



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate B - Scientific Health Opinions
Unit B3 - Management of scientific committees II

SCF/CS/NF/DOS/1 FINAL

OPINION OF THE

SCIENTIFIC COMMITTEE ON FOOD

ON

A REQUEST FOR THE SAFETY ASSESSMENT OF

THE USE OF PHYTOSTEROL ESTERS IN YELLOW FAT SPREADS

6 APRIL 2000

1. TERMS OF REFERENCE

With reference to the initial assessment carried out by the Dutch authorities, in the light of the relevant comments/objections presented by member states and pursuant to the article 11 of Regulation (EC) 258/97, the Committee is asked to assess the safety from the point of view of consumer health, of phytosterol esters in yellow fat spreads as a novel food.

2. BACKGROUND

The Commission has received the initial evaluation of a petition for an approval for the use of phytosterol esters in yellow fat spreads as a novel food. Phytosterol esters, used at levels proposed in the application, will lead to a new product with enhanced cholesterol lowering activity.

The application was made under the Novel Foods and Novel Food Ingredients Regulation 258/97/EC. The product is classified under Class1, Subclass1: a pure chemical substance or simple mixture obtained from sources already in use for food purposes in the European Community.

The petitioner first submitted an application to the Dutch competent authority for initial assessment. The Dutch Preliminary Advisory Committee on the Safety of Novel Foods performed the initial safety assessment of this new product, concluding that "...the product.....is safe for human use at the levels indicated below. The committee has assessed the full dossier and with current knowledge sees no human health concern occurring from a nutritional or toxicological point of view. However,the committee advises to restrict the dosage of the phytosterols to a maximum of 8% w/w. At this level serum cholesterol levels drop practically at the same rate as with higher doses of phytosterols, but there is less or no drop in serum carotenoid levels".

During the consultation procedure following the initial assessment by the Netherlands, comments/objections were made by a number of Member States' Authorities. The European Commission therefore decided to submit this dossier to the Scientific Committee on Food (SCF) for evaluation of the safety of this product. Major questions, concerns and recommendations made by Member States were:

- It was questioned whether the product is actually free of rDNA,
- Appropriate labelling of the phytosterol esters ingredient is needed to reach the proper target groups,
- The level of phytosterols permitted to be used in the margarine should be limited to a maximum of 8% (w/w),
- Long term clinical studies are recommended to clarify whether the reduction of cholesterol absorption will be compensated by increased endogenous cholesterol synthesis,

- The assessment of the β -carotene lowering effect should be based on the 97.5th percentile of intakes rather than the mean,
- Approval of the product will include validation of health claims,
- Time limited (1 year) permission and post-marketing information should be recommended,
- Oxidation products of cholesterol and phytosterols should be addressed,
- Health risk posed by the product to phytosterolaemic individuals should be sufficiently taken into consideration.

These questions, concerns and recommendations are addressed by the SCF in this opinion if considered relevant for the safety evaluation.

3. EVALUATION

The application submitted by the petitioner follows the Commission Recommendations (1). The product falls into Class 1, Subclass 1: a pure chemical substance or a simple mixture obtained from sources already in use for food purposes in the European Community. According to Regulation 258/97 phytosterols would fall under article 1, Paragraph 2, Section e.

The present evaluation is based on the structured schemes of the SCF as a guide to identify the different aspects required to establish the safety of the novel food (1), on the information submitted by the petitioner (2), and on the comments of the member states on the initial assessment report made by the Dutch Competent Authority.

3.1 Specification of phytosterol esters

With phytosterol esters as a novel food ingredient added to margarine, the applicant developed a yellow fat spread that enhances cholesterol-lowering activity in humans. This novel food ingredient is the esterification product of phytosterols, mainly with polyunsaturated and, in part, monoenoic fatty acids. The common or usual name of phytosterol esters is proposed to be “vegetable oil sterol esters”. Phytosterols are extracted from the edible oils (soya, maize, rapeseed, sunflower) and esterified with sunflower oil fatty acids. The product tested in genotoxicity studies had the following specification (results of the analysis of five different batches) (2):

- Free fatty acids <0.2% (w/w)
- Total fatty acids 37.0 – 37.7% (w/w), mean 37.4% (w/w)
- Fatty acid composition (of total fatty acids):

C16:0	7.5 – 7.6%
C18:0	4.8 – 4.9%
C18:1	22.6 – 22.7%
C18:2	65.0 – 65.1%
- Free sterols 10.5 – 11.8% (w/w), mean 10.9% (w/w)
- Total sterols 62.3 – 63.0% (w/w), mean 62.6% (w/w)
- Sterol profile (of total sterols):

