Phytosterols (2)

Fytosterols (2)

Assessment of safety for the consumer, in accordance with European Regulation 258/97 concerning novel foods and food ingredients
Beoordeling van de veiligheid voor de consument, volgens de Europese verordenig 258/97 betreffende nieuwe voedingsmiddelen en nieuwe voedselingrediënten

Letter to the Dutch Minister of Health, Welfare and Sport

On December 13, 2001, professor JA Knottnerus, President of the Health Council of the Netherlands wrote as follows to the Minister of Health, Welfare and Sport:

Herewith I present you an advisory report that is prepared in response to your request, also on behalf of the Minister of Agriculture, Nature Management and Fisheries regarding the safety of phytosterols and phytosterolesters for the consumer. This advice is a so called initial assessment in the context of European Regulation (EC) 258/97, concerning novel foods and novel food ingredients. The assessment is carried out by the Committee on the Safety assessment of novel foods of the Health Council of the Netherlands.

This advisory report is also presented to the Minister of Agriculture, Nature management and Fisheries.

signed
professor JA Knottnerus

Phytosterols (2)

Assessment of safety for the consumer, in accordance with European Regulation 258/97 concerning novel foods and food ingredients (confidential version)

Health Council of the Netherlands:
Committee on the Safety assessment of novel foods

to:

the Minister of Health, Welfare and Sport

the Minister of Agriculture, Nature management and Fisheries

No. 2001/04VNV, The Hague, December 13, 2001

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 to 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 Preservation & 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.

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Contents

Executive summary, conclusions and recommendations

The applicant, Archer Daniels Midland Company (ADM), has compiled a dossier on the safety of the novel food ingredient, phytosterols and phytosterol esters. These compounds are equivalent from a biological perspective, and are prepared from vegetable oils using standard procedures. Careful production and purification appears to guarantee the quality of the product. The applicant provides sufficient information about the composition. The nutritional and toxicological information in the dossier is based entirely on the scientific information on phytosterol mixtures that are added to certain foods, which have already been authorized on the European and American markets.

The applicant requests permission to use phytosterols (as such or in esterified form) in a variety of foods on the assumption that daily consumption of up to 130 mg of phytosterol equivalents per kg of body weight is safe. This is derived from investigations using experimental animals and corresponds with 9.1 grams per day for a person weighing 70 kg. But the applicant assumes that nutritional conscious consumers will limit their daily intake of phytosterols to a lower quantity, which is already sufficient to achieve the intended cholesterol-lowering effect.

Phytosterols and related compounds have already been subjected to toxicological studies in experimental animals and safety studies in humans. The applicant bases its conclusions on this scientific literature. According to the Committee, this is justified since ADM has demonstrated that the phytosterols in this application are the same as those in the phytosterol mixtures previously assessed. The Committee concludes that ADM’s novel food ingredient can be placed on the European market up to a maximum

level of 8% (w/w) phytosterol equivalents in fat spreads. Such an application was already assessed to be safe for human consumption (EC00a; SCF00). At the present time there is no scientific evidence that consumption of this type of food ingredient in a limited application presents a public health risk. The Committee is of the opinion that the other products, which the applicant wishes to be enriched with phytosterols, should not be allowed on the market. On the one hand, expansion of the product assortment increases the chance of an undesirably high intake of phytosterols by the target group; on the other, it increases the chance that other consumers will also be exposed to phytosterols. Furthermore, the committee has insufficient information on the risk of excessive consumption.

Although the concentration of β-carotene in the blood declines by 20% with long-term consumption of around 2g of phytosterols per day (in fat spreads), at the moment this does not appear to have adverse effects on health. However, there is not enough certainty about the long-term effects of such physiological changes due to the consumption of phytosterols. The Committee concludes that the safe upper limit, adopted by applicant on the basis of toxicological research in rats, is debatable given the above-mentioned effect in humans. For the time being, the Committee disapproves that people who will not benefit in any way from cholesterol reduction, such as children and pregnant women, consume phytosterol-enriched foods. The Committee also considers it undesirable for the target group to ingest more phytosterols than necessary to reach the plateau of the effect (around 2g/dag). Results of market research for two products already on the market indicate that the consumption among the target group does actually reach this level, and that consumption outside the target group is limited. The Committee advises to carry on with the restriction on the product assortment and with strict labeling.

