EXPLANATORY STATEMENT

APPLICATION A434

PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN LOW-FAT MILK & YOGHURT

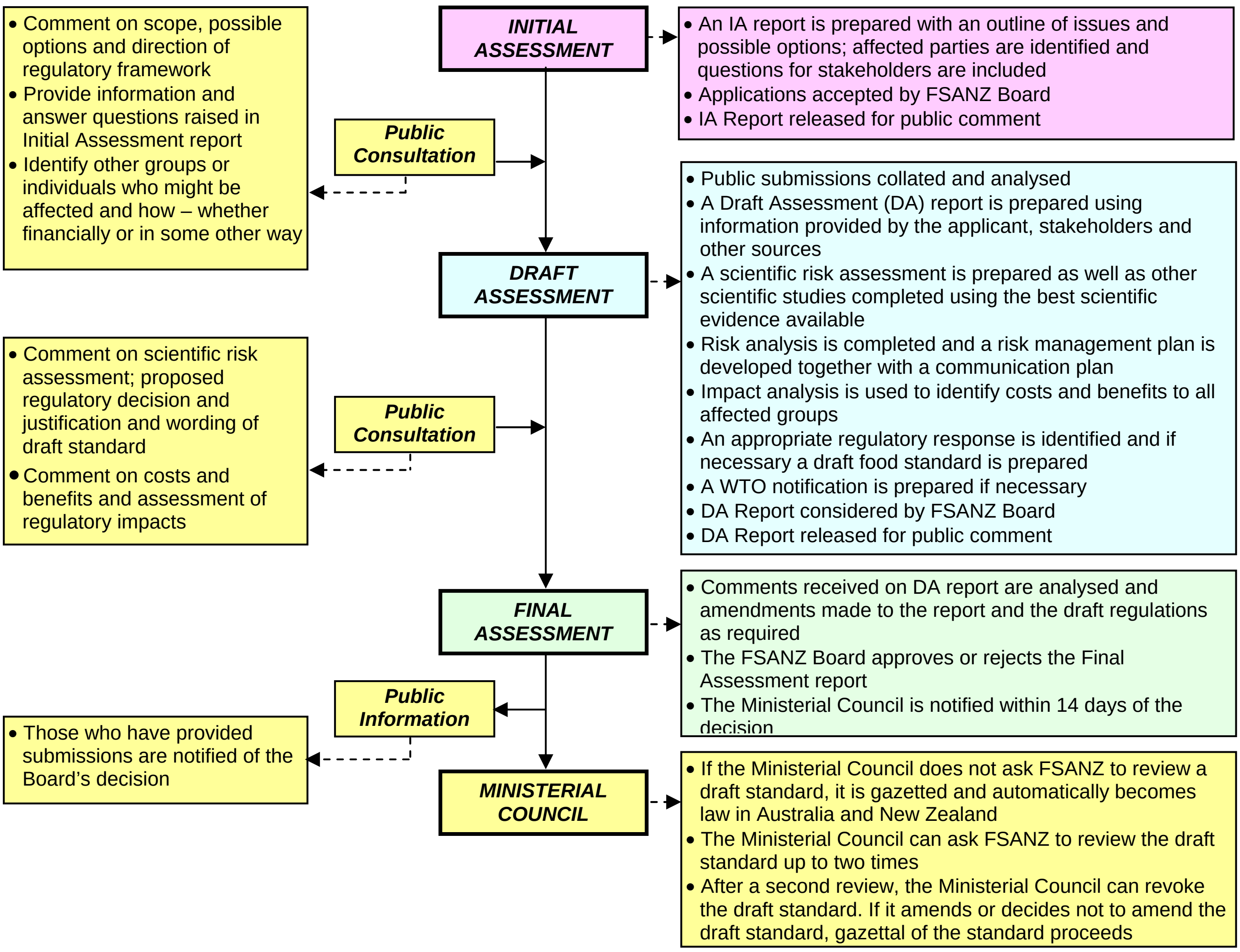
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

FSANZ's role is to protect the health and safety of people in Australia and New Zealand through the maintenance of a safe food supply. FSANZ is a partnership between ten Governments: the Commonwealth; Australian States and Territories; and New Zealand. It is a statutory authority under Commonwealth law and is an independent, expert body.

FSANZ is responsible for developing, varying and reviewing standards and for developing codes of conduct with industry for food available in Australia and New Zealand covering labelling, composition and contaminants. In Australia, FSANZ also develops food standards for food safety, maximum residue limits, primary production and processing and a range of other functions including the coordination of national food surveillance and recall systems, conducting research and assessing policies about imported food.

The FSANZ Board approves new standards or variations to food standards in accordance with policy guidelines set by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) made up of Commonwealth, State and Territory and New Zealand Health Ministers as lead Ministers, with representation from other portfolios. Approved standards are then notified to the Ministerial Council. The Ministerial Council may then request that FSANZ review a proposed or existing standard. If the Ministerial Council does not request that FSANZ review the draft standard, or amends a draft standard, the standard is adopted by reference under the food laws of the Commonwealth, States, Territories and New Zealand. The Ministerial Council can, independently of a notification from FSANZ, request that FSANZ review a standard.

The process for amending the *Australia New Zealand Food Standards Code* (Food Standards Code) is prescribed in the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). The diagram below represents the different stages in the process including when periods of public consultation occur. This process varies for matters that are urgent or minor in significance or complexity.



Final Assessment Stage

FSANZ has now completed two stages of the assessment process and held two rounds of public consultation as part of its assessment of this Application. This Final Assessment Report and its recommendations have been approved by the FSANZ Board and notified to the Ministerial Council.

If the Ministerial Council does not request FSANZ to review the draft amendments to the Code, an amendment to the Code is published in the *Commonwealth Gazette* and the *New Zealand Gazette* and adopted by reference and without amendment under Australian State and Territory food law.

In New Zealand, the New Zealand Minister of Health gazettes the food standard under the New Zealand Food Act. Following gazettal, the standard takes effect 28 days later.

Further Information

Further information on this Application and the assessment process should be addressed to the FSANZ Standards Management Officer at one of the following addresses:

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Assessment reports are available for viewing and downloading from the FSANZ website www.foodstandards.gov.au or alternatively paper copies of reports can be requested from FSANZ's Information Officer at info@foodstandards.gov.au including other general enquiries and requests for information.

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Executive Summary and Statement of Reasons

Dairy Farmers submitted an application to FSANZ seeking approval for the use of phytosterol esters derived from vegetable oils as a novel food ingredient in low-fat milk and low-fat yoghurt under Standard 1.5.1 – Novel Foods, in the *Australia New Zealand Food Standards Code* (the Code).

Standard 1.5.1 prohibits the sale of novel foods or novel food ingredients unless they are listed in the Table to clause 2 of the Standard, and comply with any special conditions of use stipulated in the Table. Approval for use requires a safety assessment to be undertaken. Current permissions to use phytosterol esters as novel food ingredients are limited to edible oil spreads and margarines. There is currently no permission to add phytosterol esters to a broader range of foods.

Purpose and scope of the Application

Free phytosterols are chemically and structurally related to animal-derived cholesterol. These properties confer the ability to interfere with the mechanism of cholesterol absorption in the human intestine. When ingested in various food matrices, phytosterol esters can potentially decrease low density lipoprotein (LDL) cholesterol levels in the blood. Products with added phytosterol esters are primarily targeted to adult consumers, particularly those over 40 years of age, interested in achieving a lower cholesterol level without major changes to their diet. The purpose of the application is to increase the range of phytosterol-enriched foods available to these consumers.

Approval of a health claim is not a consideration in this assessment. Clinical data establishing that phytosterol esters can lower LDL cholesterol levels when added to low-fat milk and low-fat yoghurt have been evaluated to ensure the validity of labelling statements associating plant sterols with a reduction in the absorption of cholesterol.

Risk assessment

Two new clinical studies were submitted in support of the Application. As well as testing efficacy in different food matrices (breakfast cereal, fibre-increased bread, low-fat milk and low-fat yoghurt), a range of physiological/biochemical parameters were also measured to detect potential adverse health effects. When incorporated into low-fat milk and low-fat yoghurt, phytosterol esters had a modest cholesterol lowering effect. Daily consumption rates between 2.6 g and 10.7 g phytosterol esters were well tolerated, and no adverse physical or physiological effects were detected. The results from the clinical studies are consistent with other published studies, some investigating consumption of phytosterols for periods up to 12 months.

The investigations into the nutritional effects of phytosterols on absorption of carotenoids and some fat-soluble vitamins found that serum β-carotene levels were most affected, showing a reduction of approximately 25%, which to some extent was dependent on the nature of the food matrix and on cholesterol-lowering effects.

However, the reduction in β-carotene levels was not associated with a reduction in retinol (Vitamin A) levels and was within a broad natural variation for this provitamin.

The results from the dietary exposure assessment which considered phytosterol-containing spreads, low-fat milk and low-fat yoghurt indicate that mean exposure to free phytosterols would be 1.6 g/day for the Australian population and 1.9 g/day for the New Zealand population. For both countries, estimated mean dietary exposure is expected to be highest for consumers aged 40-64 years, which is a major fraction of the target group. At the highest level of consumption (95th percentile), estimated exposure to phytosterols is expected to be between 4.2 g/day and 4.7 g/day for all population groups assessed.

When all proposed foods in Applications A433[1] and A434 (high fibre/moderate sugar breakfast cereal, plus low fat milk and yoghurt) are considered, the results of the dietary exposure assessment indicate that estimated mean dietary exposure from all foods did not exceed 1.9 g/day in any population group, and highest mean consumption levels were in the target population groups (over 40 years of age) in both Australia and New Zealand. At the 95th percentile of exposure, no population group exceeded 4.7 g free phytosterols per day, equivalent to 7.6 g phytosterol esters. The highest consumers of phytosterol esters are therefore likely to be well under the upper level of consumption of 10.7 g/day used in the clinical studies which produced no evidence of adverse health effects. The results also suggest that the major source of dietary exposure to added phytosterols is from edible oil spreads for all population groups assessed.

The overall conclusion of the risk assessment is that phytosterol ester-enriched low-fat milk and low-fat yoghurt are not associated with adverse health effects at the levels proposed by the Applicant, and can result in a cholesterol lowering effect. Adult consumers in the target population group are major consumers of the foods in question, and by maintaining their established dietary habits are likely to use the foods in amounts considered safe and appropriate.

Risk management

Phytosterol ester enriched foods can be consumed safely by the target population group and may assist in reducing LDL cholesterol levels. However, in general, children and pregnant or lactating women do not need to reduce cholesterol absorption, and products containing added phytosterols are therefore less appropriate for these groups.

Comprehensive risk management options have been considered, to encourage appropriate use by the target population group and discourage consumption by non-target groups. The recommended measures include (i) prescribing the maximum amount of phytosterol esters that may be added to low-fat milk and low-fat yoghurt; (ii) retaining the three mandatory advisory statements currently required under Standard 1.2.3 (for edible oil spreads and margarines), and adding one additional mandatory advisory statement to the effect that phytosterol-enriched foods do not provide additional benefits when consumed in excess of three serves per day; (iii) imposing a restriction on the maximum container size to 1 litre for milk, and 200g for yoghurt; and (iv) imposing an additional condition of use prohibiting phytosterol enriched foods to be used as ingredients in other foods.