Cholesterol	0.2 – 0.3%
Brassicasterol	2.7 – 3.1%
Campesterol	26.5 – 27.0%
Stigmasterol	17.4 – 18.0%
β-sitosterol	50.8 – 51.2%
unknown	1.2 – 1.7%

- Total volatiles <0.5% (w/w)
- Peroxide values 1.5 – 2.1 meq/kg, mean 1.9 meq/kg

Based on the variability in sourcing/seasonal variation of the plant sterols, the applicant expects the following sterol profile (2):

Cholesterol	0.0 – 2.0% of total sterols
Brassicasterol	0.0 – 9.0%
Campesterol	10.0 – 40.0%
Campestanol	0.0 – 6.0%
Stigmasterol	6.0 – 30.0%
β-sitosterol	30.0 – 65.0%
Sitostanol	0.0 – 10.0%
D5-Avenasterol	0.0 – 4.0%
D7-Avenasterol	0.0 – 2.0%
D7-Stigmastenol	0.0 – 2.0%
Other	0.0 – 5.0%

Phytosterols occur naturally in food as free alcohol, esterified with long chain fatty acids (25 – 80% of total phytosterols) and conjugated as glucosides (usually in small amounts). The majority of plant oils contains 0.1 – 0.5%, while some germ oils (rice bran, wheat germ, oats) contain up to 4% total phytosterols (3). Reduced and low fat spreads on the market contain approximately 0.3-0.4% phytosterols.

The application for this novel food ingredient covers yellow fat spreads with increased levels of phytosterols (up to 12%, on average 8%).

3.2 Effects of production processes

Phytosterols are by-products of vegetable oil refining. Phytosterols are isolated from conventional edible oils (soya, maize, sunflower, rapeseed). The conventional caustic refining procedure comprises degumming, neutralisation, bleaching and deodorization. The last step, a mass-transfer process, by which substances are evaporated from the oil under reduced pressure (2 – 10 mbar) and elevated temperature (230 – 270°C), leads to a distillate making around 0.1 – 0.3 % of oil mass and contains 8 – 20 % sterols (details in 5).

Formulation and process rules currently used to ensure safety of conventional spreads have been used for the new products. All materials are produced according to Good Manufacturing Practices. All processing materials are of food-grade or equivalent.

Storage and distribution temperatures used are the same as conventional spreads and the same Hazard Analysis and Critical Control Point (HACCP) schemes are used to control product safety and quality.

Phytosterols from oil from already approved genetically modified plant strains might be present in the mixture. The isolated phytosterols are re-esterified with fatty acids from sunflower oil.

The production process of the spread has a history of safe use for ingredients for the food industry and it does not affect the composition and structure of the components.

3.3 History of source organism

Commercially available and used plant oils from different plants, but mainly from soya, sunflower, maize, and rapeseed, are the sources for production of the novel food ingredient. These source oils are not derived from plants especially grown for this purpose and they are generally not genetically modified, although it cannot be excluded that some mixtures contain oils or isolated sterols from GMOs. In this case these can be expected to be approved organisms and derived products like the Round-up-ready soybean and its products. Thus, whenever labelling requirements exist for the use of already approved ingredients derived from GMOs, these requirements will also apply to this novel food.

3.4 Ingredients use in food

The applicant has applied to use vegetable sterol esters in new vegetable oil-based spreads at levels up to 20% (\approx 12% free sterols). The use of the new product is intended to help maintain healthy cholesterol levels as part of a diet low in saturated fat and cholesterol. The spread base contains around 40% fat, composed of edible vegetable oils which are high in polyunsaturated (PUFA), low in saturated and very low in *trans* fatty acids. The product is not intended for use in cooking.

3.5 Anticipated intake/extent and consequences of use

With normal consumption of this kind of spreads being 20 – 30 g/d, the intake of phytosterols when using the novel product will increase to about 1.6 – 2.4 g/d, amounting to an 8-12 fold increase of the current daily intake from traditional products. In the USA plant sterol esters in plant oil-based spreads at levels up to 20% are generally recognised as safe (GRAS) (4).