To summarize, the Committee on the Safety assessment of novel foods therefore objects to authorize on the European market a very wide assortment of foods containing phytosterols and related compounds. Better guarantees are needed to ensure that the consumption of phytosterols remains confined to the target group. It is also necessary to establish a clear safe level of consumption of phytosterols for lifetime exposure for the target group.

Chapter 1

Introduction

The proposed level of consumption of the phytosterols that the firm ADM wants to market in Europe is substantially higher than the quantity that the European population ingests on average. The firm has therefore requested permission to introduce them on the market in accordance with Regulation 258/97 of the European Parliament and of the Council concerning novel foods (appendix C).

In 2000 the European Scientific Committee on Food concluded that phytosterols are safe for human consumption up to a maximum level of 8% in yellow fat spreads (SCF00). This finding accords with a previous assessment of the Netherlands preliminary advisory Committee on the safety of novel foods, which advised establishing an upper limit on the use of these types of novel food ingredients.

The assessment procedure for ADM's products proceeded as follows. In August 2001 the firm sent the dossier to the Minister of Health, Welfare and Sport (ADM01). On 11 October 2001 the Committee on the Safety assessment of novel foods ('the Committee') received a request from the Minister of Health, Welfare and Sport for advice regarding the safety of ADM's phytosterols and phytosterol esters for the consumer, in accordance with the previously mentioned European novel food Regulation 258/97 (EC97) and the accompanying Recommendation of the European Commission 97/618 (EC97a).

The Committee discussed the dossier at one of its meetings. It submitted further questions to the producer concerning the equivalence of the novel food ingredients with similar products assessed earlier, on the basis of which the producer had established the nutritional and toxicological safety. After receiving additional

information, the Committee completed its assessment in December 2001. This report presents its findings.

Chapter 2

Completeness and accuracy of the dossier

2.1 Administrative data

The name and address of the producer and applicant are: Archer Daniels Midland Company (ADM), 1001 N. Brush College Road, Decatur, IL, 62521, USA.

2.2 General description of the novel food ingredient

Phytosterols are vegetable substances. Because of their structural similarity to cholesterol they prevent the (re-)absorption of cholesterol by the body which leads to reduction of the blood cholesterol concentration.

The novel food ingredients, plant sterols and sterol esters, which the applicant wishes to introduce and trade on the European market (ADM01) (hereinafter referred to as 'ADM phytosterols'), are derived from various oil seeds. It is the aim of the applicant that food manufacturers will use these ingredients in the following (end)products: fat spreads, salad dressings, health bars, health drinks, yoghurt-type products and processed meat products. At a daily intake, these foods can help to lower the blood cholesterol level.

2.3 Classification of the food ingredient for assessment

The applicant classifies the new product in Class 1, subclass 1.1 as defined in part 1 of Recommendation 97/618 of the European Commission (EC97a). This means that it is a

simple mixture of chemical substances from non-genetically modified sources and that these sources already have a history of food use in the European Community.

The Committee agrees with the applicant that the ADM phytosterols fall under category e, 'food ingredients isolated from plants', in the novel food regulation (EC97), and fall into class 1.1.

2.4 Information about the food

The applicant structured the information that is essential for a safety assessment of food ingredient consumption in accordance with the themes prescribed in Recommendation 97/618 of the European Commission (EC97a):

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

The dossier contains sufficient biochemical, nutritional and toxicological information to assess the safety of the novel food ingredient. The Committee also consulted scientific literature.

2.5 Brief summary by the applicant

The dossier, including the executive summary, was sent to the member states in accordance with article 6, section 2 of the European Regulation (EC) 258/97 (EC97).