It is proposed that the new labelling requirements apply to all foods with added plant sterols, including the edible oil spreads and margarines.

[1] Application A433 from Goodman Fielder seeks permission to add phytosterol esters to breakfast cereal.

Public consultation

Sixteen submissions were received in the first public consultation period and twenty-two submissions were received during the second consultation period. A small majority of submissions were in favour of the Application. Of those in favour, all supported increased consumer choice and improved opportunities for product innovation. The major issues of concern raised by those opposed were the potential nutritional effects, the potential for adverse effects in non-target consumers, and the choice of food products, namely milk and yoghurt which are widely consumed in Australia and New Zealand. The issues raised in public submissions have been addressed in the report and, where appropriate, through the risk management strategies outlined.

Statement of Reasons

FSANZ agrees to approve the use of phytosterol esters derived from vegetable oils in low-fat milk and low-fat yoghurt, subject to specified conditions of use, for the following reasons:

- there are no anticipated public health and safety concerns associated with the use of phytosterol esters derived from vegetable oils in low-fat milk and low-fat yoghurt when used in conjunction with the risk management measures proposed;

- there is evidence that phytosterol esters derived from vegetable oils can, following consumption, reduce levels of cholesterol in humans when incorporated into low-fat milk and low-fat yoghurt products;

- the nutrition assessment indicates that phytosterol esters derived from vegetable oils have no significant adverse nutritional effects at the proposed levels of use. The reductions in the absorption of β-carotene are within the normal variation which results from physiological and environmental factors;

- conditions of use, including an additional labelling statement, are proposed as part of a comprehensive risk management strategy to ensure appropriate use of phytosterol-containing foods by the target consumers, and to discourage use by non-target consumers;

- the proposed changes to the Code are consistent with the section 10 objectives of the FSANZ Act; and

- the Regulatory Impact Statement indicates that, for the preferred option, namely, to approve the use of phytosterol esters derived from vegetable oils as novel food ingredients in low-fat milk and low-fat yoghurt, the benefits of the proposed amendment outweigh the costs.

The proposed drafting to the *Australia New Zealand Food Standards Code* is shown at **Attachment 1** to the Draft Assessment Report.

1. Introduction

An Application was received from Dairy Farmers on 15 February 2001 seeking approval for the use of phytosterol esters derived from vegetable oils as a novel food ingredient in low-fat milk and low-fat yoghurt under Standard 1.5.1 – Novel Foods, in the Code. The Application was assigned to Work Group 2 and, by mutual agreement with the Applicant, commenced work in September 2002. Following completion of the Initial Assessment, FSANZ accepted this Application on 11 March 2003.

Phytosterol esters derived from vegetable oils can lead to a lower serum low density lipoprotein (LDL) cholesterol level when added to the diet. Phytosterol esters are currently added to lines of edible oil spreads namely Pro-activ® marketed by Unilever, and Logicol® marketed by Goodman Fielder. The Applicant seeks to extend the current permission for phytosterol esters to low-fat dairy products, in order to increase the product range available to consumers.

2. Regulatory Problem

2.1 Current Regulations

Standard 1.5.1 in the Code prohibits the sale of novel foods or novel food ingredients unless they are listed in the Table to clause 2 of the Standard and comply with any special conditions stipulated in that Table. Approval for use requires that a novel food or novel food ingredient, be subjected to a pre-market safety assessment before being offered for retail sale in Australia and New Zealand.

The current permission to use phytosterol-esters and tall oil phytosterols (TOPs) as novel food ingredients was limited to edible oil spreads and margarines primarily due to the limited safety data available and the lack of scientific evidence relating to their cholesterol-lowering effects in other food matrices. There is currently no permission to add phytosterol esters to a broader range of foods.

Dairy Farmers is seeking to extend the approval for the use of phytosterol esters to a limited number of additional food products, namely low-fat milk and low-fat yoghurt.

The Application has been open for two rounds of public comment, for eight weeks and nine weeks respectively, and is now at Final Assessment.

3. Objective

The objective of this Application is to establish if the food regulations should be changed to allow the use of phytosterol esters in low fat milk and low fat yoghurt. Before approval, an amendment to the Code must be agreed by the FSANZ Board, and subsequently be notified to the Ministerial Council. An amendment to the Code may only be gazetted once the Ministerial Council process has been finalised.

In addressing the proposed variation to Standard 1.5.1, FSANZ is required by its legislation to meet three primary objectives that are set out in section 10 of the FSANZ Act. These are:

- the protection of public health and safety;

- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying standards, FSANZ must also have regard to:

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

4. Background

Phytosterols (or plant sterols) is a collective term for cholesterol-like compounds that are naturally present at low levels in many varieties of fruits, vegetables, nuts and cereals. The most common and major plant sterols are sitosterol, campesterol and stigmasterol.

Free phytosterols occur naturally at low levels (up to 0.9%) in common vegetable oils, and are chemically and structurally related to animal-derived cholesterol. These properties confer the ability to interfere with the mechanism of cholesterol absorption in the human intestine.

Free phytosterols are extracted from vegetable oil sources, typically soybean oil. Phytosterol esters are prepared commercially by the reaction of phytosterols with fatty acid methyl esters or free fatty acids.

4.1 Previous consideration

In 1999, following consultation between the then ANZFA and Senior Food Officers in each of the Australian States and Territories and New Zealand, it was agreed that phytosterol esters derived from vegetable oils should be regarded as novel food ingredients because of a lack of history of significant consumption by the broad community, and a lack of knowledge in relation to their safety at the proposed levels of use.

The use of phytosterol esters derived from vegetable oils was assessed by the then ANZFA within Application A410. At the time, the Final Assessment Report (completed in May 2001) concluded that permission to use phytosterol esters should be limited to edible oil spreads and margarines at a maximum concentration of 13.7% (w/w) for the following reasons:

(a) The available data on phytosterol esters did not demonstrate any evidence of adverse effects at the levels of dietary exposure expected from their use in edible oil spreads and similar products;

(b) The available data at the time was not adequate to assess the safety of phytosterol esters at higher levels of dietary exposure that could occur from their use in a broader range of foods; and

(c) The available scientific evidence demonstrated that dietary phytosterol esters could reduce total and low density lipoprotein (LDL) cholesterol levels in blood when incorporated into an edible oil spread at 13.7% (w/w). Any marketing statements to this effect used by manufacturers on packaging or in advertising would therefore be consistent with this evidence. However, there were no data available in relation to the effectiveness of phytosterol esters in this regard when incorporated into other foods.

The variation to the Standard was gazetted on 14 June 2001.

4.2 Related Applications

FSANZ is currently considering two other related applications:

- A433 seeks permission to use phytosterol esters derived from vegetable oils in breakfast cereals; and
- A508 seeks permission to use tall oil phytosterols in low-fat and no-fat liquid milk products.

Dairy Farmers and the applicant for A433, Goodman Fielder, have indicated that the phytosterol-enriched foods encompassed by the two applications (breakfast cereals, breakfast cereal bars, low-fat milk and yoghurt) would be marketed to consumers in a coordinated fashion, using statements and an identifying brand name that would be consistent across the range of products. The two companies have submitted scientific information common to both applications. Due to significant similarities in terms of the safety assessment, Application A433 therefore has been considered in parallel with this application.

4.3 Additional information requested during assessment

Since the assessment period commenced in September 2002, FSANZ sought additional information from the Applicant on two occasions. Further information and validation of the clinical studies submitted with the application was sought on 22 October 2002. The Applicant requested additional time, and a response was received on 29 January 2003.

In order to more fully develop the risk management options, the statutory timeframe was interrupted by FSANZ on 3 September 2003, seeking details from the Applicant on the extent of consumer information that was intended for packaging, as well as labelling and proposed marketing strategies for the products. FSANZ received a written response on 12 December 2003, after the Applicant again sought additional time. Assessment of the Application was re-commenced on 17 December 2003.

4.4 Plant-derived sterols and stanols in other countries

Table spreads enriched with plant-derived stanols were introduced into the food supply in the mid-1990s in Finland. Over succeeding years, the use of plant sterol or stanol-based foods expanded into other countries including the United States (USA), Brazil, Switzerland (1999), Australia and New Zealand (2001). Since the EU Novel Foods approval in 2000 (EC258/97), yellow fat spreads containing phytosterols have become available in over 11 countries in the European Union including the Netherlands, Austria, Belgium, France, Germany, Greece, Ireland, Portugal, Spain, Sweden and the United Kingdom (UK).

As at September 2004, milk type products, yoghurt type products, salad dressings, spicy sauces, fermented milk type products, soya drinks and cheese type products containing phytosterols/phytostanols are authorised for placing on the market in the European Union, in addition to the permitted yellow fat spreads (Commission Decision 2004/336, 335, 334, 333/EC). Generic specifications for phytosterols and phytostanols have been established, and include the free sterols and stanols as well as those esterified with food grade fatty acids. The UK Food Standards Agency recently approved an application from Unilever seeking approval for the use of phytosterol-esters (equivalent to 1g of free phytosterols per serving) in milk and yoghurt type products.

In the USA, a number of vegetable oil sterol esters, that meet appropriate food-grade specifications and are produced by current good manufacturing practice (21 CFR section 182.1(b)), have been notified under the GRAS system. The US Food and Drug Administration (FDA) have raised no objection to a number of food products (see below) that may contain plant sterol and stanol esters in amounts up to 20%, on the basis of the GRAS notification. The FDA has not conducted an independent assessment of these compounds.

Recent phytosterol ester FDA GRAS notifications (where the FDA raised no issues) are:

- GRN 000048 (2000) - Vegetable oil phytosterols – for use in vegetable oil spreads, salad dressings, bars and yoghurt.
- GRN 000053 (2000) – Phytosterol esters – for use in vegetable oils for baking and frying, and salad dressings.
- GRN 000061 (2001) – Plant sterols/plant sterol esters – for use in vegetable oil spreads, salad dressings, health drinks, health bars and yoghurt type products.

The FDA has also issued an interim final rule (Sept 2000, 21 CFR section 101.83 [2]), which allows manufacturers of products containing added phytosterol and stanol esters to make a health claim (for reducing the risk of coronary heart disease). There are a number of specific restrictions with which the products must comply before such a health claim may be made. In the USA, a number of foods that are allowed to use this interim health claim include sterol esters in spreads and salad dressings, and stanol esters in spreads, salad dressings, snack bars and dietary supplements in soft gel form.

There is currently no permission for the use of phytosterols in foods in Canada.

4.4.1 Use of plant stanols in foods

Foods containing plant *stanol* esters (stanols esterified with fatty acids of rapeseed oil) are permitted on the market in the EU, without being subjected to review, because they were marketed in a member State before the Novel Foods Regulation came into force. Initially, the products were edible oil spreads (margarines), but this has broadened to include other foods such as fresh cheese, snack bars, salad dressing and yoghurt, and the markets include Finland, Belgium, the Netherlands, Luxembourg, UK, Ireland, Sweden, Denmark and the USA.

There is currently no permission to use phytostanol esters in food in Australia and New Zealand.