The main sources of phytosterols in the basic diet are cooking oils and margarines. Bread and cereals can also contribute significantly to total phytosterol intake (6). Reduced-fat health spreads contain 0.3 – 0.4% phytosterols, corn oil margarines are highest in phytosterols (0.5%). Vegetables and fruits contain <0.05% (based on the edible portions), except seedlings of barley, beans, peas which contain 0.1 – 0.2% phytosterols. Some seeds are also rich sources: sunflower and sesame seeds contain 0.5 – 0.7%, and legumes can contain 0.22% phytosterols.

A typical U.S. diet provides approximately 250 mg of phytosterols per day (≈ 4 mg/kg bw/d) (7). In the UK and the Netherlands phytosterol intake was estimated to be about 200 mg/d. In the adult Finnish population average intakes amounted to 300 mg/d (≈ 5 mg/kg bw/d) with an upper limit of 680 mg/d (≈ 10 mg/kg bw/d). Generally the intake of adult vegetarians and their children is higher (up to 40%) than the average for the population as a whole (7-9).

Infant formulae based on cow's milk contain 0.08 – 0.20 mmol/l β -sitosterol, 0.03 – 0.10 mmol/l campesterol and around 0.02 mmol/l stigmasterol, while the phytosterol content in human milk is negligible and can not be detected using current methods (10).

Oral phytosterol intake of about 3g/d inhibits the intestinal cholesterol absorption, probably by blocking the receptors (11). Aiming at a similar blood cholesterol modulating effect, studies with hypercholesterolaemic subjects have employed dose levels of many grams (up to 25 g/d) of phytosterols per day for up to three years (8). Such limited total- and LDL-cholesterol lowering effect can be compensated by an increased endogenous cholesterol synthesis, unlike the use of drugs suppressing synthesis or perturbing the enterohepatic cycle of cholesterol and bile acids, which might lead to very low cholesterol levels. In addition, studies have shown that drug treatment with statins to reduce cholesterol levels increased the phytosterol/cholesterol ratio by increased absorption. For example, the ratio of sitosterol/cholesterol was shown to increase by 200 % (9, 13). This means, that high intake of phytosterols could be a potential problem when ingested together with cholesterol lowering/inhibiting drugs.

From marketing data on users and usage of a similar yellow fat spread containing phytosterols in the EU, the petitioner concludes that the product is used predominantly by people who are more than 50 years old and of relatively high socio-economic standing, and that the majority of households using the product consist of one or two people. The petitioner's current sales data for yellow fat spreads containing phytosterol esters in USA and Australia indicate a comparable consumer profile.

Typical daily consumption of yellow fat spreads in Europe is between 20 and 30 g/d. In order to achieve the required cholesterol lowering effects the intake of phytosterols - according to petitioner - should amount to 1.6 – 3.6 g/d (expressed as esters 2.2 – 5.0 g/d). That means that phytosterol concentrations in the yellow fat spread should be 6 – 12% (w/w). Estimates of fat spread use of males above 50 years of age in the UK and the Netherlands show that the 95th percentile of use is approximately 57 g/d and 70 g/d respectively.

The marketing of the product is focussed on the particular section of the population that is trying to control its blood cholesterol levels.

As indicated by the applicant there is only a small number of people at risk of adverse reaction. These comprise individuals with an inborn error of phytosterol metabolism (autosomal, recessive); worldwide 50 cases are known (2). Appropriate

labelling should assure that phytosterolaemic patients can avoid consuming the product.

Although it is not intended to recommend this product to healthy young adults, or for children, these individuals may consume the product when it is available in a family home. The initial assessment came to the conclusion that children in Europe are not expected to experience negative effects from possible lowered cholesterol levels.

The new product is intended to replace other yellow fat spreads. Based on the product specification the novel food differs from other fat spreads only in the phytosterol ester content at the cost of corresponding amounts of non-fat compounds (water). Thus there will be no change in intake of nutrients and/or other compounds. The new product contains a similar amount of polyunsaturated fatty acids as other so called “heart health” products.

3.6 Nutritional information

Phytosterol esters are hydrolysed by pancreatic carboxyl ester lipase. Absorption of free phytosterols in humans and experimental animals is low: 4 – 5% for β -sitosterol and stigmasterol, 9 – 10% for campesterol and brassicasterol (12). At higher dietary intake (2000 mg/d), absorption of sitosterol by humans is reduced. In healthy subjects campestanol is better absorbed than campesterol (12.5% vs. 9.6% of intake). Phytosterol absorption in women was found to be slightly higher than in men (13) and higher in children than in adults (14).

