lactate, malate, oxide, phosphate, sulphate, tartrate or acetate salts that will be selected depending on regulations in the marketing country (1).

An unspecified number of preparations (all being mixtures of plant sterols) are used as a source of sterols in MultiBene-ingredient, either together or separately. The applicant indicates that at least three different plant sterol preparations (and the respective suppliers) are used:

- Beta-sitosterol based on tall oil;
- Phytosterol based on vegetable oil;
- FYTO 90 based on vegetable oil.

The applicant presents a certificate of analysis of residues for each of the three products above (e.g. solvents, heavy metals, PAH and PCB compounds). The applicant states that besides the proposed sources of phytosterol also other similar available phytosterol sources, manufactured by other companies, may be used in the production when the products meet the MultiBene-ingredient specification and quality criteria.

Beta-sitosterol is extracted from pine trees (*Pinus maritima* L), Phytosterol and FYTO 90 are derived from deodoriser distillate of vegetable oils.

The range of different sterols (present either as free forms or fatty esters) in the two sources is described:

Sterols (%)	Sources	
	Tall oil	Vegetable oil
Total sterol	>95	≥90
Beta-sitosterol	75-80	40-58
Beta-sitostanol	10-14	0-5
Campesterol	6-10	20-30
Campestanol	0-2	0-1
Brassicasterol	-	0-7
Stigmasterol	-	14-22
Other sterols	0-2.5	-

The applicant paid attention to the residue analyses of the raw material supplier. Beta-sitosterol contains very small amounts of some residues of dioxine (0.51 pg/g), heavy metals (less than 20 ppm), polycyclic aromatic hydrocarbons (PAH) (acenaphthylene less than 150 µg/g, naphthalene and pyrene both less than 30 µg/g, other 13 PAH showing less than 1-10 µg/g, depending on the individually considered compound) and PCB compounds (not detected), and methanol (5000 ppm).

According to the specification provided by the applicant, the plant sterol mixture is composed of beta-sitosterol/stanol 40-90%, campesterol/campestanol 8-30%, stigmasterol 0-22% and other sterols 0-10%.

The Committee agrees with the comment of some Member States that "it is true that tall oil is already used as a starting material for the production of stanols esters which are used in the Benecol products but, in contrast to vegetable oils, this is not a traditional food but a by-product of the wood-processing industry". For this reason the Committee was initially concerned by a phytosterol profile from tall oil containing only 95% total sterols as stated in a previous application but was later satisfied when the applicant submitted a higher purity profile for the sterol mixture extracted from tall oil containing >99% total plant sterols/stanols (16).

3.1.1 Kaukas Ultra Sitosterol

In response to an interim request the applicant informed the Committee that they planned to use the recognised and approved sterols purchased from different companies and possibly also food sterols from UPM-Kymmene (Kaukas Ultra Sitosterol). Their role is to prepare appropriate crystal sizes and some other technical aspects to make the incorporation of plant sterols in food in such a way that the cholesterol-lowering potential of the sterols is better than that of most other preparations.

The petitioner suggested that Kaukas Ultra Sitosterol is a wood-based sterol that should be distinguished from tall oil sterols. The process at Kaukas for the separation of wood sterols is as follows:

Wood extractives from wood chips (pine, spruce and birch) are dissolved into the heated alkaline liquor as a soap fraction. Neutral components (unsaponifiables as sterols) are separated from the soap (fatty- and resin acid soaps) by liquid extraction. Sterols are separated by crystallization from other neutral components; the sterol crystals are collected by centrifugation and washed. After a second purification step with pure solvent the formed crystals are filtered and the product dried in a vacuum drier and packed in drums.

The difference between wood-based sterols and tall oil sterols appears to be that the production of wood-based sterols utilizes the soap fraction from wood whereas tall oil sterols are derived from tall oil pitch (fractionation residue from crude tall oil distillation).

