Fytosterolen (3)

Tweede beoordeling van de veiligheid voor de consument, volgens de Europese verordening 258/97 betreffende nieuwe voedingsmiddelen en nieuwe voedselingrediënten

Phytosterols (3)

Second opinion regarding consumer safety, in accordance with European Regulation 258/97 concerning novel foods and novel food ingredients

Gezondheidsraad:
Commissie Veiligheidsbeoordeling nieuwe voedingsmiddelen (VNV)

Health Council of the Netherlands:
Committee on the Safety Assessment of Novel Foods

aan/to:

de Minister van Volksgezondheid, Welzijn en Sport/
the Minister of Health, Welfare and Sport

de Minister van Landbouw, Natuurbeheer en Visserij/
the Minister of Agriculture, Nature management and Fisheries

Nr. 2003/01VNV, Den Haag, 13 februari 2003
No. 2003/01VNV, The Hague, February 13, 2003

De Gezondheidsraad, ingesteld in 1902, is een adviesorgaan met als taak de regering en het parlement “voor te lichten over de stand der wetenschap ten aanzien van vraagstukken op het gebied van de volksgezondheid” (art. 21 Gezondheidswet).

De Gezondheidsraad ontvangt de meeste adviesaanvragen van de bewindslieden van Volksgezondheid, Welzijn & Sport; Volkshuisvesting, Ruimtelijke Ordening & Milieubeheer; Sociale Zaken & Werkgelegenheid en Landbouw, Natuurbeheer & Visserij. De Raad kan ook eigener beweging adviezen uitbrengen. Het gaat dan als regel om het signaleren van ontwikkelingen of trends die van belang kunnen zijn voor het overheidsbeleid.

De adviezen van de Gezondheidsraad zijn openbaar en worden in bijna alle gevallen opgesteld door multidisciplinair samengestelde commissies van - op persoonlijke titel benoemde - Nederlandse en soms buitenlandse deskundigen.

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect tot public health issues” (Section 21, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport; Housing, Spatial Planning & the Environment; Social Affairs & Employment, and Agriculture, Nature management & Fisheries. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

Deze publicatie kan als volgt worden aangehaald:
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Uw kenmerk : VGB/VL 2345876
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Datum : 13 februari 2003

Mijnheer de minister,

Dit schrijven dient ter beantwoording van de adviesaanvraag over de veiligheid van nieuwe voedingsmiddelen en nieuwe voedselingrediënten, die door u mede namens de Minister van Landbouw, Natuurbeheer en Visserij aan de Gezondheidsraad is voorgelegd. Aan de orde is een zogenoemde tweede beoordeling, conform de Europese verordening 258/97, van het gebruik van fytosterolesters in verschillende voedingsmiddelen. Het ingrediënt zelf is niet nieuw. De aanvrager, de firma Unilever, wil het assortiment van producten waaraan fytosterolesters mogen worden toegevoegd uitbreiden naar producten op basis van yoghurt en melk. Met melk worden in deze aanvraag, naast magere en halfvolle melk, ook melkvarianten op basis van plantaardige olie bedoeld. Uit markmonitoringsgegevens heeft de aanvrager vastgesteld dat consumptie van de al in de handel zijnde fytosterolester-houdende vetsmeersels beduidend minder is dan voorafgaande aan de markttoelating was ingeschat. Dit ziet Unilever als rechtvaardiging voor verbreden van het assortiment. De beoordeling is verricht door de Commissie 'Veiligheidsbeoordeling nieuwe voedingsmiddelen' van de Gezondheidsraad (Commissie VNV).

De eerste beoordeling van de aanvraag voor markttoelating is verricht in het Verenigd Koninkrijk door het *Advisory Committee on Novel Foods and Processes* (ACNFP) van de Engelse assortiment producten verrijkt met fytosterolesters, zoals beschreven in het veiligheidsdossier, voedselautoriteit *Food Standard Agency*. De ACNFP concludeert dat uitbreiding van het toelaatbaar is op voorwaarde dat de aanvrager zich houdt aan de afspraken over etikettering en de marktmonitoring zal voortzetten.