Absorbed phytosterols are transported in the triglyceride-rich lipoprotein (VLDL) and chylomicrons, taken up by the liver and then excreted into the bile (15). Circulating phytosterols are transported in the blood mainly in LDL and HDL fractions. Tissues with LDL receptors such as the liver, adrenals and testes may then take up phytosterols and convert them into steroid hormones (16). Since their concentration in these tissues is much lower than that of cholesterol, this will not significantly contribute to hormone synthesis. However, no information on the relative potency of hormones derived from either cholesterol or phytosterols is available. Unabsorbed sitosterol and campesterol is converted by the human colonic microflora to sitostanol/stigmastanone and campestanol/campestanone, respectively. Among a group of 31 normal North Americans, 23 high converters have been found converting a mean of $83 \pm 9\%$ sitosterol (17).

After ingestion of 8.6g phytosterols/d in healthy human adults, faecal concentrations of sterols and sterol metabolites increased from about 40 to 190 mg/g dry weight and 30 to 50 mg/g dry weight, respectively. The major sterol metabolites excreted were metabolites saturated at the 5,6-position in β -configuration or metabolites formed by oxidation at the 3-position. The faecal concentration of 4-cholesten-3-one was slightly but significantly increased (about 2 mg/g). Faecal secondary bile acid concentration was reduced. The formation of small amounts of oxysterols could not be excluded, but considered to be unlikely (18). Phytosterols in food can be oxidised, particularly at higher temperatures ($>180\text{ }^{\circ}\text{C}$) (19). Oxidation products (7-hydroxy-

and 7-keto-components) are formed at very low levels which are similar to other plant oil products containing phytosterols and are also poorly absorbed (2).

If the product is consumed on regular basis (20 – 25 g phytosterol-enriched spread daily, equivalent to 1.6 – 2.0 g phytosterols/d) then the average lowering of plasma LDL-cholesterol will be 8 to 10%, relative to initial plasma levels (4.16 ± 0.5 to 6.54 ± 0.61 mM). The reduction in blood cholesterol levels of the magnitude anticipated from consumption of phytosterol-enriched spreads is safe in those individuals who do not have elevated plasma cholesterol levels. This was confirmed by the results of the three-year Dietary Intervention Study in Children (DISC). In 8 – 11 year old children a diet low in fat, saturated fatty acids and cholesterol lead to a modest decrease in LDL-cholesterol, while maintaining adequate growth, iron status, nutritional quality and psychological well-being during the critical growth period of adolescence (20). Children and adults would not be expected to experience any adverse effect on metabolism when their blood cholesterol is lowered. The novel food is intended to be used by population groups above 50 years of age, who try to control their elevated blood cholesterol.

At levels of phytosterols in spreads of 3.4, 6.5 and 11 – 13% (w/w) in short term (21) and 8% (w/w) in a one-year follow-up study (2) the new product is equally effective in lowering LDL cholesterol by 8 – 10%, relative to the initial plasma level. At 11 – 13% of phytosterols in the fat spreads no appreciable effect on the fat-soluble vitamins calciferol, tocopherols and phylloquinone was noticed, but a 10% reduction of α - and β -carotene as well as lycopene was observed. This reduction of 10% itself seems not to be of physiological relevance, but, considering a long term exposure and taking into account the 97.5 percentile of intake, the decline of β -carotene levels might be higher.

In the initial assessment by the Dutch competent authority it was expected that a maximum of 8% (w/w) phytosterols will cause little or no drop in serum carotenoid levels.

The applicant considered the points raised by some member states after the initial assessment and commissioned a one-year follow up study (2) with healthy subjects using fat spread containing 8% (w/w) phytosterols (the preparation contained 38g fat in 100 g spread). A report with the results of this study was forwarded to the SCF. The results can be summarised as follows:

- When adjusted for total lipids no statistically significant changes after week 26 and week 52 were found for lutein, zeaxanthin, β -cryptoxanthin, lycopene and α -carotene. Only β -carotene was significantly ($p=0.037$) decreased at week 52; the level dropped by 24% (21% when lipid adjusted) as compared with the initial level at time point 0. This significant drop of β -carotene level occurred after 52 weeks despite the fact that the tested new fat spread contained a maximum of 50 mg carotenoids per kg fat (mainly β -carotene and lycopene added for coloration). The reduction was twice that observed in the short-term studies with 12% phytosterols. Nevertheless, it can be seen from the week 0 results that there is a large variation within the normal range for

plasma β -carotene levels, that there are also seasonal variations and that this reduction is within normal range (Table 1).