The applicant submitted further information on product specification of Ultra Sitosterol from Kaukas. It contains less than 3% volatiles (105 ºC), maximum 0.5% ash, and has a melting range 137-140 ºC. Its composition (by capillary gas chromatography from dry matter, %) is as follows: 87.5-90.5% β-sitosterol (including β-sitostanol), <1.0% α-sitosterol, 8.0-11.5% campesterol, and <1.5% artenols. Total sterols are higher than 98.5%.

The applicant states that contamination by components such as resin acids, resin aldehydes, terpene alcohols, terpenes, etc. can all be identified with their "quality assurance-process" (GC-MS analysis) down to a detection limit of a few ppm. So far these above-mentioned components have not been identified in Kaukas Ultra Sitosterol.

The specification of MultiBene-ingredient and specification of plant sterol mixtures are presented by the applicant as representative of samples of the raw material to be used and the products to be marketed.

3.2 Intended use and analysis of the effects that can be produced by the processes the novel food has been submitted to

The intended use of MultiBene-ingredient is in: 1) bakery products, 2) dairy products, 3) meat products, 4) dietary fats, 5) spice sauces, and 6) non-carbonated soft drinks.

The corresponding enriched foods are produced by using the traditional ingredients except for the enrichment of the novel food ingredient. Plant sterol content is 1.5% in bakery products, 0.7-1.0% in dairy products, 2.7% in meat products, 8% in dietary fats, 2% in sauces and 0.4% in non-carbonated soft drinks.

Pure beta-sitosterol is dissolved from raw tall oil pitch by hydrocarbon and aqueous methanol solution and recrystallized at the end of the process. Plant sterols from vegetable oil origin are derived from deodorised distillate from one or more of the following vegetable sources: soybean, corn, canola, sunflower seed, cottonseed and peanut.

The esterification is made through trans-esterification with food grade fatty acid esters and free sterols. Food grade oil is methylated with methanol using sodium methylate as catalyst. The resulting methyl ester is used to trans-esterify free sterols under mild vacuum and 100 ºC.

In the production process of MultiBene-ingredient, plant sterols are micronised in an air jet microniser and particle size fewer than 20 microns are obtained. Micronising process has a history of food use but application to plant sterols is claimed to be a new innovation. Esterification of plant sterols has been used for several years for Benecol products (sitostanol esters).

3.2.1 Stability of the modification introduced

The application describes (as an example) the manufacturing process of bakery products, snacks, yoghurt, ketchup and dressing (1). During the manufacture of the final product, sterols will not be exposed to especially high temperatures, high air pressure or vigorous stirring.

It can be stated that phytosterols are relatively stable compounds due to their chemical structure. The applicant presents examples of the effect of the production method on the concentration and the stability of phytosterols in final products. In bakery products, baking in the oven has not been proved to have any marked effects on the concentration or the composition of phytosterols when the sterol concentration is at desired level 1-5%. However, enrichment at higher concentrations (10-15%) is technologically problematic and results in significant losses during the process. No changes in the concentration of sterols were detected in toasted rye bread or wheat rolls, neither when flour was kept in a cold store and bread in a freezer over a two-three month period.

3.3 Information on uses and characteristics of the materials used as a source to produce the novel food

Vegetable oils used as a source are from soya, maize, rapeseed, sunflower, cotton and peanut. The food grade of isolated phytosterols has been stated by the applicant.

Similar plant stanols isolated from tall oil are already used in several EU Member States as ingredients in the existing Benecol products on the market. Flora/Becel pro-active or Take Control margarine contain plant sterols that have been isolated from vegetable oil.

Apart from plant sterols, the MultiBene-ingredient is composed of minerals that are commonly used in the manufacture of foodstuffs. The different salts of potassium, magnesium and calcium will be selected depending on regulations in the marketing country. In this respect, it has to be indicated that no provisions on fortification of foods with minerals are set out at Community level. Accordingly, the decision concerning addition of minerals to foodstuffs may be made by each Member State in the framework of its national legislation.

3.4 Anticipated intake or extent of use of the novel food ingredient

A daily intake of 1.5-2 g of plant sterols will be recommended for cholesterol-lowering in package labelling of MultiBene foods.