5. Relevant Issues

The focus of the assessment of novel foods is primarily related to the first objective identified in section 10 of the FSANZ Act, namely, *the protection of public health and safety*. However, as for all applications to change the Food Standards Code, other objectives identified in the Act must also be considered, including *the provision of adequate information relating to food to enable consumers to make informed choices*; and *the prevention of misleading or deceptive conduct*.

FSANZ has identified and addressed the relevant issues in relation to a broader use of phytosterol esters. These issues include the potential for increased dietary exposure, safety, potential nutritional effects in target and non-target consumers, truth in labelling, and the provision of appropriate consumer information, as well as some other issues raised in public submissions. The risk management measures address the issues identified in the risk assessment.

5.1 Claims concerning function or efficacy

FSANZ has previously assessed phytosterols derived from vegetable oils and TOPs primarily from a safety perspective rather than an efficacy perspective. Health claims are generally prohibited in the Code, and although there is now an abundance of published studies reporting the cholesterol-lowering effects of additional phytosterols in the human diet, approval of a health claim is not a consideration in this assessment.

However, irrespective of whether any statement on a product is considered a health claim, all statements on the label should be true and not mislead consumers. The evidence now available suggests that the nature of the food matrix in which the phytosterols are consumed is a factor in the overall cholesterol-lowering effect. As lipophilic compounds, they are suited to incorporation into lipid-rich foods such as edible oil spreads and margarines. As these physical properties may contribute to the cholesterol lowering effects, appropriate evidence is needed to demonstrate that phytosterols have similar efficacy when added to other food-types such as dairy and cereal products. Therefore, current information on the potential physiological or functional effects of phytosterol esters when incorporated into specific food matrices is relevant only in relation to the veracity of labelling statements used by manufacturers in promoting these products.

5.2 Technical properties of phytosterol esters

A detailed report on the food technology aspects of this application is provided at **Attachment 2**.

Plant sterols are natural components of cereals, fruit, vegetables and edible vegetable oils, and as such are natural constituents of the human diet. Phytosterols have a role in plants similar to one of the roles of cholesterol in mammals, that is forming cell membrane structures. The structures of the most abundant phytosterols, β-sitosterol, campesterol and stigmasterol are very similar to cholesterol. Free phytosterols are poorly soluble in most food matrices, but their sterol esters (formed by conjugation of the sterols with fatty acids) are more fat soluble.

Free phytosterols are only partially extracted when edible oils (such as soybean oil) undergo normal refining. It is estimated that 2500 tonnes of vegetable oil needs to be refined to yield 1 tonne of plant sterols. This relatively low yield ratio means that phytosterols are expensive to produce.

The current application seeks to broaden the foods containing phytosterols to low-fat milk and low-fat yoghurt. For such products, the esters are technically preferable to the free phytosterols since they have improved solubility in fats or oils used in the manufacturing process. The production and processing methods for phytosterol-enriched products are the same as for the corresponding standard products, except for the added incorporation of the phytosterol esters before further processing. Phytosterol esters are very stable to both oxidation and heat and remain unchanged during product processing, including various heat treatments. Even under severe conditions, such as deep-frying, sterol oxidation products are only formed at parts per million (ppm) concentrations.

The technical specifications for the phytosterol esters in this Application are the same as those currently listed under Standard 1.3.4 – Identity and Purity in the Code (see Attachment 2).

5.3 Safety/efficacy of phytosterol esters

An extensive database of both animal and human studies on the safety of phytosterol esters was examined during consideration of Application A410. The animal studies indicate that free phytosterols and phytosterol esters are poorly absorbed from the gastrointestinal tract, have low toxicity, are not genotoxic, and have no effect on reproductive parameters. There was also no evidence of oestrogenic activity in both *in vitro* and *in vivo* studies. Excretion is through the bowel both as free phytosterols and as phytosterol esters. The human studies provide evidence of reduced cholesterol absorption resulting in lower plasma cholesterol levels following ingestion of up to 3.3 g/day in short term studies, and ingestion of 1.6 g/day (calculated as free phytosterols) in a 1-year study. There was no evidence of adverse health effects in these studies, but the reduction in the levels of plasma β-carotene (a precursor for the synthesis of vitamin A) raised a potential concern regarding higher levels of phytosterol intake, particularly for groups that may be at risk of vitamin deficiency such as children or lactating women.

An updated safety assessment of phytosterol esters in other food vehicles and at higher levels of intake has been prepared, and is presented in two sections – a general safety assessment (at **Attachment 3**), and a nutritional assessment (at **Attachment 4**).

Clinical studies were conducted in mildly hypercholesterolaemic volunteers that examined the cholesterol lowering effects of phytosterol ester-enriched low-fat milk, low-fat yoghurt, fibre-increased bread and breakfast cereal, in a multi-centre trial. In the first study, the trial foods each provided 2.6 g/day phytosterol esters, and were consumed singly and sequentially for a period of three weeks each, in addition to a control period in which no phytosterol-enriched foods were consumed. As well as testing efficacy in the different food matrices, a range of physiological/biochemical parameters were also measured in the study participants (see Attachment 3).

The second study was an evaluation of the nutritional effects of phytosterol ester enriched breakfast cereal, fibre-increased bread, and margarine together providing 10.7 g/day phytosterol esters, consumed over a period of 12 weeks. The analyses specifically focussed on circulating levels of lipophilic nutrients such as the carotenoids and some fat soluble vitamins. In the second six-weeks of the trial period, participants were asked to consume at least 5 serves per day of fruits and vegetables, at least one from a list of carotenoid-rich fruits and vegetables, in conjunction with the phytosterol enriched foods (see Attachment 4).

The key findings of these recent studies include:

- each phytosterol-enriched trial food (low-fat milk, low-fat yoghurt, fibre-increased bread and breakfast cereal) providing 2.6 g/day phytosterol esters reduced serum LDL cholesterol levels (Study 1);

- milk was the most effective food vehicle, reducing serum LDL cholesterol levels by approximately 15%, whereas yoghurt reduced serum LDL cholesterol levels by approximately 8%;

- bread and breakfast cereal reduced serum LDL cholesterol levels by approximately 5% and 6% respectively;

- very low levels of phytosterols were detected in plasma with increases over controls in the range of 1-2 μg/ml;

- intakes of phytosterol esters of 10.7 g/day (Study 2) resulted in a similar reduction in serum LDL cholesterol as the lower intake level (2.6 g/day). However, if the milk phase was excluded from Study 1, the reduction in cholesterol at the higher intake level was approximately twice that of the lower intake, implying that there is a more significant cholesterol lowering effect when milk is used as the food vehicle;

- lipid-standardised plasma carotenoid levels were significantly reduced (14% - 27%), which varied with individual carotenoids throughout the trial, but were partially restored to baseline levels when target amounts of fruits and vegetables were consumed. The reduction in β-carotene levels is the most consistent finding across these studies; and

- no other significant changes were observed in other physiological/biochemical parameters tested in the studies.

A comparison between diets containing 2.6 g/day and 10.7 g/day phytosterols revealed that at higher ingestion levels, endogenous cholesterol synthesis increases almost proportionately as indicated by plasma lathosterol levels. This homeostatic synthesis may account for the plateau effect in reduction of serum cholesterol levels observed as ingestion of phytosterol esters increases. The effects observed in both of these studies are highly consistent with previous studies reported in the scientific literature.

As absorption of dietary cholesterol is inhibited by ingestion of phytosterols, there is a concomitant effect on the absorption of some lipophilic micronutrients.

When these nutritional effects were examined in detailed studies, reductions in α- and β-carotene, lycopene, lutein and cryptoxanthin were observed, while vitamin E and vitamin A levels remained unaffected. When the nutrient levels were adjusted to correct for lower LDL cholesterol levels, only β-carotene levels were significantly affected by ingestion of phytosterol-enriched foods. However, additional fruits and vegetables (including some that were carotenoid-rich) in the diet, when co-consumed with the phytosterol-enriched foods, partially compensated for the lower bioavailability of carotenoids in the presence of phytosterols. The detailed nutrition assessment is presented in this report at **Attachment 4**.

With some variability, consumption of phytosterol-enriched foods generally results in a reduction in β-carotene levels of approximately 20-25%. This reduction does not translate into an overt nutritional deficiency as absolute levels remain within a broad natural range and there is no measurable effect on retinol (vitamin A) levels. The nutritional significance of a reduction in β-carotene levels therefore cannot be directly measured or assessed. In terms of antioxidant status, other nutrients such as vitamin C, vitamin E and lycopene are not affected by consumption of phytosterols and other phytochemicals present in fruits and vegetables contribute to the complexity of the diet and overall health.

5.3.1 Conclusions from the safety assessment/efficacy assessment

When incorporated into foods such as low-fat milk, low-fat yoghurt, breakfast cereal, and bread, phytosterol esters have a modest cholesterol lowering effect, with milk the most effective food vehicle, followed by yoghurt, cereal and bread in order. At daily consumption rates between 2.6 g and 10.7 g, phytosterol esters are well tolerated, with no adverse physical or physiological effects detected in clinical trials over a 12 week period. Other published studies suggest that phytosterol esters are not associated with adverse effects over periods up to 12 months.

The investigations into the nutritional effects of phytosterols on absorption of carotenoids and some fat-soluble vitamins found that β-carotene levels were most affected, showing a reduction of approximately 25%, which was to some small extent dependent on the nature of the food matrix and on cholesterol-lowering effects. Some evidence was provided to demonstrate that consumption of 5 serves per day of fruits and vegetables (with at least one of these rich in carotenoids), partially restores the levels of some micronutrients, particularly α-carotene, lycopene, lutein and cryptoxanthin to baseline levels. Of primary importance, the reduction in β-carotene levels is not associated with a reduction in retinol (vitamin A) levels and is within a broad natural variation for this provitamin. On the basis of the currently available data, there is no evidence to support the view that a reduction in β-carotene levels of this magnitude would result in adverse nutritional effects.

Phytosterol ester-enriched foods can act as convenient tools for reducing circulating LDL cholesterol levels without major changes to the diet, and can be consumed safely by the target population group.

5.4 Potential dietary exposure to phytosterol esters

A detailed dietary exposure assessment has been completed based on the availability of phytosterol ester enriched low fat milk and low fat yoghurt in addition to a baseline level of exposure from existing phytosterol-enriched edible oil spreads (at **Attachment 5**).

A separate dietary exposure report has been prepared that incorporates the results of modelling for all proposed phytosterol enriched foods currently under assessment (breakfast cereals, low-fat milk and low-fat yoghurt) as well as the existing baseline exposures from edible oil spreads (at **Attachment 6**).

Since Applications A433 and A434 are being considered at the same time, the combined dietary exposure assessment was undertaken to determine the potential impact of allowing phytosterol esters to be added to all foods encompassed by the applications, as well as permitted edible oil spreads, to provide an absolute maximum exposure assessment. Both applicants propose to add phytosterol esters at a level equivalent to 0.8 g free phytosterols (1.3 g phytosterol esters) per serve. The dietary modelling was conducted for both Australian and New Zealand populations using DIAMOND, a dietary modelling computer program developed by FSANZ that uses data obtained in nutrition surveys.

5.4.1 Exposure assessment

The dietary exposure assessment took into account the existing permission under Standard 1.5.1 to add phytosterol esters to edible oil spreads and margarines (the 'baseline' scenario), but not the intrinsic level of phytosterols naturally occurring in foods. Food consumption data were derived from the 1995 Australian National Nutrition Survey (NNS) and the 1997 New Zealand NNS.