Table 1: Changes in plasma β -carotene levels in one-year follow-up study (data from ref.2, doc. ref. D99/047)

n=64 healthy adults	β - carotene (nmol)	β -carotene/lipid adjust. (nmol/mmol)
Week 0	410.4±216.8	58.3±33.1
Week 26	321.9±175.6	48.0±28.1
Week 52	310.1±190.3	46.1±28.6

The reduced plasma β -carotene levels might become more relevant when the vitamin A status is not optimal. This is the case for pregnant and lactating women as well as younger children.

- There were no significant differences in the plasma levels of retinol, 25-OH-cholecalciferol or α -tocopherol (total lipid adjusted) during 52 weeks of study. Phylloquinone status was not statistically different between test and control groups after 26 weeks of study.
- There was a significant cholesterol-lowering effect of phytosterol esters enriched margarine throughout the one-year duration of the study (2).
- There were no side effects seen in the individuals during the study.

3.7 Microbiological information

Spreads containing phytosterol esters have been tested for their microbiological stability and have been found to be similar to conventional spreads. The production process and the inherent properties of the novel products give no rise to concerns of microbiological risk. No data indicate an effect on the intestinal flora in terms of bacterial profile or metabolic activity beyond natural variations (2).

3.8 Toxicological information

The toxicological information available on phytosterols and phytosterol esters comprises data from studies on absorption, distribution, metabolism, and excretion and on (a) subchronic toxicity, (b) genotoxicity, (c) reproductive toxicity, (d) potential estrogenic activity and from (e) human studies:

- (a) In a 13-week feeding study with rats, a mixture of phytosterol esters, obtained mainly from soya bean oil and re-esterified with fatty acids from sunflower oil, was tested at dosages of 0.16, 1.6, 3.2 and 8.1% in the diet. The mixture contained 62% total sterols consisting of mainly β -sitosterol (48.7%), campesterol (25.8%) and stigmasterol (21.6%) with only 1.1.% brassicasterol.

Neither D5- and D7-avenasterol nor D7-stigmastenol were present. Apart from some minor changes in haematology and clinical-chemical parameters, no relevant toxic effects up to the highest dose of 6.6 g/kg bw/day (corresponding to 4.1 g phytosterols/kg bw/day) were found (22).

- (b) Phytosterols (47.9% β -sitosterol, 28.8% campesterol, 23.3% stigmasterol) and phytosterol-esters (47.3% β -sitosterol, 28.1% campesterol, 24.1% stigmasterol) show neither evidence of mutagenic activity in the bacterial mutation assay with *Salmonella typhimurium* (strains TA 1535, 1537, 98 and 100) nor clastogenic activity in tests on chromosomal aberrations with human peripheral blood lymphocytes *in vitro* both in the presence and absence of S-9 mix derived from rat livers.

In addition, two *in vivo* genotoxicity studies were conducted using a phytosterol ester mixture containing 0.3% cholesterol, 3.0% brassicasterol, 28.1% campesterol, 0.8% campestanol, 18.7% stigmasterol, 45.5% β -sitosterol, 2.6% β -sitostanol, 1.1% D5-avenasterol and 1.9% others. Using an *in vivo/in vitro* procedure the mixture did not induce unscheduled DNA synthesis (UDS) in the livers of orally dosed male rats (once with 2000 mg/kg). In another study in rats the plant sterol mixture did not induce micronuclei in the polychromatic erythrocytes of bone marrow of male rats treated up to 2000 mg/kg/d (2, doc. ref. D00/004).

Neither 4-cholesten-3-one, an oxidation product of cholesterol increased in volunteers fed phytosterols, nor 5 β -cholestan-3-one showed mutagenic activity when tested in the bacterial mutation assay with five strains of *Salmonella typhimurium*. Furthermore, none of the substances showed a clastogenic potential in the *in vitro* chromosome aberration assay with human lymphocytes (23,24).

- (c) A variety of effects on the reproductive system such as antiandrogenic action in rabbits and decrease in testicular weight and sperm concentration in rats have been reported for β -sitosterol and phytosterol-rich extracts (25, 26, 27, 28). These observations have been made after administration by the subcutaneous route and/or with phytosterol preparations, the purity of which was not specified.

However, in a two-generation reproduction study in rats, phytosterol esters of the same composition as in the 13-week study had no effect on the reproduction of the F0 and F1-generations, nor on the development of the F1- and F2-pups, nor on the sexual maturation of the F1-weanlings nor on oestrous cycles. A dietary phytosterol ester concentration of 8.1% was shown to be the no-observed-adverse-effect level (NOAEL). This was equivalent to a dose of 2.5-9.1 g/kg bw/day depending on the period during the study (29).

