ADVISORY COMMITTEE FOR NOVEL FOODS AND PROCESSES.

UK 2002 / 002

Opinion On An Application Under The Novel Foods Regulation To Extend The Range Of Uses Of Phytosterol Esters In Food Products

Applicant:	**Unilever**
Responsible Person:	**Dr George Gordon**
Novel Food:	**Extension In The Range Of Uses Of Phytosterol Esters**
EC Classification:	**1.1**

INTRODUCTION

1. An application was submitted by Unilever to the UK Competent Authority on 6th of August 2002 for approval of phytosterol esters for use in a range of food products. A copy of the application dossier was placed on the FSA website at the same time.

2. The applicant previously submitted, via the Netherlands, a successful application under (EC) 258/97 for the same phytosterol ester component in a single product type (yellow fat spreads). Approval was granted for use of the phytosterol ester ingredient in yellow fat spreads up to a maximum of 8% (Commission Decision 2000/500/EC). The UK discussed the issue of approval extension with the Commission who were of the opinion that, as the initial approval specified incorporation into a single product, a full application made under the terms and conditions of (EC) 258/97 was required before an extension could be granted.

3. The applicant is seeking permission to extend the current product range to include milk and yoghurt products. Although these products differ from their conventional counterparts only by the addition of phytosterol esters, the applicant is aware that this fortification will contravene EU and domestic regulations and mean that the products cannot be named milk or yoghurt. The applicant will comply with the regulatory position in Member States as necessary, and for the purposes of this opinion only, the products are referred to as milk ‘type’ and yoghurt ‘type’ products.

4. The novel ingredient has already been subject to a safety assessment and granted approval up to a maximum level of use in spreads only. Therefore, the application for an extension of the product range takes into account the existing conditions of approval. Data from post launch monitoring (PLM) that shows that intake from spreads has not reached the level anticipated in the previous application. The applicant uses data from the PLM, supplemented with dietary survey data and consumer purchase data to show that an extension of the product range will not lead to an intake of phytosterols above the level previously approved.

I. Specification of the Novel Ingredient

Information on this aspect is provided on page 4 of the application dossier.

5. The novel phytosterol esters ingredient is identical to that used in the yellow fat spreads that have been previously approved under (EC) 258/97. A full description of the ingredient and specification was given in the original application which was approved in 2000.

Discussion. *The Committee was satisfied that this ingredient is identical to that previously approved under (EC) 258/97.*

II. Effect of the production process applied to the novel food

Information on this aspect is provided on page 5 of the application dossier.

6. The production methods used to produce the phytosterol esters ingredient are identical to those used to produce the ingredient used in the yellow fat spreads that have been previously approved under (EC) 258/97.

7. The milk and yoghurt to be used are standard products. Storage and distribution temperatures are as for conventional counterparts and no additional controls are considered necessary. HACCP schemes are used to control product safety and quality. The only additional process required is to control the amount and quality of the phytosterol ester added.

8. Intended levels of fortification are the same as, or less than current yellow fat spread fortification levels of 8% and are as follows:

Yoghurt	1g free phytosterols per pot (125 – 150g)
Milk	1g free phytosterols in 250ml milk

Discussion. *The Committee was satisfied that the production process is controlled and that the in-process monitoring steps are appropriate to ensure safe and consistent products.*

Production methods

Information on this aspect is provided on page 5 of the application dossier.

9. The source organisms used to produce the phytosterol esters are identical to those used in the yellow fat spreads that have been previously approved under (EC) 258/97. The phytosterols are extracted from edible oils (soya, maize, rapeseed, sunflower).

Discussion. *The Committee was satisfied that the sources of the ingredient are identical to those used in the phytosterol esters used in the yellow fat spreads previously approved under (EC) 258/97.*

III. Anticipated intake/ extent of use

Information on this aspect is provided on page 7-19 of the application dossier.

10. A condition of approval for yellow fat spreads fortified with phytosterol esters was that the applicant should carry out a post launch monitoring scheme (PLM). The purpose of this scheme was to ensure that the target population group was being reached and that exposure levels were within the maximum stipulated in the approval.

11. The results from the monitoring scheme, which have been presented to the Scientific Committee on Food indicate that the pre-market assumptions for daily intake of the yellow fat spread products, and also 95th percentile levels were significantly higher than the actual levels consumed. At the time of approval the predicted daily intake of the spread was 20-30g, whereas the PLM indicated that the daily spread intake was 15-18g.