Assessments were conducted for the general Australian and New Zealand populations (2+ and 15+ years respectively), for two target populations for phytosterol products (those aged 40-64 years and 65+ years) and for two non-target populations for whom phytosterol exposure would offer no nutritional benefit, namely pregnant women and children (2-12 years). Food chemical concentration data were derived from levels proposed in both applications and from the maximum level of use permitted in edible oil spreads and margarines.

In the first report, which considered only the dairy products, intakes of phytosterol esters were estimated for mean and 95th percentile consumers for the target and non-target groups separately, and were considered in the context of a comparison between a baseline level of intake (assuming that all existing edible oil spreads and margarines contained phytosterols), and the estimated level of intake if all low-fat milk and low-fat yoghurt contained phytosterols. Dietary exposure estimates were conducted using the assumption that the pattern of consumption of foods containing phytosterols would not be different to the pattern of consumption of similar foods prior to the addition of phytosterol esters to these foods. The modelling assumptions and methodology were therefore conservative and provide an over-estimate of likely exposures to phytosterols from the specified foods.

5.4.2 Results

The results from the assessment considering baseline plus low-fat milk and low-fat yoghurt (Attachment 5) indicate that mean exposure to free phytosterols would be 1.6 g/day for the Australian population and 1.9 g/day for the New Zealand population. For both countries, estimated mean dietary exposure is highest for consumers aged 40-64 years, which is a major sub-set of the target group. The group with the highest 95th percentile exposure is the New Zealand population group 40-64 years.

The results from the combined assessment which considered all proposed foods (low fat milk and yoghurt plus healthy breakfast cereal) in addition to the baseline exposure (Attachment 6), indicate that estimated mean dietary exposure from all foods, expressed as free phytosterols, did not exceed 1.9 g/day in any population group assessed, and highest mean consumption levels were in the target population groups (over 40 years of age) in both Australia and New Zealand. At the 95th percentile of exposure, no population group assessed exceeded 4.7 g free phytosterols per day. The results also suggest that the major source of dietary exposure to added phytosterols is from edible oil spreads for all population groups assessed.

5.5 Risk characterisation

5.5.1 General population

The data submitted with these applications indicate that consumption of phytosterol-enriched foods providing up to approximately 10.7 g/day phytosterol esters is safe. This conclusion is supported by information from published studies. This level of intake is well above the level expected to be normally consumed, even for the high level consumer. The potential for an adverse nutritional effect is considered to be very small, however, risk management strategies should be considered to ensure appropriate use of phytosterol esters in the target group and discourage use in the non-target groups. The safety assessment also found that occasional, or inadvertent consumption of phytosterol-enriched products by non-target consumers would not raise any health concerns.

5.5.2 Children

In considering the potential impact of consuming phytosterol-enriched foods by non-target consumers such as children, the recent NHMRC Dietary Guidelines for Children and Adolescents in Australia (2003) has been considered. This guideline states that, relative to their body weight, children's nutrient and energy requirements are greater than those of adults. Furthermore, in assessing the role of fat in the diet of children, the background to the guideline states: "There is some evidence that an adequate intake of cholesterol during the growth period is important for cholesterol metabolism later in life and for myelinisation of the nervous system, neurologic development in general, the formation of hormones essential for growth and sexual maturation, and the production of bile acids."[2]

At the same time, the Guidelines emphasise the fact that the human body is capable of synthesising sufficient cholesterol for all its metabolic needs. Excluding genetic disorders and/or underlying pathology, hypocholesterolaemia does not occur in otherwise healthy children. In addition, the Guidelines state that increasing problems of obesity in childhood constitute a risk factor for a range of immediate and long-term health problems, including diabetes, high cholesterol levels, hypertension, sleep apnoea, musculoskeletal problems, liver disease and potential psychological problems. It is now established also that overweight children over the age of 7 years are at greater risk of developing obesity and cardiovascular disease as adults. However, it is also noted that saturated fats in the diet contribute more to elevated blood cholesterol levels than does dietary cholesterol.

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[2] NHMRC Dietary Guidelines for Children and Adolescents in Australia (2003), Chapter 3.6 Limit Saturated Fat and Moderate Total Fat Intake

A detailed discussion of studies investigating the effects of consumption of phytosterol esters by children (with pre-existing hypercholesterolaemia) is presented in the Nutrition Safety Assessment (Attachment 4). As expected, phytosterol consumption lowered cholesterol absorption in children, with no identified adverse effects.

On balance therefore the available evidence suggests that occasional or casual consumption of phytosterol-enriched foods by children does not present a risk to health. The modest reduction in cholesterol that may result from an increased intake of phytosterols is not likely to be physiologically or nutritionally significant.

5.5.3 Pregnant and lactating women

Pregnant and lactating women are considered to have specific nutritional needs because of their respective physiological states, and do not need to actively lower blood cholesterol levels. Phytosterol enriched products are therefore not suitable for these women.

5.5.4 Conclusions of risk characterisation

Regular consumption of phytosterol-enriched foods is not generally appropriate for children, or pregnant or lactating women since there is no necessity to lower absorption of dietary cholesterol in these groups, and they would derive no health benefit from increasing their intake of phytosterols. In contrast, for consumers over the age of 40 years, and particularly those with slightly elevated cholesterol levels, the broader availability of phytosterol enriched foods could enable them to effectively reduce LDL cholesterol, one of the known risk factors in the development of atherosclerosis and cardiovascular disease.

The results of several studies suggest daily consumption of 5 serves of fruits and vegetables, particularly those high in β-carotene, when choosing phytosterol-enriched foods, may assist in maintaining the levels of some carotenoids. The European Scientific Committee for Food (SCF) recommends that consumers be made aware of the potential β-carotene lowering effect of phytosterol-enriched products by the provision of appropriate dietary advice relating to the regular consumption of fruits and vegetables.

5.6 Risk management strategies

A number of strategies can be employed to achieve the goals of permitting broader choice in the range of phytosterol-enriched products available to interested consumers, whilst at the same time discouraging consumption by children and pregnant or lactating women, thus minimising the likelihood that non-target groups would become regular consumers. The risk management measures proposed in this assessment also aim to address the issue of appropriate consumption by the target group. These measures include:

- restricting permission to use phytosterol esters to defined products;
- restricting conditions of use;
- comprehensive labelling requirements;
- mandatory advisory statements on packaging; and
- the provision of additional consumer information.

5.6.1 *Restricting permission to defined products*

Permission to use phytosterol esters to a maximum level in low-fat milk and low-fat yoghurt represents a cautious expansion of the use of these novel food ingredients. Although milk and yoghurt are widely consumed foods, low-fat varieties are preferred by the target consumers and the dietary modelling suggests consumption rates of these products would not be excessive. Phytosterol enrichment of low-fat dairy products is also consistent with public health messages on the nature of a healthy diet.

5.6.2 *Restricting container size*

In addition to the existing conditions of use in Standard 1.5.1 pertaining to the specifications for phytosterol esters in Standard 1.3.4 - Identity and Purity, the following restrictions on use are proposed:

(i) A maximum container size of 1 litre for phytosterol-enriched low-fat milk; and
(ii) A maximum container size of 200g for phytosterol-enriched low-fat yoghurt.

Specifying the maximum container sizes for these foods discourages general household use by only permitting smaller quantities of foods that better suit individual use, rather than family use. Allowing single serve punnets of yoghurt up to a maximum weight of 200g provides manufacturers with some product flexibility to cater to the target group, but also helps consumers monitor the number of serves of phytosterol esters consumed in a day to ensure quantities are effective.

5.6.3 *Restricting conditions of use*

An additional condition of use will apply to all phytosterol-enriched foods, including the currently approved edible oil spreads and margarines:

(iii) Foods containing added plant sterols may not be used as ingredients in other foods.

Prohibiting the use of phytosterol-enriched foods in other mixed foods will prevent further extension of the phytosterol-containing product range. Thus, only those foods listed in Standard 1.5.1 will be able to have phytosterols added.

5.6.4 *Comprehensive labelling requirements*

5.6.4.1 Labelling statements relating to absorption of cholesterol

An integral part of the previous and current assessments is to consider the approach taken by manufacturers of these products in terms of advertising and promotional statements carried on retail packaging. This is particularly important in relation to the section 10 objective of the FSANZ Act relating to *the prevention of misleading or deceptive conduct*.

The previous assessment of the use of phytosterols in edible oil spreads and margarines concluded that the available evidence from human studies indicated that total cholesterol was reduced by approximately 5% and LDL-cholesterol by 7-8% by average consumption of these products.

Since approval of the edible oil spreads and margarines, statements such as: 'With plant-derived ingredients that lower cholesterol absorption' or 'With natural plant sterols which reduce cholesterol uptake' are evident on existing food packaging. At that time, no studies had been conducted to examine whether similar cholesterol lowering effects could be achieved when phytosterols were consumed in other food matrices.

The available evidence now demonstrates that modest cholesterol-lowering effects can be achieved when phytosterol esters are incorporated into low-fat milk and low-fat yoghurt. The Applicant has provided a demonstration package for each dairy product that uses a similar statement: 'With Natural Plant Sterols to Lower Cholesterol Absorption'. Statements such as these promote consumer identification of phytosterol-enriched products and also have an educational function in terms of presenting information on the nature and intended purpose of the foods.

<u>*Ingredient labelling*</u>

The existing conditions of use for phytosterol esters under the standard for Novel Foods (Standard 1.5.1), include the requirement for 'phytosterol ester or plant sterol esters' to be used when declaring the ingredient in the ingredient list, as currently prescribed in Standard 1.2.4. This requirement would be maintained for any broader permission arising from this assessment.

5.6.5 Mandatory advisory statements

Existing mandatory advisory statements on phytosterol-containing edible oil spreads are listed in the box below:

Statements to the effect that:

1. **the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables;**

2. **the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and**

3. **consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication.**

As discussed in previous assessments, it is desirable that use of phytosterols should not be seen by consumers as an alternative to responsible control of dietary cholesterol. In this regard, a healthy diet message particularly encourages low consumption of saturated fats, and adequate consumption of fruits and vegetables. As there is a clear intention to promote the beneficial effects of phytosterol-enriched foods in terms of their cholesterol lowering ability, the foods should be consistent with a healthy diet. In addition, there is evidence that consumption of at least 5 serves per day of fruits and vegetables (with at least one rich in carotenoids) significantly restores the plasma levels of carotenoids when phytosterols are added to the diet. Therefore, in broadening the use of phytosterol esters in foods, statement one (above) will be maintained.

As concluded in the risk assessment, regular consumption of phytosterol-enriched foods is not appropriate for children, and pregnant or lactating women. Potential diet-related health problems in children are better managed through improved overall dietary habits and limiting foods high in saturated fats and sugars, rather than by merely lowering cholesterol absorption. Similarly, pregnant or lactating women do not need to manipulate cholesterol levels *per se*, because of their particular physiological status. For these reasons, the current mandatory statement two (above) will be maintained for any new phytosterol ester-enriched products.