De Commissie VNV baseert haar oordeel op het rapport van de eerste beoordeling door de ACNFP en op de informatie in het dossier. Ook heeft zij de rapporten van het Wetenschappelijk Comité voor de menselijke voeding die recent zijn verschenen over verhoogde inneming van

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fytosterolen hierbij in beschouwing genomen (SCF02, SCF02a). De commissie beoordeelde zelf al eerder de veiligheid van fytosterolen en fytosterolesters (GR01a) en fytostanolesters* (GR99). De Commissie VNV is het grotendeels eens met de ACNFP dat consumptie van fytosterol-houdende melk- en yoghurtachtige producten veilig is in de hoeveelheden die de aanvrager voorstelt, ook in combinatie met consumptie van fytosterolverrijkte vetsmeersels.

In de eerdere rapporten heeft de Commissie VNV gepleit tegen uitbreiding van het productassortiment. De resultaten van de marktmonitoring die door de aanvrager is uitgevoerd maken echter voldoende aannemelijk dat de huidige consumptie van fytosterolen verwerkt in vetsmeersels achterblijft bij de verwachting. Door consumptie van andere producten met toegevoegde fytosterolen kan de totale dagelijkse fytosterolenconsumptie toenemen tot het niveau van inneming waarvoor in 2000 reeds toestemming is verleend door de Europese Commissie (Beschikking 2000/500/EG).

Aanvullend op de eerste beoordeling constateert de Commissie VNV dat het niet duidelijk is hoeveel verschillende zuivelachtige producten met toegevoegde fytosterolen de aanvrager op de markt wil brengen. De commissie pleit er voor dat het totale productassortiment voldoende beperkt blijft om de fytosterolinneming te kunnen beteugelen. Zij stelt dat assortimentsverbreding alleen toelaatbaar is onder voorbehoud dat er garanties moeten zijn dat consumptie tot de doelgroep beperkt blijft. Te meer daar bepaalde zuivelachtige dranken mogelijk ook andere bevolkingsgroepen dan de doelgroep aanspreken. Alhoewel het niet aan de commissie VNV is definitief te besluiten welke producten wel en niet voor verrijking met fytosterolen in aanmerking komen, beschouwt zij het als noodzakelijk dat hierover in Europees verband regie wordt gevoerd (zie ook hieronder).

De Commissie VNV brengt onder de aandacht dat waarschijnlijk een deel van de cholesterol-bewuste consumenten geneigd is meer dan de aanbevolen hoeveelheid van fytosterolverrijkte producten te gaan gebruiken. Om ongewenst hoge innemingen te voorkomen (stapeling) is naast beperking van productassortiment strikte etikettering noodzakelijk. De commissie is het eens met de ACNFP dat de toelating van deze aanvraag, en daarmee samenhangend de etiketteringsvoorschriften, niet los kan worden gezien van de andere aanvragen voor

* Fytosterol is de bioactieve component van de fytosterolester. Aan fytosterolen verwante verbindingen zijn de fytostanolen ('verzadigde fytosterolen') met een vergelijkbare cholesterolverlagende werking

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Gezondheidsraad Vice-voorzitter
Health Council of the Netherlands

Onderwerp : Tweede beoordeling veiligheid Fytosterolen (3)
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markttoelating van allerlei producten met fytosterolen en vergelijkbare verbindingen, die nu worden beoordeeld op Europees niveau door het Wetenschappelijk Comité voor de menselijke voeding (SCF02b). Niet alleen de Commissie VNV (GR01, GR01a), ook het Europese Wetenschappelijk Comité heeft geconcludeerd dat er meer onderzoek nodig is naar mogelijke langetermijneffecten van inneming van toegevoegde fytosterolen (SCF02a).