12. The monitoring also confirms that the yellow fat spread product is reaching the target consumers (those over 45) and that intake per household remained constant irrespective of the number of people in the household, indicating that usage was predominantly by a single individual. The yellow fat spread product has a 0.1-2.5% market share and the applicant is of the opinion that as the new products are intended for the same target consumers, then there will not be any increase in the market share for each food category.

13. As pre-market assumptions regarding the target population are confirmed by the PLM data, and the daily consumption figures showed that spread intake is lower than anticipated, the applicant seeks approval to increase the product range, and can demonstrate that if the products are used as recommended on the labelling, then the intake would remain within the 2-3g free phytosterols per day range. This level of intake reflects the anticipated levels for use of yellow fat spreads containing 8% phytosterol approved in 2000.

14. In order to support this claim further, the applicant has used two types of data to predict the daily consumption of spreads, yoghurt and milk type products.

These data are based on figures available for the daily consumption of similar (unfortified) products, and the consumption of individual product types, and also consumption in combination with the others can be estimated. In addition, data showing current intake of all similar (fortified) products are also presented.

(a) Dietary Survey Data

15. These data were obtained by consumers logging their food intake over a fixed time period. The applicant accessed data for the UK and the Netherlands. Survey data for other MS were not deemed sufficiently detailed, out of date or not available to third parties.

16. As the consumption information is obtained using un-fortified products the implicit assumption that **all** spreads, yoghurts and milk consumed **are** fortified, is made. Such an assumption is likely to lead to an overestimation of phytosterol fortified products as no allowance can be made for the purchase of both phytosterol fortified and unfortified products. In addition any restrictions on consumption of the fortified product such as effective labelling would not be seen.

17. As food consumption is not normally distributed, the applicant has used the median (50^{th} percentile) and 95^{th} percentile figures as a basis for comparison. In all cases data are presented as g phytosterols/person/day.

18. *UK NDNS data (Application dossier pp 11-15).*
The highest potential intake is in the age range 65+. Median values were below 3g per day irrespective of whether 1 product or all three products were consumed. All consumers ate at least one of the product and 11% consumers all three. Consumption patterns are similar irrespective of age group and, as listed on p13 Annex 1, 95^{th} percentile data are in the range 2.16 - 3.67 for consumption of any one product, and 3.22 - 5.01 for consumption of all three.

19. *Netherlands data (Application dossier pp 11-15)*
The Dutch data are grouped according to sex, with higher potential intake by males. Median values were highest in the 46-65 age group at 4.58 (95^{th} percentile 6.63). Although the highest 95^{th} percentile value was for males aged between 6 and 16, because this group consumes the highest amounts of the unfortified products, the group is unlikely to be seeking cholesterol lowering products, and the applicant would not target products at such an age group.

(b) Consumer Purchase Data

20. The applicant has purchased consumer purchase data for all EU countries where such data are made available. No data were available for MS in Southern Europe. UK Consumer Purchase Data were obtained from AC Neilsen (Consumer Panel 2002) who collate information obtained from

households scanning barcodes after purchase.

21. As for the dietary survey, data are presented as median (50th percentile) and 95th percentile values and potential intakes of phytosterols are calculated with the same assumption that all products purchased contain phytosterol. A number of other assumptions likely to lead to an over estimation of phytosterol intake have been made. These are: All the 'milk' and 'yoghurt' products that are purchased are consumed during the 12 or 26 week period of data collection; there is no spoilage or wastage of the food that is purchased; use is also by individuals that live in the house. A further assumption, that the products are not both purchased and consumed outside the home, is an unlikely scenario, given the limited availability of the products.

22. As the data are collected at household level it is not possible to determine who is actually consuming the product, if there is more than one person in the house. However as reasonable estimates of intake can be obtained from one member households these data are used.

23. Data showing consumption for one or all three products, were consistent with the dietary survey data indicating that the highest consumption would be in the target population group. The highest estimated intake of phytosterols in the UK was for all three products and were 2.44 (median) and 5.75 (95th percentile). Similar highest consumer age ranges and intake values were calculated for France and Germany.

Consumption of existing cholesterol lowering foods

24. Although data presented to date indicate consumption levels of phytosterols based on the consumption of all milk, yoghurt and yellow fat spreads, the consumer purchase data also enabled consumption of phytosterol (Flora pro.activ) and phytostanol (Benecol range) fortified products currently on the market in the EU to be assessed. These data are particularly useful in that they deal with a small, highly relevant product range, reflecting current purchase patterns for equivalent products.