- (d) Orally administered β -sitosterol of unknown purity increased uterine weight in rats receiving a low dose for 30 days (6.2 μ g/dl in drinking water). This weak oestrogenic response was not observed at higher doses (12.4 μ g and 18.6 μ g/dl) (30).

In contrast to these studies, uterotrophic assays with immature female rats orally gavaged with phytosterols (47.9% β -sitosterol, 28.8% campesterol,

23.3% stigmasterol) and phytosterol esters (47.3% β -sitosterol, 28.1% campesterol, 24.1% stigmasterol) in doses of 5, 50 and 500 mg/kg bw/day for 3 days did not reveal any oestrogenic response using uterine weights as the end point. In addition, phytosterols of the same composition did not display oestrogenic activity in a recombinant yeast assay for oestrogenic potential, nor did they show binding in a rat uterine cytosol oestrogen receptor binding assay (31). These studies, together with the two-generation reproduction study, provide sufficient reassurance of absence of endocrine effects via the oral route.

- (e) In a 3-week study with 12 men and 12 women who consumed 5.8 g phytosterols (in 40 g margarine) per day no changes in the sex hormone levels in females was shown (18). Two double-blind placebo-controlled 14-week tests did not provide evidence for any adverse effects on haematological and clinical parameters (21,32). These trials and the one-year follow-up study using phytosterol esters (8% w/w expressed as phytosterols) in the fat spreads were carried out primarily with the view to assessing the cholesterol lowering effect of phytosterol esters. These tests have not reported any toxic effects relating to the phytosterols.

Phytosterol preparations are used for the medical treatment of benign prostatic hyperplasia. A number of placebo-controlled, double-blind clinical trials was conducted with preparations of uncertain compositions said to be mainly β -sitosterol. With doses of 20 mg β -sitosterol three times per day (33) and 130 mg β -sitosterol daily (34), significant improvements in symptoms and urinary flow parameters were reported (35). The mechanism of this effect and the active ingredient remains to be determined. Side effects have not been reported.

4. CONCLUSIONS

- The Committee considers that the dossier and the additional information submitted during 1999 and 2000 is complete and follows the SCF recommendations. The novel food, phytosterol esters in yellow fat spreads, has been correctly classified as Class1, Subclass1, a pure chemical substance or simple mixture obtained from sources already in use for food in the European Community.
- The new yellow fat spread differs from conventional fat spreads/margarine by its phytosterol origin (obtained from edible vegetable oils), their chemical structure (esters with long chain unsaturated fatty acids of sunflower oil) and concentration (about 16 – 24-fold higher than the conventional product). This concentration will increase the total intake of phytosterols by 8 – 12 times, compared with traditional products.
- Based on extensive toxicological testing of phytosterol preparations in a 13-week feeding study with rats, in a two-generation feeding study with rats, in studies on

oestrogenic potential and in tests on genotoxicity, no safety concerns were apparent.

The safety in use of phytosterols has been demonstrated for mixtures of predominantly β -sitosterol, campesterol and stigmasterol and/or their esters with fatty acids, to which the specification of the new product should be restricted. The phytosterol profile of 30-65 % β -sitosterol, 10-40 % campesterol, 6-30 % stigmasterol and a total of 5% other phytosterols, based on total sterol content (w/w), is considered acceptable by the Committee.

- The Committee considers that the very small number of people with inborn error of phytosterol metabolism (phytosterolaemia) should be made aware of the presence of higher levels of phytosterols in this product and that patients on cholesterol-lowering medication should only consume the product under medical supervision.
- Ingestion of 20g per day for one year of products containing 8 % free phytosterols reduced plasma β -carotene concentrations by 20%. Although the β -carotene concentration was still within the normal range and within normal seasonal variations, such a reduction in plasma β -carotene levels might become more relevant for persons whose vitamin A status is not optimal. The Committee is therefore of the opinion that this β -carotene lowering effect should be communicated to the consumer, together with appropriate dietary advice regarding the regular consumption of fruits and vegetables.
- Given the overall evaluation of the submitted information the Committee concludes that the use of phytosterol esters in yellow fat spreads at a maximum level corresponding to 8% free phytosterols is safe for human use.
- The Committee is of the opinion that the applicant should perform, in accordance with Chapter XI in the Annex of Commission Recommendation 97/618/EC (1), 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 Committee will wish to review this information when it becomes available.

5. REFERENCES

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