2.6 Other assessments

Unilever uses ADM phytosterols as one of the phytosterol ingredients in their fat spread. This product was assessed in accordance with the European novel food regulation 258/97 (SCF00) and authorized for placing on the European market in 2000 (EC00a).

In April 2001 the ADM phytosterols were certified by the Food and Drug Administration in the United States (US FDA) as '*generally recognized as safe' (*GRAS*)*. These phytosterols will be added to fat spreads, salad dressings, health bars,

health drinks and yoghurt-type products, such that per serving 1 gram phytosterol equivalent is consumed.

Phytosterols from ADM Nutraceutical (USA) are a component of the phytosterol mixture that the firm Oy Karl Fazer Ab wants to use in bakery products, grain based snacks and gum arabic pastilles. An application to introduce these novel ingredients to the European market was made in 2000, which is being dealt with in accordance with Regulation 258/97 and Recommendation 97/618/EC (HCN01).

2.7 Proposal for labeling by the applicant

Labeling should comply with Directive 2000/13/EC (EC00) and article 8 of Regulation (EC) 258/97 (EC97). In the Netherlands, the labeling proposal is being discussed at the Regular Consumer Goods Act Consultations and is not assessed in this advisory report.

Chapter 3

Interpretation and evaluation of the data presented

3.1 I Specification of the novel food ingredient

This application concerns a mixture of phytosterols, or a mixture of the corresponding esterified forms (see section 3.2), and consists primarily of β-sitosterol, campesterol and stigmasterol. The specification of the product provided by the applicant is:

- total phytosterols > 90 %
- β-sitosterol 40-58 %
- campesterol 20-30 %
- stigmasterol 14-22%
- brassicasterol 0-6 %
- sitostanol 0-5 %

The product also contains <15 mg/g of tocopherols and less than 10 mg of heavy metals per kg. The ranges found are caused by the natural variation in phytosterol content arising from different input oilseed crops, and from seasonal growing condition variations.

The dossier contains the physical characteristics of the phytosterol mixture, but no description of the analytical methods used nor data on the chemical stability. The Committee assumes that validated standard procedures were followed for this.

The Committee concludes from the data provided for the composition of five phytosterol mixtures that there is little variation within a production period of one

year. It assumes that the product specifications are representative for the ADM phytosterol food ingredients to be placed on the market.

3.2 II Effects of the production process applied to the food ingredient

According to the applicant, the oil extraction and purification procedures followed are traditional processes in the food industry. Phytosterols are a by-product of vegetable oil refining. Solvents, lecithins, free fatty acids, color bodies, off-odors and off-flavors are removed from the crude vegetable oil. The oil fraction remaining after steam distillation contains the phytosterols and phytosterol esters. The naturally esterified phytosterols are then converted into free phytosterols and subsequently all phytosterols are isolated and further purified by crystallization from a heptane solution. With the free phytosterols as end-product, phytosterol esters can again be synthesized by standard estification processes using fatty acids from vegetable oils.

The applicant reports that apart from phytosterols, a small quantity of other oil constituents remain after purification (<10 %): mono-, di- and triglycerides, and intermediates in the biosynthesis of sterols (squalene). The product meets European quality standards for food (EC93).

Analyses of twenty organochlorine compounds demonstrated that no measurable residues of pesticides are present.

The information in the dossier provides the Committee with sufficient insight in the various phases of the production process. The procedures used are familiar in the edible oil industry. It concludes that the phytosterol mixture contains no contaminants that are harmful for public health.

3.3 III History of the organism used as the source of the food ingredient

The phytosterols are derived from the seeds of various plants. The primary material that the firm uses is a mixture of crude edible oils, whose main component is soybean oil (from *Glycine max*). In addition, seed oils from corn (*Zea mays*), rapeseed (*Brassica campestris*) and palm (*Elaeis guineensis*) are incorporated.

The fatty acids for the esterification derive preferentially from soybean oil, sunflower oil, safflower oil and canola oil, but corn oil, cotton seed oil, palm oil and peanut oil may also be used as sources.