The calculations on anticipated intake, based on a study of food consumption in Finland, Sweden, Denmark and Great Britain are the following:

Product	Portion/day (g)	Phytosterol (%)	Intake of phytosterols (g/day)
Bakery products	100	1.5	1.5
Yoghurt	150	1	1.5
Ice cream	120	0.7	0.9
Meat products	75	2.7	2
Condiment sauces	30	2	0.6
Drinks	250	0.4	1

Higher use (90^{th} percentile) could result in an intake of 1.4-3.8 g phytosterol per product group or even in an intake of 8.5 g from single MultiBene foods (i.e. dairy products including cheese in Sweden) (1).

Using a modelling method the applicant considers that it could be stated that a simultaneous use of several products fortified with phytosterols, especially by men, may result in a daily intake of sterols exceeding 4 g and could be as high as 9 g per day.

The applicant presents a list of dietary supplements containing phytosterols marketed in Finland and Germany, which can be considered as an additional intake source.

Plant sterol-enriched food (Benecol margarine, containing esterified stanols) was first retailed in 1995 in Finland. Later on, other Benecol products (fresh cheese, snack bars, salad dressing and yoghurt) were launched on the market in Finland, Benelux, UK, Ireland, Sweden, Denmark and the USA. The recommended intake is based on 2 g/day of plant stanols. Yearly about 200,000 Finns eat Benecol products every day. By the year 2001, more than 12.5 million Benecol-product packages with either Benecol margarine or fresh cheese have been sold in Finland (14).

Also Flora/Becel pro-active margarine has been launched on the EU food market. The recommended daily portion of Flora/Benecol pro-active contains 1.6 g phytosterol.

Results of the use of phytosterol-enriched margarine during a follow-up period of one year has been published (3, 6). According to a report on Post-Launch Monitoring of pro-activ reviewed by the Committee (15) the product is being bought by the target population and intakes are lower than the assumptions made in the original novel food application.

The Committee notes the difficulty in the control of the portion size in the case of soft beverages, which can be particularly relevant when taking into account the potential consumption of these beverages by children.

3.5 Nutritional information: composition and foreseeable impact in the population's diet

A number of studies have been taken into account by the petitioner to asses the effects of plant sterols on serum vitamin concentration, which were already considered by the Committee (14). In particular, the applicant included various human studies to support that the effects of plant sterols on serum vitamins and pro-vitamins could not be so marked as previously thought and they appear not clearly dose-related.

The applicant also included several animal studies with MultiBene-ingredient, to support the efficacy of the novel food ingredient.

However, in a recent study (5) high intake of esterified plan sterols (9 g/day) resulted in a clear reduction of β-carotene blood levels which was statistically significant even when expressed in proportion of β-carotene to cholesterol. In this study 84 free-living men and women consumed reduced-fat spread and salad dressing providing 0.0 g/day (n=21), 3.0 g/day (n=21), 6.0 g/day (n=19) or 9.0 g/day (n=23) of phytosterols as esters for an eight-week treatment period. There were no product-related serious adverse events and no changes in clinical laboratory values in response to phytosterol intake. Alpha- and β-carotene levels were reduced in the 9.0 g/day group *vs.* control ($p < 0.05$). All groups receiving phytosterols had significant increases in serum campesterol *vs.* control ($p < 0.001$), but beta-sitosterol responses did not differ from control.

According to a previous opinion of the Committee (14), in general, the sterol-enriched foods are expected to replace the ordinary foods in the diet of cholesterol conscious consumers. If the novel foods are equivalent in composition (other than in the added compounds) to their traditional counterparts, no further nutritional effects (other than from the added compounds)

should in principle be expected from their consumption. However, there is not enough data to anticipate the potential impact of the introduction of the novel food ingredient on the consumption patterns and dietary habits in the population. Post- launch monitoring studies should address the above issue.

As already stated (14), the Committee noted that plant sterols and stanols interfere with the absorption of carotenoids and perhaps other fat-soluble vitamins like vitamin E.

3.6 Microbiological information

With regard to microbiological quality, there is no reason to expect particular problems from the production processes, materials, and other aspects of the intended use of the present novel food ingredient.