25. The information was collected over a 26 week period. As there were insufficient numbers of one member households, throughout the age range, such data have only been included for individuals within the 45-64 (50-65 Finland) and 65+ age group, although 'per household' data have also been included. In summary, median levels are not higher than 0.66g in the one member households, whilst 95th percentile values do not exceed 2g (2.75 in Finland).

26. It should be noted that these figures are significantly less than for "total" yoghurt, milk and yellow fat spread consumption and this is likely to be because non-fortified equivalent products were also purchased during this

period. Up to 90% of single member households in the target group also purchased non-fortified spreads and yoghurt.

Determination of the estimated daily intake from new product range

27. This is discussed in para 39.

Labelling

28. The current approval for phytosterols in yellow fat spreads notes that they are not nutritionally appropriate for certain individuals such as infants and lactating or pregnant mothers.

29. In view of the need for clear and unambiguous labelling which must be maintained if the product range is increased, the applicant has sought to clarify the labelling of products in terms of recommended daily intake, and the amount of individual products that can be consumed. The applicant will also include a statement to the effect that extra servings will not provide any additional cholesterol lowering benefit.

30. In response to a large number of applications under (EC) 258/97 for approval of phytosterol ingredients in a range of food products, the SCF are currently considering the issue of elevated levels of phytosterols from multiple dietary sources. The use of appropriate labelling may be considered as a means of avoiding excess daily consumption and the applicant has indicated that the new product range will be covered by a comprehensive labelling regime. Furthermore the applicant has indicated a willingness to amend their application in response to the SCF discussions.

Discussion. *The Committee was content that the PLM data showed that consumption levels for fortified yellow fat spreads was lower than anticipated. The Committee reviewed the data obtained from the dietary surveys and was content that the increase in the product range would not lead to consumption of phytosterols at levels greater than those approved previously.*

The Committee expressed concerns that although present levels of phytosterol consumption are currently limited by a small product range, as more fortified product become available the potential for over consumption increases and any clearance should reflect any decisions made by the European Commission.

The Committee also sought reassurance that the any labelling for additional product types should not only inform the consumer of the recommended number of daily servings, but should also make the consumer aware that there are a range of similar products on the market, including those from other manufacturers.

IV. Information on Previous Exposure

Information on this aspect is provided on page 20 of the application dossier

31. Although there has been no exposure to phytosterol esters in 'milk' and 'yoghurt' products, the ingredient has been consumed in yellow fat spreads and there is low level consumption of 'free' phytosterols in a normal diet. Individuals have had significant exposure to phytostanol esters (hydrogenated phytosterols) in a range of products including 'milk' and 'yoghurt' products.

Discussion *The Committee accepted that the novel ingredient has been consumed previously and that there were low levels of phytosterols in a normal healthy diet.*

V. Nutritional Aspects

Information on this aspect is provided on page 21 of the application dossier

32. The ability of phytosterols to reduce cholesterol absorption is well documented.

33. Data submitted by Unilever for the original approval have been considered previously, and the applicant commissioned research that addresses specific issues raised by the SCF. These include the PLM and the effect of consumption of phytosterols in conjunction with cholesterol lowering drugs. Studies have also looked at the effectiveness of phytosterols in children with familial hypercholesterolaemia. Research in both areas indicated the beneficial effect of phytosterols although the applicant does not intend to market the product to either group.

34. The cholesterol lowering effect of phytosterols is not influenced by the food matrix. The applicant has summarised research that shows that yoghurts and milk fortified with phytosterols, were as efficacious in the reduction of LDL-cholesterol as other foods containing this ingredient.

Effect on carotenoids

35. Studies indicate that the consumption of phytosterols can lead to modest reduction in carotenoids, particularly the most lipophilic carotenoids such as ß-carotene. The applicant has updated studies in this field. Given that this application does not seek to increase the amount of phytosterols in the diet beyond that originally approved, the previous risk assessment conclusions from the SCF in response to the original application are still appropriate.

Discussion *The Committee was content that the fortification of foods with phytosterols to help reduce cholesterol absorption is well recognised, provided appropriate labelling is included on the products indicating that they are not considered appropriate for certain subgroups of the population and that no new safety issues will be raised by the extension of this product range.*

The Committee agreed that there was no effect of the food matrices on the effectiveness of the ingredient.