The Committee confirms that the phytosterol sources have a history of safe use and are used worldwide in the oil and fat industry.

3.4 IX Anticipated intake and extent of use of the food ingredient

Phytosterols reduce the absorption of cholesterol in the intestines. The intention is to add these novel food ingredients to various foods to help lower the blood cholesterol level and keep it at this lower level. The applicant has based the phytosterol enrichment levels of the end products on the following European food intake data sources:

- Eurostat Data Shop (report 1998-99) includes data from 8 European countries based on production and availability of foods, which will overestimate the actual intake. The applicant uses the average values.
- Report by TNO Nutrition and Food Research on food consumption surveys among the Dutch population in 1997-98.

For the use of phytosterols in fat spreads the applicant proposes an enrichment level of 8% as recommended by the European Scientific Committee on Food (SCF00). According to Eurostat, the average 'consumption' of fat spreads in Europe is 27g/day (ranging from 2g in England to 65g in Belgium). This corresponds with the 90th percentile of the intake according to food consumption surveys by the Institute of European Studies and is slightly higher than the 22 g/day for Dutch people (TNO report). The anticipated intake of phytosterols from fat spreads is 2.2 g/day (27 x 0.08).

The anticipated intake of phytosterols from the other enriched products is stated to be 1 gram per daily serving. For salad dressings, at a daily intake of 14 grams (Eurostat: dressing and mayonnaise) the phytosterol level should be 7.1%. For yoghurt-type products, with a daily intake of 30 grams (Eurostat) the phytosterol concentration should be 3.3%. These products may also include soy-based and other protein-based formulations. The applicant defines health bars as 'cereal bars containing high protein and/or high energy and/or fortified with vitamins and minerals and/or reduced or low in fat, consumed by nutritionally-conscious individuals'. There are no data available on consumption of these bars in Europe. The applicant assumes daily intake of 50g (compared with 40-60g in the United States) and so the phytosterol enrichment level becomes 2%. The category of health drinks may include liquid and reconstituted meal replacements and dry powder non-reconstituted products, as well as sport drinks. There are no intake data of these products in Europe. The applicant assumes a daily consumption of 250g (approximately ¼ liter) and so fixes the phytosterol concentration at 0.4%. For processed meat products such as sausages, prepared ham, meat pastes and pates, with a daily intake of 50g (Eurostat) the phytosterol enrichment level should be 2%.

The applicant assumes a maximum safe daily intake level of 7.8g of phytosterol equivalents per person weighing 60 kg (or 130 mg/kg body weight per day; see section 3.8). The applicant believes excessive consumption of phytosterols is unlikely since consumers of the proposed products are well educated and nutritional conscious. Even if an entire set of enriched products is consumed each day, in amounts that are normally expected to be consumed, the total phytosterol exposure would be 7.2 g (including dietary intake from natural sources). In other words, it still falls under the safe upper limit adopted by the applicant. The applicant also suggests that appropriate labeling of the end product can prevent excessive exposure by indicating the phytosterol quantity per portion. This label could also indicate that the product is not intended for children, pregnant women or people with phytosterolemia (a rare abnormal storage of fat).

The Committee has noted the way in which the phytosterol enrichment levels for the various products was derived. However, the consumption of certain products appears to vary greatly between the various European member states (for fat spreads, see above; for yoghurt, see HCN01), and in the case of health bars and drinks is even unknown. Furthermore, part of the intake data is not based on sound scientific results. The Committee therefore concludes that the averages for the intake in Europe reported by the applicant are not justified. The Committee is also not convinced that with an expanded assortment of phytosterol-enriched products, the consumer will be as nutritionally conscious as the applicant suggests.