3.7 Toxicological information

Specifications and safety studies on phytosterol esters as ingredients have already been considered by the Committee for a particular novel food in the case of yellow fat-enriched spreads (13), in general from multiple dietary sources (14), and recently for various phytosterol-enriched products (16). A review of toxicological information (17, 22, 21) but no new toxicological studies have been provided.

The available toxicological data on phytosterol esters have been already considered relevant for the evaluation of the free phytosterols as well (16). Thus, toxicological information in *in vivo* animal studies and the extensive information from human trials which is available (see 14) can be considered reassuring. This is because in the human gut, plant sterol esters are hydrolysed to fatty acids and free sterols by pancreatic carboxyl ester lipase (13, 8).

The first evaluation of the Committee on yellow fat spreads with added phytosterols did not assess phytostanols. There are however a number of available studies in both experimental animals and in humans on safety of stanols not showing relevant adverse effects, as recently revised by the Committee (14, 16).

In addition to data on oestrogenic effects, the applicant refers to a human study made with margarine enriched with vegetable oil plant sterols showing no differences, either in women or men, in serum female sex hormone levels between the intervention (plant sterol intake 8.6 g/d) and control group (1a). No effect on sex hormones was either found in the study (2 g/day) of Volpe *et al.* (2001) described later (20).

The anticipated effects of the products concerned by the application at proposed consumption levels are not likely to be more marked than the effects of those phytosterol-enriched products that are already on the market.

3.8 Information on the effects of total or partial exposure of human populations

A number of human studies on the intake of plant sterols and stanols have already been reviewed by the Committee (13, 14, 15, 16). Very recently (16) the Committee reviewed the hypocholesterolemic effect of sterols as studied in 71 (19) and 73 (19a) hypercholesterolemic subjects, in double-blind, placebo-controlled clinical trials that were performed with three different food items (bread, jam in yoghurt, meat products containing slightly elevated levels of calcium, magnesium and potassium) enriched (0.9 to 4.2 g/day) with a tall oil-derived plant

sterol mixture (79% β-sitosterol, 11% sitostanol, 7.5% campesterol). It was concluded that the presence of mineral nutrients in doses recommended for blood pressure-lowering did not interfere with the cholesterol-lowering efficacy of the sterols (19).

In a clinical trial (10) a three-week intake of MultiBene-enriched frankfurters and cold cuts, representing 2.1 g/day of plant sterols, containing tall oil-derived plant sterols, potassium, calcium and magnesium as part of habitual Finnish diet, reduced serum cholesterol significantly in hypercholesterolemic subjects without overt evidence of adverse effects. No changes in blood pressure nor in HDL-cholesterol or triglyceride concentrations were observed. A lower dose of 1.2 g was without effect on blood cholesterol. The mineral enrichment of test products seemed to have no additional or synergistic effect with plant sterols on serum cholesterol concentration.

A clinical randomised, placebo-controlled, double-blind parallel study design with six-week intervention period (7) showed that the yoghurt, low-fat cheese and low-fat fresh cheese containing plant sterol mixture (mainly sitosterol) reduce total serum cholesterol by 4.0-8.3% and LDL-cholesterol by 8.7-11.2%. One hundred and sixty-four mildly or moderately hypercholesterolemic subjects participated in the study. They were randomised into six groups, which were sterol yoghurt, placebo yoghurt, sterol fresh cheese, placebo fresh cheese, sterol hard cheese and placebo hard cheese groups. The subjects consumed either 150 g of yoghurt, 50 g of fresh cheese or 50 g of hard cheese per day. The plant sterol intake was around 2 g. Serum total amount of plant sterols increased by around 10% (12.3±4.2 *vs.* 11.5±4.4) in the sterol group, mainly related to a significant increase (62%, 4.4±1.7 *vs.* 2.6±1.2) in sitosterol concentrations. There were no significant differences between groups in plasma γ-tocopherol, retinol, vitamin K_1 and vitamin D during the trial. Beta-carotene and α-tocopherol levels were decreased in the sterol diet group while differences lost statistical significance when concentrations were related to serum total cholesterol.