The cholesterol lowering effects of phytosterol esters can vary according to the food matrix. The clinical studies confirm that when various food vehicles are compared under controlled conditions, there is, to some extent, a variable outcome in terms of cholesterol-lowering effect. Milk has been shown to be a particularly effective food vehicle while phytosterol-enriched breakfast cereal is somewhat less effective. In general however, the cholesterol lowering effects of phytosterol-enriched foods cannot be equated with the efficacy expected of specific lipid lowering medication.

Consumers who use medication prescribed for the treatment of hypercholesterolaemia therefore should not substitute their medically supervised treatments for phytosterol-enriched foods with the expectation that they will have similar results. Mandatory advisory statement three (above) will also be maintained.

In addition to these three statements, it is proposed to add the following mandatory advisory statement:

4. consuming greater than 3 serves per day of products containing plant sterols provides no additional benefit.

The evidence indicates that consuming phytosterol esters in amounts above approximately 3 g/day does not improve the cholesterol lowering effects. This additional statement will serve to limit unnecessary levels of consumption of phytosterol esters while maintaining consistency with the data that demonstrate the safety of phytosterols for high consumers within the target group. At the same time, it promotes integrity in manufacturers’ statements relating to the cholesterol lowering effects of plant sterols, where these effects do not increase with increased consumption of phytosterol esters (over approximately 3g per day). It also achieves a consistent message for consumers across all phytosterol-containing foods and ensures an effective minimum amount is consumed.

5.6.6 Consumer information provided by the manufacturer

The marketing plans for the products encompassed by the two applications using phytosterol esters equate one serving of product with 1.3g phytosterol esters (0.8 g of free phytosterols). The manufacturers have designated serving sizes for each of the proposed products. In the case of milk, one serving is 250 ml (1 cup), one serving of yoghurt is provided in individual punnets, and one serving of breakfast cereal (muesli-type) is 45-50 g. The CSIRO studies confirm that consumption of between 1-4 g of free phytosterols achieves a measurable reduction in LDL-cholesterol using these food vehicles. Thus, two to three servings of a phytosterol ester-enriched product (either milk, yoghurt, breakfast cereal or the existing table spreads) provides the optimal amounts of phytosterols associated with reduced cholesterol levels.

The Applicants seeking a broader permission for phytosterol esters also produce one of the permitted phytosterol enriched table spreads currently on the market, and have provided details of symbols that would be used on all phytosterol ester-containing products, across a single brand name associated with their products. The pictorial representation clearly communicates to consumers that consumption of 3 serves per day is desirable, from a choice of cereal, yoghurt, table spread or milk. The symbol also communicates appropriate serving sizes for each of these products (see diagram below). In addition to the marketing symbol for the branded products, serving sizes pertaining to the food in question are stipulated in the nutrition information panel.

Proposed consumer information to appear on packaging for low-fat milk and low-fat yoghurt products, depicting serving sizes for all phytosterol enriched products.	Proposed consumer information to appear on breakfast cereal packaging to depict serving size and appropriate use of all phytosterol enriched products.
	

The Applicants have also outlined a detailed package of marketing activities they propose to use on an ongoing basis to inform consumers about the products. This includes brochures/fact sheets, fresh product sampling to target consumers, provision of support material and samples to health professionals (eg dietitians), education through Consumer Advisory Centres, and informative advertising. These comprehensive measures are considered to adequately address the issues of appropriate consumption by consumers interested in these products.

5.7 Additional risk management issues

5.7.1 Pricing of products

The applicants claim that, because of the high cost of the phytosterol esters, there will be a pricing regime on products containing these novel food ingredients that will discourage family or larger household use. This is claimed to lessen the possibility that family members other than those in the target group would have access to these products. However, although the existing phytosterol enriched edible oil spreads and margarines are more expensive than their conventional counterparts, price discounting on these products does occur. A price premium for phytosterol-enriched foods therefore cannot always be guaranteed. Price does not reflect a robust risk management tool to ensure use only by target consumers.

5.8 Issues raised in public submissions

At Draft Assessment stage, FSANZ prepared responses to a range of issues that were identified from first round public submissions. These issues and the responses can be found in this report following the summary of first round submissions (at **Attachment 7**).

The following issues were identified from submissions received in the second round of public consultation.

5.8.1 Medicalisation of the food supply

Queensland Health, the Tasmanian Department of Health and Human Services, the South Australian Department of Health, and the Public Health Association of Australia express almost identical views relating to the presence of phytosterols in the diet. They question the need for phytosterol-enriched foods for the purpose of reducing serum LDL cholesterol. Instead, they contend that for the prevention and management of certain chronic diet-related diseases, consumers are better advised to adopt more balanced, health conscious eating patterns that do not unduly rely on particular foods or dietary interventions to achieve a desired outcome. They advise that current nutritional and epidemiological evidence supports a diet high in fruits and vegetables and wholegrains, moderate in lean meat and dairy foods, and low in saturated fat and sugar as providing the most effective health outcomes.

In addition, there is an assertion that because consumption of phytosterols is, at present, contained to a recommended number of serves per day, a therapeutic dosage is implied which is not appropriate to the food supply.

5.8.1.1 Response

The primary function of FSANZ in regulating the entry into the food supply of novel foods or novel food ingredients such as phytosterol esters is to ensure the protection of public health and safety. Once the safety of these substances has been established in the context of the Application, and the appropriate risk management measures have been put in place to control their use by the food industry, market forces will determine whether there is consumer demand for the products in question. It is not appropriate therefore for FSANZ to assess whether phytosterol esters are needed in the food supply.

In approving a broader range of phytosterol-enriched foods, FSANZ is not suggesting that these foods are an alternative to healthy eating patterns. Rather, as discussed in the risk management section under 5.6.5, phytosterol esters are to be confined to foods with a healthy compositional profile. Thus, phytosterol-enriched foods merely add to the increasing range of products that the food industry develops in response to public health messages regarding the role of diet in the development of certain adverse health conditions. In this regard, the expanding range of reduced fat foods is also a form of industry exploitation of these public health messages concerning the nature of a healthy diet.

It should also be noted that many people with slightly elevated cholesterol levels are already eating a diet that would be considered compatible with healthy eating guidelines. For these people, consumption of phytosterol-enriched foods involves a conservative dietary change that can assist them with achieving individual health related goals or dietary preferences.

FSANZ considers that it is not appropriate to consider a mildly elevated LDL cholesterol level as a disease. Rather, elevated cholesterol levels can be attributable to a range of diet and lifestyle related variables that, over time, are associated with the onset of certain chronic diseases (eg. atherosclerosis, coronary artery disease). There are multiple dietary interventions that are appropriate for reducing cholesterol levels in these circumstances, such as reducing intake of saturated fats, in combination with increasing intake of fruits and vegetables, or consumption of phytosterols, which generally lead to reductions in this risk factor.

Taking account of the modest reduction in cholesterol levels associated with consumption of plant sterols, there can be no pretence that these novel food ingredients act as a therapeutic agent. Pharmacological therapies are generally required in combination with changes to the diet when cholesterol levels exceed a clinically significant threshold, taking account of individual medical circumstances and other known risk factors. The mandatory advisory statement relating to the need for medical advice on the use of phytosterol enriched products *in conjunction with* cholesterol-lowering medication emphasises to consumers that phytosterol enriched foods are not substitutes for prescribed medication.

Modifications to the fat content of foods on the basis of the role that diet may play in the development of disease represents the medicalisation of food. The removal of fat from foods that naturally contain high levels of saturated fats (for example dairy foods) has become a special area of interest for public health prevention and intervention initiatives in response to an increasing prevalence of, for example, obesity and diabetes. Nutritional guidance over a period of time has condemned the consumption of large amounts of saturated fats, particularly of animal origin (excluding fish), for the purpose of improving general (cardiovascular) health.

However, as previously noted, fat modified foods are neither suitable for, nor wanted by, the whole population. In addition, there is a need to distinguish between certain types of fats, as some are essential while others are detrimental to health if eaten in excess. In general, the perceived benefits to the health of the population brought about by reducing intake of fats have outweighed any adverse nutritional impact arising from the widespread removal of fat from foods.

One clear function of dietary fat is to facilitate the intestinal absorption of essential fat-soluble nutrients such as the carotenoids, including β-carotene, and vitamins A, D, E and K. Recent research (Brown *et al*., 2004[3]) clearly demonstrates that a substantially greater proportion of dietary carotenoids (α- and β-carotene, lutein, lycopene and zeaxanthin) is absorbed by the body when consumed with full-fat foods compared with reduced-fat or no-fat foods.

The benefits of consuming reduced-fat foods therefore are only relevant in terms of reducing risks for some chronic conditions, such as obesity and diabetes, but may also come at some nutritional cost with respect to the bioavailability of essential fat-soluble nutrients. In this respect, reduced-fat foods may be compared with phytosterol-enriched foods as both offer certain groups of consumers some benefits in terms of their general (cardiovascular) health that potentially overrides any unwanted nutritional effects.

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[3] Brown, M.J., Ferruzzi, M.G., Nguyen, M.L., Cooper, D.A., Eldridge, A.L., Schwartz, S.J. and White W.S. (2004) Carotenoid bioavailability is higher from salads ingested with full-fat than with fat-reduced salad dressings as measured with electrochemical detection. Am. J. Clin. Nutr. **80**, 2: 396-403.

A recommended number of servings for phytosterol enriched foods represents the appropriate amounts required to achieve the optimal cholesterol lowering effect (as determined in multiple studies) and to convey to consumers the important message that unlimited consumption will not increase this effect. This information assists consumers who choose phytosterol-enriched foods to take full advantage of the potential benefits without incurring unnecessary expense.

Given that the safety evidence identified no health risks associated with the consumption of phytosterol-enriched foods, and the generally agreed benefits of blood cholesterol levels within a normal narrow range, there is no basis for maintaining the restriction on phytosterol-enriched foods to currently approved edible oil spreads.

5.8.2 Effects on β-carotene

Most submissions in favour of maintaining the restriction on the use of plant sterols to currently approved edible oil spreads express concerns relating to the lower plasma β-carotene levels that accompanies a reduction in LDL cholesterol when phytosterol enriched foods are consumed.

The Draft Assessment Reports for Applications A433 and A434 refer to a 'natural range' for plasma β-carotene levels. Both Queensland Health and the Tasmanian Department of Health call for an explanation of the term 'natural range' when referring to measurable serum β-carotene levels.

5.8.2.1 Response

Numerous studies on the effects of plant sterol-enriched foods show that lower levels of LDL-cholesterol in the blood are generally associated with lower levels of β-carotene, up to 25%. However, the nutritional significance of a reduction in β-carotene cannot be readily interpreted, especially when the only directly measurable physiological effect of β-carotene (i.e. retinol activity) is not affected by consumption of plant sterols.

Studies consistently report no reduction in vitamin A levels in consumers of phytosterol-enriched foods. In the case of the CSIRO Clinical Study 2 presented with this application, no reductions in retinol levels occurred even in people who consumed up to 10.7 g free phytosterols per day for 12 weeks (see Nutrition Assessment Report at Attachment 4). The levels of phytosterol esters tested in this study are almost three times above the amounts required to achieve an optimal cholesterol lowering effect. FSANZ therefore considers that the available scientific information provides evidence for a substantial margin of safety with respect to the β-carotene effects, and supports the safety of consuming phytosterol-enriched foods on a daily basis to achieve a small reduction in LDL cholesterol.