Ten overvloede merkt de Commissie VNV op dat de veilige bovengrens van dagelijkse fytosterolinneming, die in het dossier wordt vermeld, verwijst naar de waarde die de aanvrager zelf heeft afgeleid op basis van subchronisch toxicologisch onderzoek bij ratten. Deze is niet afkomstig van evaluaties door de *Joint FAO/WHO Expert Committee on Food Additives* zoals de ACNFP stelt. Volgens de Commissie VNV en het Europese Wetenschappelijk Comité voor de menselijke voeding kan er op basis van het huidige totaal aan beschikbare gegevens nog geen veilige bovengrens worden afgeleid voor levenslange, dagelijkse fytosterolinneming (SCF02a).

Ik onderschrijf de conclusies en aanbevelingen van de Commissie VNV.

Hoogachtend,

prof. dr JGAJ Hautvast

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Letter to the Dutch Minister of Health, Welfare and Sport

On Februari 13, 2003, professor JGAJ Hautvast, Vice-president of the Health Council of the Netherlands wrote as follows to the Minister of Health, Welfare and Sport:

This letter has been prepared in reply to your request for advice regarding the safety of novel foods and food ingredients, also made on behalf of the Minister of Agriculture, Nature Management and Fisheries. The subject in question is a second opinion, in accordance with European Regulation 258/97, concerning the use of phytosterol esters in a range of food products. The ingredient itself is not novel. The applicant, the company Unilever, would like to extend the range of products which are permitted to contain added phytosterol esters, to include yoghurt and milk. The milk type products referred to in the application include skimmed and semi-skimmed milk, as well as vegetable-oil-based milk variants. The applicant concludes from post launch monitoring results that consumption of the phytosterol-fortified yellow fat spreads already available on the market is considerably lower than the level of consumption assumed in the original Novel Foods submission. Unilever regards this as a justification for broadening the range of phytosterol-fortified products. This assessment has been carried out by the Committee on Safety Assessment of Novel Foods (VNV Committee) of the Health Council of the Netherlands.

The initial assessment of the application for market introduction was carried out in the United Kingdom by the Advisory Committee on Novel Foods and Processes (ACNFP) of the Food Standards Agency. The ACNFP concludes that it is acceptable to extend the range of uses of phytosterols as described in the application dossier. Any

approval should, however, be subject to a requirement for further post launch monitoring and labelling measures.

The VNV Committee bases its findings on the report of the initial assessment by the ACNFP and on the information contained in the dossier. In addition to this, it has also considered the recently published reports by the Scientific Committee on Food which examine increased intake of phytosterols (SCF02, SCF02a). The VNV Committee itself has previously assessed the safety of phytosterols and phytosterol esters (GR01a), and of phytostanol esters* (GR99). The Committee largely agrees with the British assessment that it is safe to consume phytosterol-fortified milk and yoghurt type products in the amounts proposed by the applicant, also when combined with an intake of yellow fat spreads with added phytosterols.

In its previous reports, the VNV Committee objected to extension of the product range. However, the post launch monitoring results presented by the applicant provide sufficient evidence that the actual consumption of phytosterols incorporated in fat spreads does fall short of expectations. By using other products with added phytosterols, consumers can increase their total daily phytosterol intake to the level of intake already approved in 2000 by the European Commission (Decision 2000/500/EC).

In addition to the first assessment, the Committee notes that it is not clear how many different fortified dairy products the applicant intends to introduce on the market. The Committee advices that sufficient restrictions should be imposed on the total range of products with a view to curbing phytosterol intake. It concludes that extension of the product range is only acceptable provided that there will be guarantees that consumption remains confined to the target group, especially since certain dairy drinks may also appeal to individuals outside the target group. Although it is not the VNV Committee's task to decide which products are suitable for fortification with phytosterols, it does regard European regulation of this issue as essential (see also below).