A recent study (20) reported the effect of consumption of a yoghurt-based drink enriched with 1 and 2 g plant sterols/day on serum lipids, transaminases, vitamins and hormone status in patients with primary moderate hypercholesterolemia. Thirty patients were randomly assigned to one of two treatment groups: a low-fat low-lactose yoghurt-based drink enriched with 1 g plant sterol extracted from soybean/day *versus* low-fat low-lactose yoghurt, for a period of 4 weeks. After a 2-week wash-out period, patients were crossed over for an additional 4-week period. After a 4-week wash-out period, eleven patients were treated with 2 g plant sterols/day in a second open part of the study for a period of 8 weeks. There were only slight, not statistically significant, differences in serum transaminases, vitamin and hormone levels. It was concluded that a low-fat yoghurt-based drink moderately enriched with plant sterols may lower total cholesterol and LDL-cholesterol effectively in patients with primary moderate hypercholesterolemia.

The applicant states that in Finland, there are already six years experience from the use of stanol-enriched fat spreads. No harmful effects have been reported from phytosterol-enriched foods on the market although such data has not been subjected to active systematic collection.

In summary, no adverse effects have been reported in man, but the studies carried out on human beings and presented in the application are limited.

3.8.1 Sensitive groups

While it is recognized that plant sterols are not recommended for people with sitosterolemia, the applicant does not consider it necessary to mention this consumer group in package labelling. Studies (4, 11) show that intakes around 3 g/day equally affected or minimally increased sitosterol plasma concentrations in heterozygotes compared to that seen in healthy controls. Although sitosterolemia is an infrequent genetic disease, no precise data of its occurrence has been established.

The applicant accepts that pregnant and lactating women can be considered as sensitive groups because studies in this area are lacking and effects on mother and foetus/infant are not known.

Based on several published studies, many of them already considered by the Committee (14), the effects of intakes of plant sterols were considered by the applicant to be safe for children and therefore, the applicant considers unnecessary to have restrictions for children on package labelling for MultiBene products.

In an intervention study (18) 81 children from a randomised prospective trial, aimed at reducing exposure of young children to known environmental atherosclerosis risk factors, were recruited to a double-blind crossover study at 6 years of age. In randomised order the families were advised to replace daily 20 g of the child's dietary fat intake with plant stanol ester margarine or control margarine for 3 months. The wash-out period lasted 6 weeks. The mean daily plant stanol consumption was 1.5 g. The conclusion was that plant stanol ester margarine significantly diminishes serum total and low-density lipoprotein cholesterol concentration without adverse clinical effects in healthy children who already consume a low-saturated-fat, low-cholesterol diet but decreases the serum β-carotene to low-density lipoprotein cholesterol ratio.

In a study of children with severe familial hypercholesterolemia (2) no abnormalities in sonography of the liver and gallbladder after both sitosterol (6 g/day) and sitostanol (1.5 g/day) capsule feeding were noted. Neither were any changes in stool pattern found. Plant sterol administration did not cause any increase in serum sitosterol concentrations (2). In the study of Tammy *et al.* (18) the serum sitostanol concentration after three-month treatment was about 1/6000 of the concentration of serum cholesterol even though the children ingested a 10-fold greater amount of sitostanol than cholesterol.

It can be summarised that in children, transferrin concentration increased while all other laboratory values remained practically unchanged during sitostanol treatment/therapy (2, 18). However, as with adults, the dietary use of plant stanols seems to affect the absorption of fat soluble vitamins or their precursors in children.

The applicant proposed several statements to be included in the package labelling for the sterol-enriched foods, referring to the amount (%), targeted population, recommended daily use, daily intake that gives the maximal cholesterol effect (MCE) (1.5-2 g), and the portion of MCE per g of food, and also indicating that "effects of this food on pregnant and breast-feeding women have not been studied" and that "this food should be used as part of a healthy diet". It is considered that the reference to MCE could be confusing for the consumer because some of the foods enriched or targeted to be enriched with MultiBene have not been directly tested or assessed for efficacy of the intended effect. Scientific evidence on the efficacy should be provided on a case by case basis in marketed MultiBene-enriched foods.