β-carotene range

Numerous physiological, environmental and genetic factors all play a part in determining the intestinal uptake of carotenoids. As discussed previously, β-carotene molecules are more hydrophobic than the other main carotenoids and this physical property may in part provide an explanation for the small differences seen in the restoration of levels of other carotenoids with increased consumption of carotenoid-rich fruits and vegetables. Other known factors that particularly affect the bioavailability of β-carotene include:

- the nature of the food source e.g. β-carotene in some fruits has been found to be more bioavailable than β-carotene in carrots;
- whether the carotenoid-containing food is eaten raw or cooked;
- the amount of fat in the diet, as uptake of β-carotene is facilitated by full-fat foods;
- the amount of fibre in the diet, as uptake of β-carotene is impeded by dietary fibre;
- digestive and intestinal health of the consumer;
- smoking;
- LDL cholesterol levels; and
- natural broad fluctuations in β-carotene in fruits and vegetables due to seasonal and geographical variations.

The result of this large number of variables impacting on levels of β-carotene is a broad natural range. This is reflected in nutritional data from the United States in the National Health and Nutrition Examination Survey (NHANES III)[4] published in 1999 using a pool of over 22,000 individuals. Although the data reflect United States levels, they are indicative of the range that would at least be expected in the Australian and New Zealand populations, on the basis of a reasonable expectation that consumption of fruits and vegetables is equal to or higher in New Zealand/Australia than in the United States.

For all individuals (ages 4 to 71+), serum β-carotene levels ranged from 3.0 μg/dL at the lowest (1st percentile) level, to 82.6 μg/dL at the highest (99th percentile) level. The mean serum level was identified at 18.9 μg/dL. The data also show that for adults in the target age range (over 40 years of age), the difference in serum β-carotene levels between the 1st percentile and the 5th percentile is almost 100% (i.e. a doubling overall). Therefore, even for consumers of phytosterol-enriched foods already down at 5th percentile level for serum β-carotene, a decrease of 20-25% would be relatively insignificant and not place them outside of the existing broad natural range.

Vitamin A is obtained either directly from foods (eg. milk, fish liver oils) or from fruits and vegetables that contain the main precursor β-carotene (as well as α-carotene and β-cryptoxanthin), which is converted into retinol in the body. Vitamin A levels therefore are an appropriate measure of the sufficiency of β-carotene as a nutrient in the diet. Where the levels of vitamin A remain unchanged following consumption of foods enriched with plant sterols, a measurable decrease in serum β-carotene that is linked to the decrease in LDL cholesterol is expected and not a cause for concern.

[4] Institute of Medicine (2000). *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*, page 448-449

Antioxidant status and chronic disease

The carotenoids have received much attention in terms of their antioxidant properties. Beta-carotene has historically been the focus of studies to elucidate the potential role of antioxidants in association with a range of diseases including cardiovascular disease and cancers. However, as previously discussed in the Draft Assessment Report, studies on the antioxidant effects of β-carotene have yielded disappointing findings. The studies were largely based on early evidence from observational studies of dietary carotenoid intake in fruits and vegetables.

A recent scientific review by Fairfield and Fletcher[5] evaluates a range of studies in which the antioxidant properties of β-carotene were examined in the context of cancers (particularly lung, colorectal, prostate and breast) and coronary heart disease. In all cases, the significance of the association of β-carotene with these diseases has been moderated because of the lack of a direct cause and effect relationship. On the antioxidant role of carotenoids, the review states: '…some caution must be used in interpreting the findings [of carotenoid studies]. Associations between diet and disease in observational studies may be due to the specific carotenoids, other vitamins or compounds in fruit and vegetables, or substitution for dietary meat and fat. Genetic predisposition, underlying nutritional status, smoking, and tissue-specific effects may be important'.

FSANZ has considered a number of published studies provided by submitters on β-carotene levels in patients with diabetes. In general the studies do not report a direct causal relationship between low serum β-carotene and diabetes. Type II diabetes is a chronic disease in which a host of metabolic disturbances are manifest. In addition, the studies generally do not assess confounding dietary factors, accommodate for serum cholesterol levels or account for other significant risk factors such as genetic background, obesity, a sedentary lifestyle, consumption of alcohol or smoking.

As noted in the Nutrition Assessment (at Attachment 4), β-carotene is one of a host of plant nutrients with potential antioxidant activity. Others include vitamin C, vitamin E and lycopene which are not affected by consumption of plant sterols. Lycopene is the dominant carotenoid compound in tomatoes, although the content differs between varieties and increases as the fruit ripens. Despite the restricted occurrence in foods, lycopene is the most abundant carotenoid in human plasma (Kaplan *et al*. 1987) and various tissues, and has significantly higher antioxidant activity than β-carotene.

Therefore, at the present time, the totality of evidence does not support the view that a potential reduction of up to 20-25% in serum β-carotene levels following phytosterol intake could be considered a health risk.

5.8.3 Yoghurt products

At Draft Assessment, FSANZ proposed that phytosterol ester-enriched yoghurt would be (i) limited to a maximum container size of 140 g; and (ii) allowed a maximum fat content of 3 g per 100 g food.

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[5] Fairfield, K.M. and Fletcher R.H. (2002). Vitamins for Chronic Disease Prevention in Adults, JAMA **287**, 23:3116-3126.

In addition, permission to use phytosterol esters in drinking yoghurt was explicitly excluded. Several submitters have raised a number of minor issues with respect to drafting of the proposed permission for low-fat yoghurt.

The New Zealand Food Safety Authority has advised that a single serve punnet of yoghurt in New Zealand generally contains 150 g, not 140 g as stipulated in the Draft Assessment Report. The National Heart Foundation conducted a small survey on punnet sizes in Australia and NZ and found that manufacturers use a range of single serve container sizes up to 200 g for almost all currently available yoghurt products. They contend that the proposed limitation on punnet size is therefore overly restrictive, particularly as the dietary modelling assumed the whole category of yoghurts was phytosterol enriched, which resulted in highly conservative exposure estimates.

Dairy Australia and Nestlé Australia Ltd questioned the need to exclude drinking yoghurts from the proposed regulations, when the composition of these products is virtually identical to traditional yoghurt. In addition, the National Heart Foundation has identified that the total fat content of low-fat liquid products can contain no more than 1.5 g/100g according to the Code of Practice on Nutrient Claims (CoPoNC). Moreover, a level of 3 g total fat/100 g does not represent low-fat yoghurts in the marketplace.

5.8.3.1 Response

The proposed limitation on the container size for yoghurt is being proposed to assist consumers with a quantity of yoghurt equivalent to one serve of phytosterol esters. FSANZ initially considered that in simplifying a single serve of phytosterol-enriched foods, consumers would be more aware of appropriate amounts to consume, thus contributing to the effectiveness of the risk management messages.

However, 1.3 g (one serve) of phytosterol esters can be incorporated into a single serve container of yoghurt of several different sizes, without increasing the amount of phytosterols consumed. Moreover, as the products will be targeted primarily to adults, a punnet size larger than the proposed 140g is likely to be more appropriate, especially for adult males. Therefore, FSANZ acknowledges the unnecessary restrictions that this limitation would place on food manufacturers, and has accordingly made minor changes to the drafting to allow a container size up to a maximum of 200g for yoghurt.

In addition, as drinking yoghurt is substantially similar to yoghurt, FSANZ agrees that the exclusion on drinking yoghurts was not justified, particularly where the restrictions on container size would also apply to these products. Finally, FSANZ acknowledges that it is appropriate to treat low-fat yoghurt and low-fat yoghurt beverage in the same way and therefore a maximum fat content of 1.5g/100g is consistent with the existing CoPoNC specifications.

The amended drafting for this Application, incorporating these minor changes, is at **Attachment 1**.

5.8.4 Production variations

The Australian Food and Grocery Council (AFGC) noted that, at Draft Assessment, the proposed permissions for phytosterol esters in low-fat milk and low-fat yoghurt was fixed at 5.2 g/litre and 1.3 g /punnet respectively. The Council points out that this does not allow for any production variations, so milk containing 5.18 g/litre would not technically be permitted. A similar argument applies also to manufacturing variations for yoghurt products. Dairy Australia advises that production can introduce variations in ingredients up to 10% of specified amounts.

5.8.4.1 Response

FSANZ acknowledges that production variations occur as a normal part of food manufacture and therefore agrees to make minor amendments to the drafting in order to standardise the regulations across all phytosterol-enriched foods. The current permissions for addition of phytosterols to edible oil spreads allow use up to a prescribed maximum level, and this approach has been applied to breakfast cereal under Application A433. Consequently, minor changes have been incorporated into the drafting (at **Attachment 1**) to permit the use of phytosterol esters in low-fat milk and low-fat yoghurt to no more than a prescribed maximum level for each food type.

These changes will have no effect on consumers of phytosterol-enriched foods, but are more practical in terms of enforcement and provide a less restrictive manufacturing environment for the food industry.

5.8.5 Mandatory advisory statements

The National Heart Foundation (NHF) expresses the view that the mandatory advisory statements proposed at Draft Assessment may raise unnecessary concerns in consumers in relation to the safety of phytosterol-enriched foods that are not justified on the basis of the available scientific information. In particular, the NHF recommends that the statement referring to infants, children and pregnant or lactating women should be modified to reflect that the caution for these non-target groups is related to effects on blood carotene levels, and not due to any direct harmful effects of phytosterols.

The NHF also considered that the requirement for an increased number of mandatory advisory statements on packaging represents an unnecessary labelling burden on food manufacturers.

5.8.5.1 Response

FSANZ is conscious of the number and complexity of mandatory advisory statements for phytosterol-enriched foods recommended for inclusion under Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations. However, three of the four mandatory advisory statements recommended at Draft Assessment are already in force for the edible oil spreads and margarines, and manufacturers are accustomed to their use on packaging. The additional statement relating to the optimal number of serves of phytosterol enriched foods is considered desirable as part of the educational process while consumers adjust to the greater choice of phytosterol-enriched foods in the marketplace.

FSANZ has adopted a cautious approach to the extension of the permissions for use of phytosterols esters and tall oil phytosterols, and does not consider the requirement for an additional statement as overly burdensome on manufacturers. Indeed, none of the submissions from the food industry have raised this as an issue of concern to them. On the contrary, all of the applicants (Goodman Fielder, Dairy Farmers and Parmalat Australia) and other submissions from industry express support for the labelling provisions outlined at Draft Assessment, including the mandatory advisory statements.

When all proposed risk management measures and industry initiatives are in place, consumers will have many avenues for obtaining information about phytosterol-enriched foods to enable them to make an individual choice on the suitability of the products for their dietary needs. Review of the existing mandatory advisory statements already in force as part of this assessment concluded that the current statements are warranted, as they provide consumers with information about phytosterol-enriched products in direct association with the foods in question.

5.8.6 Dietary exposure data

It was noted in several submissions that the dietary exposure assessment used consumption data derived from the National Nutrition Survey (NNS) conducted in Australia in 1995 and in New Zealand in 1997. They contend that the information used to model potential consumption of phytosterol-enriched foods is therefore outdated and cannot be considered reliable or reflective of current eating patterns.