The Committee would also like to point out the likelihood that some cholesterol-conscious consumers will tend to exceed the recommended amount of phytosterol-fortified products. Apart from limits on the product range, strict labelling is also required to prevent cumulative intakes from different products. The Committee agrees with the ACNFP that approval of this application, and the attendant labelling requirements, cannot be considered independently of the other applications for admission to the market of various products with added phytosterols and related compounds, currently being assessed at European level by the Scientific Committee on Food (SCF02b). Both the VNV Committee (GR01, GR01a) and this European Scientific

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* Phytosterol is the bioactive component of the phytosterol ester. Compounds related to phytosterols are the phytostanols, which are 'saturated phytosterols', having similar cholesterol-lowering effects.

Committee have reached the conclusion that additional research is needed to evaluate the possible effects of long-term exposure to elevated levels of phytosterols (SCF02a).

Finally, the Committee would like to point out that the safe upper daily intake level of phytosterol stated in the dossier refers to the value that has been deduced by the applicant itself, based on sub-chronic toxicological studies in rats. This value does not come from evaluations of exposure to phytosterols conducted by the Joint FAO/WHO Expert Committee on Food Additives, as the ACNFP suggests. The VNV Committee and the European Scientific Committee on Food agree that the sum of the available data does not yet provide a basis for determining a safe upper level of lifelong daily phytosterol intake.

I endorse the conclusions and recommendations of the VNV Committee,

(signed) professor JGAJ Hautvast

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SCF02a General view of the Scientific Committee on Food on the long-term effects of elevated levels of phytosterols from multi dietary sources, with particular attention to the effects on β-carotene (opinion expressed on 26 september 2002). Brussels, Scientific Committee on Food of the EU, 2002.

SCF02b Minutes' statement of the Scientific Committee on Food on applications for approval of a variety of plant sterol-enriched foods (expressed on 4 December 2002). http://europa.eu.int/comm/food/fs/sc/scf/out152_en.pdf

SSC99 Opinion of the Scientific Steering Committee on microbial resistance, Brussels, Scientific Steering Committee of the EU 1999.

WHO91 Strategies for assessing the safety of foods produced by biotechnology. Report of a joint FAO/WHO Consultation. Geneva, WHO 1991.

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A	De adviesaanvraag/Request for advice
B	De commissie/The committee
C	EU-procedure/EU-procedure
D	Samenvatting van het dossier/Executive summary of the dossier
E	Eerste beoordeling/First assessment

Bijlagen/Annexes

Bijlage **A**

De Adviesaanvraag/Request for advice

Op 18 augustus 1999 schreef de Minister van Volksgezondheid, Welzijn en Sport aan de Voorzitter van de Gezondheidsraad (brief kenmerk GZB/VVB 993428):

Sinds mei 1997 is in de Europese Unie de Verordening (EG) 258/97 van kracht inzake nieuwe voedingsmiddelen en nieuwe voedselingrediënten. Daarmee werd de veiligheidsbeoordeling onderdeel van een communautaire procedure.

Met u is reeds de mogelijkheid besproken de beoordeling door de Gezondheidsraad te laten uitvoeren. Ik verzoek u dan ook mede namens de Staatssecretaris van Landbouw, Natuurbeheer en Visserij, in deze eerste fase van uitvoering van de Europese Verordening (EG) 258/97 gedurende een aantal jaren, de veiligheidsbeoordeling gestalte te geven. Voor het onderbrengen bij de Gezondheidsraad pleit het experimentele karakter dat de beoordeling de eerste jaren zal hebben. Dit experimentele karakter komt voort uit het feit dat het een nieuw soort beoordeling betreft van deels nieuwe categorieën van voedingsmiddelen of voedselingrediënten. Het is namelijk een veiligheidsbeoordeling vóór het op de markt brengen van met name voedingsmiddelen van een genetisch gemodificeerde oorsprong en zogenaamd functional foods (nutriceutica). Daarnaast ga ik ervan uit dat de onafhankelijke wetenschappelijke advisering door de Gezondheidsraad het vertrouwen van de Europese Commissie en de andere lidstaten in het Nederlandse oordeel nog versterkt.

