www.food.gov.uk

Dr James Barnett
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6 June 2006 Reference: NFU 592

Dear Dr Barnett,

OPINION ON THE SUBSTANTIAL EQUIVALENCE OF PHYTOSTEROLS

The Advisory Committee on Novel Foods and Processes (ACNFP) has now completed your request for an opinion on the equivalence of your phytosterols (Nutraphyl^{TM}) with the phytosterols marketed by Forbes Medi-Tech. The Committee's opinion is enclosed.

I am pleased to inform you that, in view of the positive opinion given by the ACNFP, the Food Standards Agency, which is the UK Competent Authority for all novel food issues, is content that your phytosterol ingredient meets the criteria for equivalence, as defined in Article 3(4) of regulation (EC) 258/97.

This opinion is issued on the basis that your phytosterol ingredient is to used in yellow fat spreads, salad dressings, milk type products, fermented milk type products, soya drinks and spicy sauces in accordance with the conditions specified in Commission Decisions 2004/333/EC, 2004/334/EC and 2004/336/EC and 2004/845/EC.

We also advise that you inform all customers that food products containing plant sterols should be labelled in accordance with Regulation (EC) 608/2004.

Please note that, in accordance with Article 5 of (EC) 258/97, you should notify the European Commission when you first intend to market your phytosterol ingredient. You should also list the intended uses of your ingredient and indicate that the final products will be presented as detailed in Article 2 of the above mentioned Commission Decisions. You should send this notification to Mr Andreas Klepsch at the following address:

Andreas Klepsch
European Commission
DG SANCO
Rue de la Loi 200
B-1049
Brussels
Belgium

If you have any query, please contact me.

Yours sincerely,

(By e-mail only)

Annie-Laure Robin
Novel Foods, Additives and Food Supplement Division

Enc.: ACNFP opinion

OPINION ON SUBSTANTIAL EQUIVALENCE OF PHYTOSTEROLS CONSIDERED UNDER ARTICLE 5 OF THE NOVEL FOODS REGULATION

Applicant	**DDO Processing** **17 Southside Ave.** **Cincinnati, OH 45204** **United States**
Responsible Person	**Dr James Barnett**

Introduction

1. A request was submitted by the American company DDO Processing to the UK Competent Authority, in November 2005, for an opinion on the equivalence of its phytosterols (Nutraphyl™) to be used in yellow fat spreads, salad dressings, milk type products, fermented milk type products, soya drinks and spicy sauces with the phytosterols marketed by Forbes Medi-Tech.

2. Forbes Medi-Tech initially gained authorisation for use of its phytosterols in milk based beverages through Commission Decision 2004/845/EC, in March 2004. A subsequent authorisation, based on an opinion on substantial equivalence from the Finnish Competent Authority in April 2005, extended the range of Forbes Medi-Tech products to include yellow fat spreads, salad dressings, fermented milk type products, soya drinks, cheese type products, yoghurt type products, spicy sauces and milk based fruit drinks with added phytosterols/phytostanols. DDO Processing is therefore seeking a view on equivalence for the use of their phytosterol ingredient in the food categories included in Forbes Medi-Tech original authorisation and the two subsequent notifications granted by the Finnish Competent Authority.

3. According to Article 3(4) of (EC) 258/97, the notification procedure applies to "foods or food ingredients …which on the basis of the scientific evidence available and generally recognised or on the basis of an opinion delivered by one of the competent bodies … are substantially equivalent to existing foods or food ingredients as regards their:
   - composition,
   - nutritional value,
   - metabolism,
   - intended use and
   - level of undesirable substances contained therein."