Unilever recently presented the results of market research (so called post launch monitoring) of the consumption of the fat spread ‘Becel pro.active’ with phytosterol esters (8 g phytosterol equivalent per 100 g; Hep01). This study in five West European countries covered 2,000 households that have bought this product. The majority of these households consist of 1 or 2 persons, and no more than 20 g fat spread was daily consumed, predominantly by one person. Most consumers of Becel pro.active are cholesterol-conscious and older than 45 (87%), which suggests that the target group is being reached. In addition, it appears that in 10-20% of these households there are young children. These results show that the actual consumption of the product by the target group roughly corresponds with the recommended intake. The Committee notes that even now with a limited product assortment, people outside the target group consume phytosterol-enriched products. Discussion about expanding the range of products containing these novel food ingredients can only take place, after reliable consumption pattern analysis for the different EU member states have been collected.

3.5 X Information from previous human exposure to the food ingredient or its source

Phytosterols are natural components in fruit, vegetables, legumes, seeds, nuts and grains. In Europe, 0.2g of phytosterols per day are usually ingested with the normal diet. Vegetarians consume about 0.3–0.4g per day. The anticipated daily intake of ADM phytosterols is 5 to 10 times greater.

The applicant reports that in the numerous human studies with phytosterols in recent decades no clinically relevant adverse side-effects have been observed. In addition, the applicant refers to other commercial products, with phytosterols and related compounds, which have already been authorized on the American and European markets. No significant adverse effects were reported among the users, who consumed 0.7–3.0g phytosterol equivalent per day.

The Committee is aware that at the current level of use no adverse side-effects have been reported that are considered of clinical importance.

3.6 XI Nutritional information on the food ingredient

The applicant summarizes the scientific data explaining the cholesterol-reducing effect. In the human body only about 10% of phytosterols, consumed as such or released in the gastrointenstinal tract after enzymatic hydrolysis of phytosterol esters, are absorbed. These are then quickly eliminated by the liver and excreted (via the bile) with the feces together with the unabsorbed phytosterols. Phytosterols themselves have no direct nutritional value but displace the cholesterol in the micelles in the small intestine, and consequently lower the absorption of cholesterol in the blood. A lower cholesterol level is regarded as beneficial because it reduces the risk of cardiovascular disease.

The applicant extensively evaluates the concerns about the possible consequences of the effect of phytosterols on the intake of fat-soluble vitamins or carotenoids. Human studies have clearly demonstrated that exposure to phytosterols can lower the plasma levels of certain carotenoids, even if changes in plasma lipid concentrations have been taken into account. This relates in particular to the most hydrophilic carotenoids, α- and β-carotene (pro-vitamines A) and lycopene. The applicant explains that, like cholesterol, these carotenoids depend for their absorption on the micelle lipid composition. Given the fact that the decrease in the plasma level of these carotenoids through consumption of phytosterols is based on the same mechanism as with cholesterol, the question is whether this phenomenon has any nutritional or public health significance, particularly in the long term.

The applicant concludes on the basis of seven arguments, which are discussed in detail, that the observed decrease in carotenoids does not represent a public health risk in the European population.

In the evaluation of potentially adverse effects of phytosterols on blood levels of fat-soluble vitamins, the applicant concentrates on α-carotene, β-carotene and lycopene because changes in the blood levels of other carotenoids or vitamins A, D, E and K have not yet been clearly demonstrated. The Committee agrees. The Committee has evaluated recently published research results (Dav01) which show that daily consumption of 9 grams of phytosterols over a period of 8 weeks significantly reduces the α- and β-carotene plasma levels (which only holds for β-carotene after correction for plasma total cholesterol level). The lower doses tested of 3 and 6 g/day did not have this effect. None of the three doses had a significant effect on the plasma levels of fat-soluble vitamins A, D, E, and K. The Committee notes, however, that prolonged consumption (1 year) of 1.6 grams of phytosterols per day reduces the serum β-carotene level by 20%, even if the fat spread containing the phytosterols is enriched with carotenoids (HCN01, SCF00).

In these studies the blood carotenoid concentrations still remained within the normal ranges, which are determined in part (1st argument of the applicant) by the normal seasonal variation (40%). According to the Committee, however, it is not known to what extent this also applies after long-term or lifetime consumption of phytosterols from a wide variety of products (Gra00).