Mijn beleid is erop gericht een zo groot mogelijke openheid en transparantie te realiseren van de gevolgde procedure en de beoordeling om de consument vertrouwen te geven in de veiligheid van de

nieuwe voedingsmiddelen. Ik verzoek de Gezondheidsraad hieraan bij te dragen door bijvoorbeeld inzage te geven in de dossiers waarvoor een aanvraag wordt ingediend, waarbij uiteraard bedrijfsvertrouwelijke gegevens worden beschermd en door de criteria, waarop de veiligheid zal worden beoordeeld, te publiceren.

De Minister van Volksgezondheid, Welzijn en Sport,
w.g. dr E Borst-Eilers

English translation

On 18 August 1999, the Minister of Health, Welfare and Sport wrote as follows to the President of the Health Council of the Netherlands (under reference GZB/VVB 993428):

Since May 1997, Regulation (EC) 258/97 concerning novel foods and novel food ingredients has been in force in the European Union. Under the Regulation, the safety of novel foods has to be assessed as part of a community procedure.

Following discussions regarding the possibility of the Health Council making such assessments, the State Secretary for Agriculture, Nature Management and Fisheries and I wish the Council to take responsibility for safety assessment for a period of several years during the fist phase of implementation of European Regulation (EC) 258/97. It is considered appropriate that the Health Council should initially take on this role because the assessment activities will be of an experimental nature, involving both a new form of assessment (i.e. pre-marketing assessment) and, in many cases, new categories of foodstuff (primarily foodstuffs with a genetically modified basis and functional foods or nutraceuticals). We also feel that if assessments are made by a body with the Council's independent scientific status, this will support the validity of the Netherlands' opinion in the eyes of the European Committee and other member states.

My wish is to make the procedure and the assessment as open and transparent as possible, so as to enhance consumer trust in the safety of novel foods. I would like the Health Council to support this objective by, for example, allowing perusal of the application dossier (insofar as consistent with the need to protect the confidentiality of commercially sensitive information) and publishing the criteria upon which safety assessments are made.

The Minister of Health, Welfare and Sport,
(signed) dr E Borst-Eilers

Bijlage **B**

De commissie/The committee

- Prof. dr LM Schoonhoven, *voorzitter/chairman*
  emeritus hoogleraar entomologie; Wageningen Universiteit en Researchcentrum/
  emeritus professor of entomology; Wageningen University and Research centre
- Prof. dr CAFM Bruijnzeel-Koomen
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  professor of dermatology/allergology; Academic Hospital Utrecht
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- Dr JMA van Raaij
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- Ir R Top, *adviseur/advisor*
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  Ministry of Health, Welfare and Sport; The Hague
- Prof. dr WM de Vos
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  Committee on Genetic Modification, The Hague
- Dr RA Woutersen
  toxicoloog; TNO Voeding, Zeist/
  toxicologist; TNO Nutrition and Food Research, Zeist
- Dr ir M Rutgers, *secretaris/scientific staff member*
  Gezondheidsraad, Den Haag/
  Health Council of the Netherlands, The Hague

Administratieve ondersteuning/Administrative assistance: CL Vuijst; Gezondheidsraad, Den Haag/Health Council of the Netherlands, The Hague.
Lay-out: J van Kan; Gezondheidsraad, Den Haag/Health Council of the Netherlands, The Hague.