Evaluation

(a) Composition

4. DDO Processing is proposing to produce its phytosterols and phytosterol esters from crude tall oil, using a patented production process. The applicant does not specify the exact source of its crude tall oil but indicates that it is generally derived from by-product of paper pulp production from tree sources such as pine trees. This process involves the hydrolysis and saponification of the crude tall oil pitch (distilled tall oil), followed by the removal of the soaps. The crude sterols are then re-dissolved, crystallised and purified through filtration and washing with heptane. After removal of the solvent, the sterol crystals are finally prilled (granulated) for packaging. To obtain phytosterol esters, DDO Processing will trans-esterify its phytosterols using fatty acids derived from oilseed. The final product contains >99% sterols and stanols.

5. The applicant indicates that their production process is similar to those used by Forbes Medi-Tech and others to produce existing phytosterol ingredients from tall oil, although it leads to a slightly higher beta-sitosterol content. The applicant initially provided certificates of analysis for six batches of its tall oil derived phytosterol. The results of these analyses showed that the composition of the final tall oil product complies with the specification laid down in Commission Decision 2004/845/EC, apart for beta-sitosterol.

6. The data initially submitted by the applicant indicated levels of beta-sitosterol up to 87% compared to 80% for Forbes Medi-Tech phytosterols. The applicant carried out analysis of four additional batches of his phytosterol product with a more accurate and representative method based on gas chromatography–flame ionisation detection. The maximum beta-sitosterol level obtained was 81%, which the applicant considers to be a more accurate measurement. The proposed specification for DDO Processing ingredient is indicated below:

Composition (%)	**Commission Decision 2004/845 (Forbes Medi-Tech)**	**Proposed Tall oil plant sterols(*)**
Beta-sitosterol	<80%	<81%
Beta-sitostanol	<35%	<35%
Campesterol	<40%	<40%
Campestanol	<15%	<15%
Stigmasterol	<30%	<30%
Brassicasterol	<3%	<3%
Other phytosterol	<3%	<3%

(*) purity of > 99%

Discussion: *The first phytosterols authorised in the EU in 2000 had a maximum beta-sitosterol content of 65%. A higher limit of 80% was accepted by the Scientific Committee on Food in 2003[1], on the grounds that beta-sitosterol esters and beta-sitosterol had been the main constituents in the sterol mixtures originally tested for sub-chronic toxicity, genotoxicity, reproductive toxicity and oestrogenic activity studies, without showing effects causing concern. In addition, the SCF had reviewed*

[1] SCF Opinion on Applications for Approval of a Variety of Plant Sterol-Enriched Foods (March 2003), see http://europa.eu.int/comm/food/fs/sc/scf/out174_en.pdf

additional animal studies on sterol mixtures with a high content of beta-sitosterol derived from tall oil.

The Committee was satisfied that the slightly higher upper limit of 81% for beta-sitosterol, compared to 80% for Forbes Medi-Tech phytosterols, did not have significant consequences for the safety or biological properties of the product, whose composition could be regarded as "substantially equivalent" to the authorised product marketed by Forbes Medi-Tech. This is consistent with the approach taken in the UK for other applications for opinions made under Article 3(4) of the novel foods regulation, for which minor variations in composition are accepted[2]*.*

(b),(c) Nutritional value and metabolism

7. There is no information to suggest that the nutritional value or metabolism of DDO Processing phytosterols will be any different to those used by Forbes Medi-Tech. The phytosterols content of both products is at least 99%.

8. The applicant mentions that the anticipated intake of phytosterols is not likely to be increased as the ingredient is to be used in the same range of products already approved, as an alternative to existing ingredients from other manufacturers.

Discussion: *The Committee did not comment on the above information provided by DDO Processing.*

(d) Intended use

9. DDO Processing intends that its phytosterols will be used in yellow fat spreads, salad dressings, milk type products, fermented milk type products, soya drinks, spicy sauces. These products are the same as those authorised to be placed on the market when containing Forbes Medi-Tech phytosterols.

Discussion: *The Committee was content that DDO Processing phytosterols are to be consumed at the same levels than phytosterols sold by Forbes Medi-Tech in the same range of products mentioned above.*

(e) Levels of undesirable substances

10. The applicant has not carried out analyses to check for the presence of protein allergens but they point out that it is unlikely that allergens would be found in the final product after the heating and distillation operations. Residues of solvents used in the manufacturing process (methanol and heptane) were initially reported to be below 10 mg/kg. The applicant has also provided additional information indicating that his ingredient has a heptane residue level below 0.1 mg/kg.