5.8.6.1 Response

FSANZ is aware of the lapse of time since the previous National Nutrition Survey and of the urgent need to generate new survey data that documents the changes that may have occurred in the eating patterns of consumers over the last decade. However, when considering the foods encompassed by the current phytosterol applications (namely breakfast cereal, low-fat milk and low-fat yoghurt) FSANZ considers that minimal change is likely to have occurred since the mid 1990’s in terms of consumption of these foods, as they were already established, staple foods in both New Zealand and Australia. The data and information provided by the previous surveys in this case is likely to be appropriate and valid for current times.

5.8.7 Consumption by adolescents

The Dietitians Association of Australia considers that adolescents are increasingly being diagnosed with hypercholesterolaemia and are therefore a population group who may potentially consume large quantities of plant sterol enriched foods.

5.8.7.1 Response

The dietary exposure assessment included adolescents in modelling performed for the whole population (2+ years for Australia and 15+ years for New Zealand). In addition, the modelling looked specifically at females in the 16-44 year age group in both countries. Due to a number of assumptions on which the modelling is based (for example, that *all foods* in the relevant category would contain plant sterols), the dietary exposure estimates are highly conservative.

Based on these results and the conclusions from the nutrition assessment, FSANZ considers that there are no safety concerns for non-target consumers of phytosterol-enriched products, even at the 95th percentile level of exposure.

5.8.8 Long term studies

The New Zealand Dietetic Association, the Public Health Association of Australia and others noted that there is currently only one published study that considers usage of phytosterol-enriched foods for one year. The remainder of studies evaluate phytosterols over shorter periods of consumption.

5.8.8.1 Response

This issue was discussed in the Draft Assessment Report (see Attachment 7). FSANZ considers that there is a considerable weight of evidence in support of the safety of phytosterol esters from the published studies conducted over varying periods of time from 4 weeks up to 1 year, using plant sterols, sterol esters, stanols and stanol esters in quantities that would often exceed expected daily consumption. Extensive toxicological information was available and assessed by FSANZ in 1999, prior to the approval of phytosterol esters and tall oil phytosterols as novel food ingredients in 2000. None of the clinical parameters measured indicate a potential for more significant effects over a longer period of exposure.

Phytosterols are only poorly absorbed by the body, and there have been no reports of adverse effects, although sterol- and stanol- enriched foods have been on the market in Europe for over 10 years. A reduction in serum carotenoids with consumption of phytosterol esters is the most reported effect, however this is partially compensated by consuming nominally 5 serves per day of fruits and vegetables where at least one serve is rich in carotenoids. The clinical studies have shown that the effects on carotenoids are rapidly reversed when there is no consumption of phytosterols.

5.8.9 Case-by-case assessments

Queensland Health and South Australia express disappointment that phytosterol ester-enriched foods are being assessed on a case-by-case basis, rather than through a broader, holistic approach in which resources of government, industry and other stakeholders could be utilised more efficiently.

On the other hand, the National Heart Foundation considers it important to consider each category of food separately in order to determine appropriate qualifying criteria.

5.8.9.1 Response

Although there is no consideration of a health claim for the phytosterol Applications (A433, A434 & A508), manufacturers are currently labelling products containing plant sterols in such a way that the cholesterol lowering effects of plant sterols are openly communicated to consumers. When originally approved under the novel foods Standard, evidence of safety and efficacy was only available for the edible oil spreads and margarines. Since this time, further studies using other specified food matrices have reported similarly efficacious cholesterol lowering effects.

The CSIRO clinical studies demonstrate a variable cholesterol lowering response with food matrices such as fibre-increased bread, breakfast cereal, low-fat milk and low-fat yoghurt, although all of these foods are efficacious to some extent. In terms of ensuring truth in marketing statements therefore, there is a need for manufacturers to provide evidence that supports any claims relating to their products. A case-by-case approach ensures that there is evidence to support the manufacturers statements in the marketing of phytosterol enriched foods, and facilitates a cautious expansion of the use of these novel food ingredients on the basis of a limited history of use.

5.8.10 Safety of plant sterols

A scientific reference[6], provided by Valerie James (NZ), reports on the comparative health effects of phytosterol enriched margarines on rats with a genetic predisposition to haemorrhagic stroke. The authors claim that the results of their study suggest plant stanols provoke haemorrhagic stroke in stroke-prone spontaneously hypertensive (SHRSP) rats to a slightly greater extent than plant sterols.

5.8.10.1 Response

An earlier study by the same authors (Ratnayake *et al.*) using plant sterols (not stanols) was considered by FSANZ in 2000 as part of the safety assessment of phytosterol esters derived from vegetable oils as a novel food ingredient. These studies are not relevant in terms of studying the effects of consumption of phytosterols in humans eating a normal diet.

The use of SHRSP rats as a model for investigating the effects of phytosterols in humans was considered inappropriate for several reasons. Firstly, the genetic strain of rat used in these studies has been developed as a model for the study of haemorrhagic stroke and displays an abnormally high intestinal absorption rate and decreased biliary excretion of phytosterols, resulting in the over-accumulation of phytosterols in the body. This is not representative of the situation in humans. Secondly, the rats also have abnormally low cholesterol levels and benefit from the inclusion of cholesterol in their diet, factors which confound the significance of the results with respect to morbidity and mortality from stroke. It has therefore been suggested that the SHRSP rat strain could more appropriately be used as a model for phytosterolaemia, a very rare inherited disease in humans (see Attachment 4).

In terms of published studies, it has been consistently reported that there is only very low absorption of plant sterols in humans. At levels of phytosterol intake up to 3.3 g/day or in the long-term (1 year) plasma phytosterol levels represented less than 1% of the total sterols in plasma. This pattern was reinforced by the findings of the CSIRO studies, which reported an increase in the measured levels of the major sterols in plasma following consumption of various food vehicles containing the sterol esters, although the absolute levels of plant sterols in plasma remained low.

The conclusion from a large number of observational studies is that there is no association between total blood cholesterol and risk of stroke and that lowering of blood cholesterol levels will not increase the likelihood of stroke.

[6] Ratnayake, W.M., Plouffe, L., L'Abbe, M.R., Trick, K., Mueller R. and Hayward, S. (2003) Comparative health effects of margarines fortified with plant sterols and stanols on a rat model for hemorrhagic stroke. Lipids, **38** (12): 1237-47.

6. Regulatory Options

6.1 Option 1 – do not permit the use of phytosterol esters in low-fat milk and low-fat yoghurt

This option maintains the status quo by not permitting the use of phytosterol esters in low-fat milk and low-fat yoghurt, while retaining the current permission on the use of phytosterols in edible oil spreads and margarines only.

6.2 Option 2 – approve the use of phytosterol esters in low-fat milk and low-fat yoghurt

This option will result in an amendment to the Code to permit the addition of phytosterol esters at specified levels to a low-fat milk and a low-fat yoghurt product under Standard 1.5.1.

6.3 Option 3 – approve the general use of phytosterol esters

This option will result in an amendment to the Code to permit the use of phytosterol esters as ingredients in foods to a maximum permitted level.

7. Impact Analysis

7.1 Affected parties

- consumers, especially target population groups such as adults over 40 years of age with health concerns about high blood cholesterol, and non-target population groups such as children and pregnant or lactating women;
- dietitians and allied health professionals providing dietary advice to consumers;
- the manufacturing and retail sectors of the food industry; and
- Government generally, where a regulatory decision may impact on trade or WTO obligations, and State, Territory and New Zealand enforcement agencies.

7.2 Impact Analysis

In the course of developing food regulatory measures suitable for adoption in Australia and New Zealand, FSANZ is required to consider the impact of all options on all sectors of the community, including consumers, the food industry and governments in both countries. The regulatory impact assessment identifies and evaluates, though is not limited to, the costs and benefits of the proposed regulation, including the likely health, economic and social impacts.

The following analysis of the costs and benefits of the identified regulatory options is based on an assessment of the information supplied by the applicant and from public submissions to FSANZ, as well as knowledge from the previous considerations relating to the use of phytosterol esters in the food supply. The relative costs and benefits may be different for sub-groups of consumers.

7.2.1 Option 1

Option 1 provides no major benefits to consumers. As permission to use phytosterol esters would apply only to edible oil spreads and margarines, there may be a limited benefit in terms of reducing the possibility of excessive intakes of phytosterol containing foods.

Option 1 represents a potential cost to adult consumers in terms of restricting the choice and availability of phytosterol-enriched food products, particularly for those who are actively seeking dietary measures to reduce the risk of cardiovascular disease, or who find the current edible oils spreads and margarines unsuitable. Similarly, there is an identifiable cost to the food industry in terms of a restriction to product range, and limiting associated marketing opportunities.

There would be no immediate impact on government if the status quo is maintained.

7.2.2 Option 2

Option 2 represents potential benefits to consumers especially in the target group in terms of access to a greater range of phytosterol-enriched food products. Dietitians and other health professionals may also benefit from a broader permission to use phytosterols in foods because of the availability of products that may be more compatible with individual needs and general ‘healthy diet’ messages to the public. The costs to consumers not in the target group is likely to be minimal, because of the mandatory labelling statements that would be required on phytosterol enriched low-fat milk and yoghurt products.

Option 2 also provides potential benefits to food manufacturers in terms of increased product range and potential greater market share. In addition, there are potential marketing opportunities for food retailers.

In terms of a potential impact on Government, Option 2 is unlikely to have any significant impact on monitoring resources, as there is already a permission for use of phytosterols in edible oil spreads and margarines.

7.2.3 Option 3

In terms of the target consumer group, option 3 would provide the greatest range of phytosterol ester-enriched products. At the same time, a broad permission would be likely to increase the possibility of over-consumption by the target group, and inappropriate consumption by non-target consumer groups, because of the likely significant expansion of products (based on information from overseas applications) and a significantly increased presence in the marketplace of products enriched with plant sterols. Furthermore, increased intake of phytosterols is not associated with an increased benefit in terms of lowering cholesterol, and therefore option 3 may be confusing or misleading for consumers, especially in relation to the amount of phytosterol enriched products required to achieve the optimal cholesterol-lowering effect. The risk management strategies proposed in this application may not be as successful where the range of available products is unrestricted, and therefore the costs would be more likely to apply to consumers in general, rather than only to non-target groups.

Option 3 provides benefits to the food industry in that it represents the least restrictive regulation of phytosterols in the food supply, allowing the greatest innovation of products (within inherent technological limitations). However, there is likely also to be costs to manufacturers associated with a broader approval in terms of increased competition in the marketplace for products that are aimed only at a defined group of consumers, albeit a group that is likely to grow in size as the population ages. Thus, by definition, the potential market is smaller than for products aimed at a more general market. In addition, as phytosterol esters are costly ingredients to produce, a broad product range directed at a limited consumer market may mean that Option 3 is likely to be less viable economically for manufacturers.

In terms of government resources, unrestricted use of phytosterol esters in foods would broaden enforcement requirements generally.

8. Consultation

8.1 Public consultation

8.1.1 First round

FSANZ received sixteen submissions in response to the Initial Assessment Report. Seven of the submitters supported approval for the use of phytosterol esters in low-fat milk and low-fat yoghurt, subject to assessments for nutritional safety and dietary exposures. Of those in favour, several supported a general permission to use phytosterol esters in foods. Submitters in favour included the food industry, The Australian Dairy Corporation, food technologists, and the Dietitians Association of Australia.