Bijlage **C**

EU-procedure/EU-procedure

Als een fabrikant een nieuw voedingsmiddel op de markt brengt, dient de veiligheid voor de consument gewaarborgd te zijn. In 1997 werd de Europese verordening van kracht waarin de procedure is geregeld voor de goedkeuring voor marktintroductie van een nieuw voedingsmiddel (EG97). Bij deze procedure zijn verschillende actoren betrokken. De aanvrager moet beoordelen of het product werkelijk 'nieuw' is, dat wil zeggen dat het nog niet eerder in de Europese Unie in substantiële mate voor menselijke voeding is gebruikt en ook niet wezenlijk gelijkwaardig is aan een bestaand product. (Voor een wezenlijk gelijkwaardig product kan worden volstaan met een kennisgeving van de marktintroductie.) Ook moet het niet gaan om een levensmiddelenadditief, aroma of extractiemiddel, omdat deze producten op een andere wijze worden beoordeeld. Voor een nieuw voedingsmiddel in de zin van de Europese verordening moet de aanvrager een veiligheidsdossier overleggen volgens aanbevelingen van de Europese Commissie (EG97a). Deze aanbevelingen zijn gebaseerd op rapporten van verschillende instanties die zich met het onderwerp nieuwe voedingsmiddelen bezighouden, te weten de OECD (OECD93, OECD96) en de WHO/FAO (FAO96, WHO91). Ook de Gezondheidsraad heeft zich al eerder over dit onderwerp gebogen (GR92). Sinds het verschijnen van de aanbevelingen van de EU wordt in internationaal verband gewerkt aan explicitering en aanpassing aan de stand van de wetenschap (FAO01, OECD98, OECD00, SCF99, SSC99, WHO00).

De fabrikant levert het volgens de richtlijnen samengestelde dossier in bij het land waar het product het eerst op de markt zal komen. Daarop komt de nationale veiligheidsbeoordelingsautoriteit in actie. In Nederland is dat de Minister van

Volksgezondheid, Welzijn en Sport. Zij heeft de Gezondheidsraad verzocht haar van advies te dienen. De Voorzitter van de Gezondheidsraad heeft hiertoe de commissie Veiligheidsbeoordeling nieuwe voedingsmiddelen (commissie VNV) ingesteld.

De commissie beoordeelt op basis van de huidige stand van de wetenschap of de door de fabrikant geleverde gegevens juist en volledig zijn en of zij het eens is met diens conclusies. Zij maakt een verslag van haar bevindingen — ook volgens de Europese aanbevelingen (EG97a, deel III) — en biedt dat de minister aan. De minister formuleert het Nederlandse oordeel over een voedingsmiddel en brengt dat in bij het Europese overleg in het Permanent Comité voor levensmiddelen. Alle Europese lidstaten worden uitgenodigd hun oordeel (de zogeheten tweede beoordeling) te geven over het dossier en over de eerste beoordeling alvorens genoemd Comité een eindoordeel velt. Als een dossier veel vragen oproept, gaat er een adviesvraag van de Europese Commissie naar het Wetenschappelijk Comité voor de menselijke voeding. Komt men dan nog niet tot overeenstemming dan beslist de Europese Ministerraad.

English translation

When manufacturers bring novel foodstuffs onto the market, consumer safety has to be ensured. In 1997, a European Regulation (EG97) came into force, laying down the procedure for approving the market introduction of novel foodstuffs. The procedure recognizes various actors. The applicant must decide whether a product is a novel foodstuff, i.e. a substance that has not previously been available for human consumption to any substantial extent within the European Union and is not substantially equivalent to any existing product. (If a foodstuff is substantially equivalent to any existing product, it is sufficient to inform the authorities of its market introduction). Food additives, aromas and extracts are excluded from the provisions of the directive, since they fall within the scope of an established assessment regime. Before marketing a novel foodstuff, the applicant must compile a safety dossier that complies with the Recommendations of the European Commission (EG97a). These Recommendations are based on reports by a number of bodies that have studied the issue of novel foodstuffs, in particular the OECD (OECD93, OECD96) and the WHO/FAO (FAO96, WHO91). The Health Council of the Netherlands has also considered the question earlier (GR92). Since publication of the EU recommendations, international efforts have been made to clarify and adapt the latest scientific knowledge in the field (FAO01, OECD98, OECD00, SCF99, SSC99, WHO00).