[2] ACNFP guidelines for the presentation of data to demonstrate substantial equivalence between a novel food or food ingredient and an existing counterpart (March 2005), see http://www.food.gov.uk/multimedia/pdfs/seguidelines.pdf

11. The applicant has provided no information on the levels of a range of other undesirable components which were previously reported to be at low levels or undetectable in plant sterols manufactured by Forbes Medi-Tech[3].

12. The applicant also highlights that the purity of its tall oil phytosterols is above 99% and therefore complies with the purity criteria set in Commission Decision 2004/845/EC for tall oil derived phytosterols.

13. The safety and the quality of the ingredient will be controlled through HACCP schemes which are used on conventional foods. The applicant also indicates that products containing DDO Processing plant sterols will be controlled for their quality and safety using Good Manufacturing Practice (GMP).

Discussion: *The Committee noted that DDO ingredient complies with recommendations from the Scientific Committee for Food and EFSA that plant sterols derived from tall oil should contain more than 99% sterols/stanols, and should comply with solvent limits set out in directive 88/344/EEC[4] (which defines a limit of 50 mg/kg for methanol and does not include a limit for heptane). It was not clear to the Committee whether the use of solvents in the manufacture of phytosterols was within the scope of Directive 88/344/EEC. The Committee also noted that the residues of heptane reported by the applicant were very low (<0.1 mg/kg) and that residue levels of 5,000 mg/kg were accepted for use in the manufacture of pharmaceuticals, although this does not necessarily mean that heptane should be permitted in food production. The Committee concluded that the heptane residues in DDO's ingredient were unlikely to present a safety concern.*

Additional information

14. **Labelling** DDO Processing will advise its customers that all products containing its phytosterols must be labelled in accordance with the requirements set in Commission Regulation (EC) No. 608/2004[5].

15. **Safety assessment** The applicant refers to the equivalence of phytosterols and phytosterol esters in relation to their low order of toxicity (except in individuals with sitosterolemia), metabolic handling and cholesterol lowering activity, which had been assessed by the SCF.

Discussion: *The Committee did not comment on this additional information provided by DDO Processing.*

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[3] EFSA opinion on novel food application from Forbes Medi-Tech for approval of plant sterol-containing milk-based beverages (November 2003), see http://www.efsa.eu.int/science/nda/nda_opinions/216_en.html

[4] Council Directive 88/344/EEC of 13 June 1988 on the approximation of the laws of the Member States on extraction solvents used in the production of foodstuffs and food ingredients.

[5] Commission Regulation (EC) N0 608/2004 of 31 March 2004 concerning the labelling of foods and food ingredients with added phytosterols, phytosterol esters, phytostanols and/or phytostanol esters.

Conclusion

16. The Committee concludes that DDO Processing has demonstrated the equivalence of their phytosterols (Nutraphyl™) to be used in yellow fat spreads, salad dressings, milk type products, fermented milk type products, soya drinks and spicy sauces with the existing Forbes Medi Tech phytosterol ingredient, according to the criteria set out in Article 3(4) of the Novel Food Regulation (EC) 258/97.

17. Therefore, the phytosterols produced by DDO Processing can be considered to be substantially equivalent to the existing phytosterol ingredient marketed by Forbes Medi Tech used in the same range of products.

18. DDO Processing has indicated they will ensure that its customers are aware that the labelling of products containing their phytosterols must comply with Commission Regulation (EC) 608/2004 concerning the labelling of foods with added phytosterols, and that the conditions set out in Article 2 of this regulation must be respected.

19. The Committee notes that phytosterol ingredients must comply with all relevant legislation, which may include the extraction solvents directive 88/344/EEC.

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