VI. Microbiological Information

Information on this aspect is provided on page 24 of the application dossier

36. The microbiological stability of the 'milk' and 'yoghurt' products containing phytosterol-esters is governed by the same principles as conventional products.

37. The accepted principles of Good Manufacturing Practice used for conventional milk and yoghurt will be used to control quality and safety during manufacture.

Discussion *The Committee was content with the information supplied by the applicant and considered the production process, the quality control measures and the nature of the final product to be sufficient to ensure no unintentional microbiological contamination of the products*

VIII Toxicological Aspects

38. There is a history of safe consumption for phytosterols within the normal dietary intake of 200-400mg/day. Given that the use of phytosterol esters in yellow fat spreads would lead to a 5-10 fold increase, a thorough toxicological examination of the product was carried out. Based on this assessment the SCF set the limit of fortification at 8% in yellow fat spreads. The toxicological examination of the novel ingredient did not identify any adverse health effects up to the maximum dose levels it was possible to test, and human trials involving large daily intakes of phytosterols have not reported any adverse health effects.

Determination of the estimated daily intake

39. The Joint FAO/WHO Expert Committee on Food Additives, (JECFA) NOAEL Safety Factor for free phytosterols is 137mg/kg/day, equivalent to 9.6g/person/day for a 70kg adult, although this is a conservative estimate as an effect level could not be established. The applicant notes that if the products are used as recommended on the labelling then the intake will not exceed 2-3g free phytosterols per day. The applicant also estimated the highest intake levels if the labelling is ignored and all three fortified products are consumed. These data (irrespective of source) list the highest potential daily consumption for each country. The highest UK consumption is 2.7g/5.8g (median/95th percentile), (age group 45-64).

40. The applicant will extend their Post Launch Monitoring to take account of consumption of all fortified products by the target groups, to assess levels of phytosterol consumption and monitor any potential adverse health events.

Discussion *The Committee was content that providing the levels of fortification did not exceed those stipulated in the original approval, there were no specific toxicological issues that had not been covered in the previous approval.*
The Committee agreed that if the products were labelled as described in the application dossier no new toxicological issues would arise.
The Committee agreed that it would discuss consumption of phytosterols from multiple sources in the light of the views expressed by the Scientific Committee on Foods.

OVERALL DISCUSSION

41. This applicant company is seeking to extend their product range of phytosterol fortified products. Currently they have approval for a single product, yellow fat spreads. This product was approved under (EC) 258/97 in 2000 and they wish to extend the range to include two further product types. Phytosterol esters in yellow fat spreads have already been approved and the product specification data, and the production process are unchanged. Although the intention is to add the phytosterol esters to different products, the current production processes are well monitored, with quality control and safety measures in place. The products are manufactured using a standard method, which has been shown to be reliable and reproducible, the only additional process is to control the amount and quality of phytosterol esters added.

42. No nutritional, toxicological or microbial safety concerns have been raised. Phytosterols are already present in human diets, occurring naturally in foods at low levels and in fortified yellow fat spreads.

43. No issues were raised regarding the anticipated intake and extent of use as sufficient data were provided to demonstrate that an increase in the product range would not lead to an increase in the consumption of phytosterols beyond those previously approved.

44. If the product extension is approved, the Applicant Company will impose strict labelling criteria on the entire product range. These will clearly define the daily servings required to affect a reduction in cholesterol and will also state that consumption in excess of the recommended number of daily servings daily servings will not provide additional cholesterol lowering benefit. The Committee previously expressed their concerns regarding the over consumption of phytosterol fortified products when they have been asked to comment on previous applications made under (EC) 258/97. The Committee agreed that the issue of over consumption should take into account all products currently on the market, and those awaiting clearance under (EC) 258/97 and should be dealt with by the Commission. Members also

acknowledged that the Scientific Committee for Foods had drafted a report entitled “View on the long term effects of the intake of elevated levels of phytosterols from multiple dietary sources”. The company has stated that they will act in accordance with any decisions made by the Commission in the light of this SCF report.

45. In view of the concerns of over consumption, and the stipulated requirement for PLM in the previous approval for the fortified yellow fat spreads the company are willing to undertake a similar exercise if approval for the extension of product range is given. The Committee recommends that any approval for this extension in the product range is subject to a requirement for further PLM.

CONCLUSION

The Advisory Committee on Novel Foods and Processes is satisfied by the evidence provided by Unilever that the extension of the range of uses of phytosterol esters as described in the application dossier is acceptable, subject to the labelling and PLM requirements described above.

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