The applicant argues that a loss of 25% of the carotenoids possibly corresponds with just 2% of the total vitamin A nutrition. The large supply vitamin A in the liver plays an important role, and is probably part of the reason why the vitamin A plasma level does not decline through long-term consumption of phytosterols. The Committee agrees with the applicant that the reduced contribution of carotenoids to vitamin A is not a problem in individuals with an adequate vitamin A intake.

Apart from their role in the production of vitamin A, carotenoids may have positive health effects. But intervention studies with high doses of β-carotene have not shown a causal relationship between β-carotene and a reduced risk of cardiovascular disease or certain forms of cancer (Gra00, Wat01).

The Committee can agree with ADM's conclusion that the decrease in β-carotene does not cause a public health concern, but only with respect to the limited phytosterol concentration in fat spreads. However, the applicant wants to use the novel ingredient in a wider range of foods, which increases the chance of higher and broader (ie. outside the target group) intake.

3.7 XII Microbiological information on the food ingredient

The Committee agrees with the applicant that microorganisms are unlikely to be present in the phytosterol mixture, because of the high temperatures used in the production process and the generally very low moisture content of oils.

3.8 XIII Toxicological information on the food ingredient

The applicant states that there is no report of allergenicity caused by phytosterols. There are no protein fragments present in the novel food ingredient, thanks to the strenuous processing conditions.

The applicant provides no results of own toxicological investigations. It refers to the conclusion of experts, who assessed the GRAS status of phytosterol esters for the firm Lipton, that phytosterol esters are safe for human consumption. ADM submitted, together with its application, the food safety section from Lipton's dossier on the basis of which the FDA confirmed the GRAS status in 1999. This contains an extensive evaluation of the scientific literature and the results of toxicological research by Unilever concerning the absorption, distribution, metabolism and excretion of phytosterols, genotoxicity, reproduction toxicity, and sub-chronic exposure. The applicant adopts the ADI* that was determined by Lipton's panel of experts: 130 mg phytosterols / kg of body weight / day. This is based on the NOAEL of 3.9 g phytosterols/kg/day, which was the average intake in sub-chronic studies with the longest-lasting exposure (13 weeks) in rats in which no negative effects were observed.

The applicant does not explicitly discuss genotoxic research. The Committee stresses that the results of detailed genotoxic studies have not produced any indication that phytosterol and cholesterol metabolites have genotoxic properties (HCN01a). According to some scientists (Gra00), it is conceivable that as a result of specific changes in the lipid composition in the intestinal tract, abnormalities in the large intestine could arise later. The Committee is of the opinion, however, that there are no indications that the consumption of phytosterols in the recommended quantities can lead to such abberations. It also emerges from exploratory epidemiological research that there is no clear negative or positive correlation between phytosterol intake and the risk of cancer of the colon or rectum (Nor01).

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* According to the Committee, this term is used incorrectly. The ADI (acceptable daily intake) is defined by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) as ' the amount of a food additive, expressed on a body weight basis that can be ingested over a lifetime without appreciable risk'.

In addition, the applicant refers to the report of the European Scientific Committee on Food which assessed the safety of phytosterol esters as a novel food ingredient for which Unilever requested authorization for placing on the market (ADM01, SCF00). The applicant quotes that it was concluded, on the basis of extensive *in vitro* and *in vivo* toxicological research, that exposure to phytosterols is no reason for safety concerns.

The effect of phytosterol consumption on the absorption and hence the plasma levels of fat-soluble vitamins and carotenoids was discussed in section 3.6.

The Committee agrees to references by the applicant to earlier reported safety assessments of phytosterol esters, used in yellow fat spreads, on the basis of the following arguments:

1 The specification of the phytosterol mixture provided in the ADM dossier corresponds with those in the dossiers of Unilever and its daughter company Lipton to which the applicant refers (SCF00, ADM01). The Committee agrees with the applicant that scientific data on oral exposure to phytosterols and phytosterol esters are both relevant given their physiological behaviour in the gastrointestinal tract. It confirms that the free and esterified forms are equivalent in biological terms, on the basis of their comparable capacity to lower the blood cholesterol concentration as well as that of the carotenoids.
2 So far as the Committee is aware, no data have been reported from new, more recent studies with phytosterols (and related compounds such as phytostanols and esterified forms) that do not support the scientific data already evaluated.