Having compiled a dossier in line with the guidelines, the manufacturer has to submit it to the competent authority in the country where the product is to be marketed first. This dossier is assessed by the national safety assessment authority. In the Netherlands, this is the Minister of Health, Welfare and Sport, who is advised by the

Health Council. The President of the Health Council has created a Committee on the Safety Assessment of Novel Foods (VNV Committee) to advise the minister on behalf of the Council.

On the basis of the scientific state of the art, the committee has to decide whether the information provided by the manufacturer is accurate and complete and whether the manufacturer's conclusions are sound. The committee then draws up a report on its findings for the minister; this report must also comply with the European Recommendation (EG97a, part III). After considering the report, the minister formulates the Netherlands' opinion regarding the foodstuff in question, which is discussed at European level in the Standing Committee on Foodstuffs. All other European member states are invited to express a 'second opinion' regarding the dossier and the first opinion. The Standing Committee then arrives at a final judgement. If a dossier is particularly contentious, the European Commission calls upon the Scientific Committee on Food for advice. If consensus still cannot be reached, the issue is referred to the European Council of Ministers.

Bijlage **D**

Samenvatting van het dossier/ Executive summary of the dossier

PHYTOSTEROL-ESTERS:

USE IN A RANGE OF FOOD PRODUCTS

SUMMARY

AUTHOR: LINDA LEA

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Date : July 2002
Document reference: D02-027

SEAC

PHYTOSTEROL-ESTERS:

USE IN A RANGE OF FOOD PRODUCTS

CONTENTS

1. ADMINISTRATIVE DATA

Applicant:	Unilever Plc Unilever House Blackfriars London EC4P 4BQ
Manufacturer:	Unilever Bestfoods UK Limited Brooke House Manor Royal Crawley RH10 2RQ
Person responsible for the dossier:	Linda Lea Safety and Environmental Assurance Centre Unilever Colworth Sharnbrook Bedfordshire MK44 1LQ UK Tel: 0044 1234 264746 Fax: 0044 1234 264711

2. APPLICATION

This application seeks approval for the use of phytosterol-esters to be included as a cholesterol-lowering ingredient in 'milk' and 'yoghurt' type products. This is in addition to the approved use in Yellow Fat Spreads.

The 'milk' type products would include skimmed, semi-skimmed and vegetable oil based milk variants. The 'yoghurt' type products would include a range of natural and fruit flavoured yoghurts. It is understood that, under EU milk legislation (EC Directive 95/2) and the varying national legislation across member states covering yoghurt, the addition of phytosterol-esters, and other ingredients required to stabilise the products, will prevent the use of the term 'milk' and 'yoghurt', to describe these Novel Foods.

Phytosterol-esters are considered to be the Novel Food Ingredient and the 'milk' and 'yoghurt' type products with added phytosterols-esters the Novel Foods.

3. IDENTIFICATION OF ESSENTIAL INFORMATION REQUIREMENTS

The structured scheme (Table II, Part I under EC Regulation No. 258/97) has been followed to determine which of schemes I-XIII are essential to provide data permitting a safety and nutritional evaluation of the Novel Food Ingredient.

With phytosterol-esters falling into Class 1.1 the following information should be provided:

I. Specification of the Novel Food
II. Effect of the production process applied to the Novel Food
III. History of the organism used as the source of the Novel Food
IX. Anticipated intake/extent of use of the Novel Food
X. Information from previous human exposure to the Novel Food or its source
XI. Nutritional information on the Novel Food
XII. Microbiological information on the Novel Food
XIII. Toxicological information on the Novel Food

This information is provided in document D02-018 'Phytosterol-esters: use in a range of food products'. Where appropriate, reference has been made in D02-018 to Unilever's previous application for the use of phytosterol-esters in Yellow Fat Spreads which was approved under Regulation (EC) No 258/97 in European Commission Decision 2000/500/EC of 24 July 2000.