3.8.2 Post-market follow-up

No systematic post-marketing follow-up studies on the nutritional, allergenic or other adverse effects or on the efficacy of phytosterol-enriched foods are available at present. However, results of the use of phytosterol-enriched margarine during a follow-up period of one year have been published (see 15). The applicant considers the establishment of a post-market follow-up programme in line with the Commission Decision 2000/500/EC. The aim of the program would be to show who the consumers are, how often and which amounts of MultiBene foods are used by consumers and what are the effects of these foods on cholesterol levels.

4. CONCLUSIONS

The available toxicological data on phytosterol esters are considered relevant for the evaluation of free phytosterols. The safety assessment of the plant sterol ingredient can largely be based on the data reviewed and evaluated by the Committee in its previous opinions on phytosterol esters in yellow fat spreads (13), on long-term effects of elevated levels of phytosterols from multiple dietary sources (14), and on a variety of plant sterol-enriched foods (16).

A daily intake of 1.5 to 2 g of plant sterols will be recommended for cholesterol-lowering in package labelling of MultiBene foods. Provided that these enriched food products are not consumed in amounts resulting in total phytosterol intakes above 3 g/day, the Committee concludes, on the basis of the available toxicological and nutritional data on phytosterol esters and phytosterols in accordance with the previous opinions (13, 14, 15, 16), that the use of phytosterols in these foods is safe.

However, the Committee noted that the average intake of phytosterol (calculated from the average intake of bakery products, dairy products and processed meat products, condiment sauces and soft drinks) would vary considerably between the four countries considered. Simultaneous use of several products fortified with phytosterols, especially by men, may result in a daily intake of sterols exceeding 4 g and could be as high as 9 g per day. High consumers (90^{th} percentile) in one of the countries could have an intake of 8.5 g from a single MultiBene food (i.e. dairy products including cheese in Sweden) (1).

The Committee reiterates the previous recommendation that appropriate risk management measures should be developed to minimise the likelihood of a daily intake exceeding 3 g phytosterols/phytostanols, in particular from the cumulative intakes of different types of products (SCF, 2002; SCF 2003). The Committee notes that the Commission is working with Member States to develop such risk management measures.

The Committee also reiterates the recommendations:

- that the small number of people with inborn error of phytosterol metabolism (phytosterolaemia) should be made aware of the presence of higher levels of phytosterols in the product,

- that patients on cholesterol-lowering medication should only consume the products under medical supervision, and

- that the potential β-carotene lowering effect should be communicated to the consumer, together with appropriate dietary advice regarding the regular consumption of fruits and vegetables.

The Committee notes again that consumers should be made aware of the presence of higher levels of phytosterols in food products. In addition, in the case of ingredients, the Committee stresses that it should be ensured that any labelling requirement must be subsequently complied by those who use the ingredient in various finished food products and taking into account the potential from cumulative intake.

Apart from plant sterols, the MultiBene-ingredient is composed of minerals that are commonly used in the manufacture of foodstuffs. The different salts of potassium, magnesium and calcium will be selected depending on regulations in the marketing country. In this respect, it has to be indicated that no provisions on fortification of foods with minerals are set out at Community level. Accordingly, the decision concerning addition of minerals to foodstuffs may be made by each Member State in the framework of its national legislation.

The vegetable oil-derived phytosterol mixtures do not fully comply with the phytosterol profile accepted by the Committee (13, 16). The mixtures must not contain more than 3% brassicasterol and 3% total other sterols.

The sterol mixture extracted from tall oil differs from the phytosterol profile already accepted by the Committee (16). Any contamination of the sterol mixture with non-sterol constituents from crude tall oil should be avoided. Wood-based sterols containing at least 98.5% sterols/stanols does not raise concern. Phytosterol preparations derived from tall oil or wood-based should contain at least 99% sterols and be along the line of the maximum limits of the Council Directive on extraction solvents (23) and the recommendations on potential contaminants in the Report of the Committee on smoke flavourings (24).

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