The Committee has noted the toxicological studies using experimental animals. However, it is of the opinion that the outcome of these studies does not provide sufficient basis to establish an ADI, acceptable daily intake. There is insufficient scientific support for the safe upper limit of 9.1g of phytosterols for a person weighing 70 kg, which the applicant adopts. Biological effects do occur in humans, not only at this level of intake but also at the far lower recommended doses. There is not yet sufficient insight into the clinical relevance of these effects in the long term (see also section 3.6).

Literature

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EC97 Regulation (EG) 258/97 (van het Europees parlement en de Raad van 27 januari 1997 betreffende nieuwe voedingsmiddelen en nieuwe voedselingrediënten. Publikatieblad van de Europese Gemeenschappen 1997; L43: 1-60)

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WHO91 Strategies for assessing the safety of foods procuced by biotechnology. Report of a joint FAO/ WHO consultation. Geneve, WHO 1991.

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A Request for advice

B The committee

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D Executive summary of the dossier

Annexes

Annex **A**

Request for advice

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

Since May 1977, 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 reponsibility 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 applicants (insofar as consistent with the need to protect the

conficentiality 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

Annex **B**

The committee

- Prof. dr LM Schoonhoven, *chairman*
  emeritus professor of entomology; Wageningen University and Research centre
- Prof. dr CAFM Bruijnzeel-Koomen
  professor of dermatology/allergology; Academic Hospital Utrecht
- Ir EJ Kok
  toxicologist; State Institute for Quality Control of Agricultural Products, Wageningen
- Dr CF van Kreijl
  molecular biologist; National Institute of Public Health and the Environment, Bilthoven
- Prof. dr P van der Laan
  professor of statistics; Technical University Eindhoven
- Dr B Loos, *advisor*
  Committee on Genetic Modification, The Hague
- Prof. dr FM Nagengast
  gastro enterologist; Academic Hospital Nijmegen
- Dr ir JMA van Raaij
  food physiologist; Wageningen University and Research centre
- Prof. dr ir G Schaafsma
  professor of nutrition; TNO Nutrition and Food Research, Zeist
- Prof. dr EG Schouten
  professor of epidemiology; Wageningen University and Research centre

- Dr GJA Speijers
  toxicologist; National Institute of Public Health and the Environment, Bilthoven
- Prof. dr WJ Stiekema
  professor of bioinformatics; Wageningen University and Research centre
- Ir R Top, *advisor*
  Ministry of Health, Welfare and Sport; The Hague
- Prof. dr WM de Vos
  professor of microbiology; Wageningen University and Research centre
- Dr RA Woutersen
  toxicologist; TNO Nutrition and Food Research, Zeist
- Dr ir M Rutgers, *executive secretary*
  Health Council of the Netherlands, The Hague

Administrative assistance: C Nederpelt-Brussee; Health Council of the Netherlands, The Hague.

Annex **C**

EU-procedure

When manufacturers bring novel foodstuffs onto the market, consumer safety has to be assured. In 1997, a European Regulation (EC97) came into force, laying down the procedure for approving the market introduction of novel foodstuffs. The procedure recognises 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 substiantially equivalent to any existing product. (If a foodstuff is substiantially equivalent to any existing product, it is sufficient to inform the authorities of its market introduction). Foodstuff 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 (EC97a). 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 (WHO91, FAO96). The Health Council of the Netherlands has also considered the question earlier (HCN92). Since publication of the EU recommendations, international efforts have been made to clarify and adapt the latest scientific knowledge in the field (FAO01, SCF99, SSC99, OECD98, OECD00, 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) 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 (EC97a, 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.

Annex **D**

Executive summary of the dossier