4. SUMMARY

Under Regulation (EC) No 258/97 on Novel Foods and Food Ingredients, Unilever received approval for the use of phytosterol-esters as a novel food ingredient in Yellow Fat Spreads in European Commission Decision 2000/500/EC of 24 July 2000 (EC, 2000). Under Article 3 of this decision, Unilever was required to establish a surveillance programme to accompany the marketing of the product. The results of this surveillance programme, referred to as Post Launch Monitoring, showed that intakes of the spread were lower than that assumed in the Novel Foods submission with no evidence of adverse health effects.

This indicates that there is an opportunity to offer consumers alternative or additional healthy foods to deliver optimal cholesterol-lowering benefits without increasing the intake of phytosterols above the level already approved. This application seeks approval for the use of phytosterol-esters to be included as a cholesterol-lowering ingredient in 'milk' and 'yoghurt' type products. This is in addition to the approved use in Yellow Fat Spreads.

The phytosterol-esters to be used in the 'milk' and 'yoghurt' type products are identical to those currently used in Yellow Fat Spreads. The 'milk' and 'yoghurt' type products containing phytosterol-esters have been tested for their microbiological and chemical stability over time, including the impact of pasteurisation, and these have been found to be similar to standard products.

The phytosterol-esters will be added to the product such that a 250ml serving of the 'milk' type product will provide 1g of free phytosterols. The 'yoghurt' type product will be produced in individual serving pots with phytosterol-esters added such that each individual pot provides 1g free phytosterols. The recommended intake will be 2-3g free phytosterols/day.

The cholesterol-lowering effect of phytosterol-esters has been demonstrated in various food types including 'milk' and 'yoghurt' type products. The effect is comparable to that seen with Yellow Fat Spreads.

The range of products will be labelled with clear instructions on how to eat an appropriate amount of the spreads, 'milk' or 'yoghurt' type products to obtain an average of 2-3g of free phytosterols per day to optimise cholesterol-lowering benefits. Consumers will also be informed that consuming higher amounts will not provide any significant additional cholesterol-lowering benefit. Labelling will continue to include the information from the original approval indicating target consumers, lack of suitability for children, pregnant and lactating women and advice to those receiving cholesterol-lowering medication. This will be adapted, if necessary, in line with the Scientific Committee on Foods current deliberations on multiple intakes of phytosterol products.

If consumers use the product as recommended on the labelling then it is anticipated that the intake will be 2-3g of free phytosterols per day. This level of intake does not exceed that originally expected from the use of Yellow Fat Spreads containing 8% phytosterol-esters approved by the EC.

There is no evidence to suggest that consumers will not follow the labelling advice regarding recommended intakes, particularly as this states that there is no additional cholesterol-lowering benefit from eating more than the recommended 2-3g free phytosterols/day. However, should consumers not follow the labelling advice then the potential daily intake of phytosterols has been modelled based on the consumption patterns of unfortified products. This has been done using both intake data from dietary surveys and consumer purchase data. This shows that even if consumers do replace all spread, 'milk' and 'yoghurt' type product intake with phytosterol-ester products the potential daily intake of phytosterol-esters is still within the range of intakes considered in the original risk assessment and does not raise any toxicological concerns.

However, it is highly unlikely that consumers will replace all intakes of spread, 'milk' and 'yoghurt' type products by the equivalent phytosterol-ester products in this way. Post Launch Monitoring data and studies of consumer purchase data of phytostanol-ester products in Finland and the UK indicates that intakes of cholesterol-lowering foods are lower than those of the unfortified counterparts. This is confirmed by UK consumer purchase data that indicates that consumers who buy phytosterol/stanol-ester products also buy unfortified products.

In conclusion, this application demonstrates that extension of the range of phytosterol-ester products available in the EU to include 'milk' and 'yoghurt' type products in addition to Yellow Fat Spreads will not lead to over-consumption of phytosterols resulting in adverse public health effects.

Bijlage **E**

Eerste beoordeling/First assessment

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.*

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.

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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.

November 2002