Six submissions were opposed to the application, primarily because of safety or nutritional concerns. Submitters not in favour of the application included Queensland Health, nutritionists, and the New Zealand Dietetics Association.

Summaries of first round public submissions and responses to the major issues identified in these submissions are at **Attachment 7**.

8.1.2 Second round

The Draft Assessment Report was open for public comment for a period of 9 weeks, and FSANZ received twenty-two submissions (summaries at **Attachment 8)**. The submitters encompassed a broad cross-section of the community including government (Departments of Health and advisory bodies), non-government organisations (National Heart Foundation, Public Health Association), organisations representing health professionals (New Zealand Dietetics Association, Dietitians Association of Australia), the food industry (Dairy Australia, the Australian Food and Grocery Council, Unilever, Nestlé, Masterfoods, Sanitarium), and members of the general public including health professionals.

In general, submissions either supported all three Applications (A433, A434 & A508), or opposed all applications.

More than half of the submissions were in favour of broadening the permission for the use of phytosterol esters to low-fat milk and low-fat yoghurt. Those in favour included individual health professionals and their organisations, food technologists and food manufacturers.

Most submissions supported the mandatory advisory statements and conditions of use proposed by FSANZ as risk management strategies to promote appropriate use of the foods by consumers. However, food manufacturers generally considered some elements of the proposed permissions overly restrictive.

Eight submissions were opposed to the broader use of phytosterols. In general, broadening the range of phytosterol-enriched foods was considered unnecessary or inappropriate for addressing diet related health issues. Concerns about the nutritional aspects of phytosterol-enriched foods were also expressed.

The issues identified in the public submissions have been addressed in section 5.8 of this Report. Several minor changes to drafting (at **Attachment 1**) are recommended for clarification, as a result of the public consultation.

8.2 World Trade Organization

As members of the World Trade Organization (WTO), Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade. This enables other member countries of the WTO to make comment.

Amending the Code to permit the use of phytosterol esters derived from vegetable oils as novel food ingredients in low-fat milk and low-fat yoghurt will not be notified to the WTO under either the Technical Barrier to Trade (TBT) or Sanitary and Phytosanitary Measure (SPS) agreements, as the permission is unlikely to have a significant effect on international trade, particularly since FSANZ would be expanding an existing permission. There are no relevant international standards and the potential food uses of phytosterol esters under the proposed variation are limited in terms of market size. Because the products containing phytosterol esters may be more expensive, the products are likely to be targeted at consumers looking for foods with particular attributes.

9. Conclusion and Recommendation

FSANZ recommends the approval of the use of phytosterol esters derived from vegetable oils in low-fat milk and low-fat yoghurt, subject to specified conditions of use, for the following reasons:

- there are no anticipated public health and safety concerns associated with the use of phytosterol esters derived from vegetable oils in low-fat milk and low-fat yoghurt when used in conjunction with the risk management measures proposed;

- there is evidence that phytosterol esters derived from vegetable oils can, following consumption, reduce levels of cholesterol in humans when incorporated into low-fat milk and low-fat yoghurt products;

- the nutrition assessment indicates that phytosterol esters derived from vegetable oils have no significant adverse nutritional effects at the proposed levels of use. The reductions in the absorption of β-carotene are within the normal variation which results from physiological and environmental factors;

- conditions of use, including an additional labelling statement, are proposed as part of a comprehensive risk management strategy to ensure appropriate use of phytosterol-containing foods by the target consumers, and to discourage use by non-target consumers;

- the proposed changes to the Code are consistent with the section 10 objectives of the FSANZ Act; and

- the Regulatory Impact Statement indicates that, for the preferred option, namely, to approve the use of phytosterol esters derived from vegetable oils as novel food ingredients in low-fat milk and low-fat yoghurt, the benefits of the proposed amendment outweigh the costs.

The proposed drafting to the *Australia New Zealand Food Standards Code* is shown at Attachment 1 to the Draft Assessment Report.

10. Implementation and review

Following consideration and approval of the Final Assessment Report by the FSANZ Board, a notification will be made to the Ministerial Council and it is anticipated that this will be completed by the end of 2004. The amendments to the Code with respect to Standard 1.5.1 – Novel Foods, and other relevant Standards, would come into effect shortly thereafter upon gazettal, subject to any request from the Ministerial Council for a review.

The existing stock-in-trade provisions allow a period of 12 months for industry to comply with the new labelling requirements for all phytosterol enriched foods.

ATTACHMENTS

1. Draft variations to the *Australia New Zealand Food Standards Code*
2. Food Technology Report
3. Safety Assessment Report
4. Nutrition Assessment Report
5. Dietary Exposure Assessment – Application A434
6. Dietary Exposure Assessment – Applications A433 & A434
7. Summary of issues in first round public submissions and FSANZ responses
8. Summary of second round public submissions

ATTACHMENT 1

Draft Variations to the *Australia New Zealand Food Standards Code*

To commence: On gazettal

[1] ***Standard 1.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in* column 2 *of the* Table to clause 2 *corresponding to the entry for* Phytosterol esters –

May only be added to milk in accordance with Standard 2.5.1. May only be added to yoghurt in accordance with Standard 2.5.3.

[2] ***Standard 2.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting after the* Editorial note *to clause 4 –*

5 Phytosterol Esters

Phytosterol esters may only be added to milk –

(a) that contains no more than 1.5 g/100 g of milkfat; and
(b) that is supplied in a package, the labelled volume of which is no more than 1 litre; and
(c) where the total phytosterol ester added is no more than 5.2 g/litre of milk.

[3] ***Standard 2.5.3*** *of the Australia New Zealand Food Standards Code is varied by inserting after the* Editorial note *to clause 3 –*

4 Phytosterol Esters

Phytosterol esters may only be added to yoghurt –

(a) that contains no more than 1.5 g total fat per 100 g; and
(b) that is supplied in a package, the capacity of which is no more than 200 g; and
(c) where the total phytosterol ester added is no more than 1.3 g.

ATTACHMENT 2

FOOD TECHNOLOGY REPORT

APPLICATIONS A433 AND A434 - PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS

Introduction

Phytosterols (plant sterols) are natural components of cereals, fruits, vegetables and edible vegetable oils such as sunflower seed oil and, as such, are natural constituents of the human diet.

Incorporation of free sterols into edible fats/oils is not readily achieved because of their insolubility, whereas sterols esterified to fatty acids are more fat soluble. In the intestine, most sterol esters are hydrolysed to free sterols as part of the normal digestive process. Plant stanols are the hydrogenated counterparts of the plant sterols but are less abundant in nature than the corresponding plant sterols. Consequently, the normal dietary intake of plant stanols is much less than that of plant sterols [1].

These Applications are an extension to a previous Application (A410), which resulted in the approval for the use of phytosterol esters, sourced from vegetable oils, in edible oil spreads and margarines to a maximum amount of 13.7%. The Applicants are seeking to extend the use of phytosterol esters into new food matrices, namely breakfast cereals, low-fat milk and low-fat yoghurt products. The phytosterol esters under consideration in Applications A433 and A434 are identical to those previously assessed within A410.

Structure of plant sterols and stanols

Plant sterols have a role in plants similar to that of cholesterol in mammals, e.g. forming cell membrane structures. Plant sterols fall into one of three categories: 4-desmethylsterols (no methyl groups); 4-monomethylsterols (one methyl group) and 4,4-dimethylsterols (two methyl groups). The most common plant sterols are ß-sitosterol, campesterol and stigmasterol and structurally these are very similar to cholesterol, belonging to the class of 4-desmethylsterols (Fig. 1, reference 1).

Plant stanols belong to the group of 4-desmethylsterols. Plant stanols are hydrogenation products of the respective plant sterols, e.g. campestanol/campesterol and ß-sitostanol/ ß-sitosterol (Fig. 1), and are found in nature at very low levels.

When edible oils undergo normal refining, plant sterols are partially extracted together with some tocopherols (in the process of natural vitamin E production). It is estimated that 2500 tonnes of vegetable oil needs to be refined to produce 1 tonne of plant sterols [1]. Plant stanols are obtained by hydrogenation of the plant sterols. Another source of plant sterols is tall oil, derived from the process of paper production from wood and approximately 2500 tonnes of pine is required to produce 1 tonne of plant sterols. Tall oil also contains a higher proportion of plant stanols (primarily ß-sitostanol) than do vegetable oils [1].

In nature, plant sterols can be in the free form or predominantly esterified with long chain fatty acids or with phenolic acids as in rice bran oil (ferulates) and shea butter (cinnamates). In the intestine, most sterol esters are hydrolysed to free sterols as part of the normal digestive process [1]. Details provided in the applications and from comparable products internationally indicate that 1.3 g of the phytosterol esters is equivalent to 0.8 g of free phytosterols.

Production of phytosterol esters

Phytosterols are by-products from the traditional vegetable oil refining process. The crude vegetable oil is refined to remove solvents (if used in extraction), lecithins, free fatty acids, colour, and various off-odours and off-flavours. One of these refining steps is steam distillation (deodorisation) where the resulting distillate contains the phytosterol fraction. This fraction is further refined to remove fatty acids, lecithins and other compounds by fractional distillation, ethanolysis/transesterification, distillation and crystallisation from an organic solvent. The phytosterols are further purified by recrystallisation. These processes are considered standard methods traditionally used for the production of phytosterols.

The phytosterol esters are then produced from the phytosterols using food grade vegetable oil-derived fatty acids or triglycerides and applying standard methods for esterification or transesterification commonly used in the fats and oils industry [8].

Solubility

The solubility of phytosterols in edible oil products is relevant for other food matrices. The solubility of free sterols in oil is around 2 percent, while the solubility of sterol esters in oil exceeds 20 percent. Therefore, the free plant sterols are typically esterified with fatty acids from sunflower to improve solubility.

For foods such as milk, yoghurt and cereal, the esters are preferred to free phytosterols since they have improved solubility properties in oils, analogous to their solubility in edible oil spreads. For the dairy products, low-fat milk and low-fat yoghurts, the phytosterol esters are initially solubilised in a vegetable oil base which is then dispersed and homogenised into the milk, in a similar fashion to the production of low-fat milk. For breakfast cereal bars, the esters are directly added to the mixture as an ingredient during manufacture.

Phytosterol ester-enriched products are produced using the same processes and procedures as the corresponding conventional products. The additional processing step controls the amount and quality of the phytosterol esters incorporated into the product prior to further processing (including heat treatment).

The improved solubility of phytosterol esters creates a palatable product and is associated with more uniform distribution both in the product and in the gastrointestinal tract.

Stability

The physical and chemical properties of phytosterols are similar to cholesterol, since they differ only with respect to the side chain. Phytosterols and their fatty acid esters are basically very stable compounds and experience only limited damage during processing [3].

Phytosterols and phytosterol esters are known to be stable to both oxidation and heat, and remain unchanged during product processing, including the various pasteurisation treatments used to produce milk and yoghurt type products. The applicants state for the milk and yoghurt type products these treatments are:

- standard treatment for milk products (HTST – High Temperature Short Time pasteurisation) 76°C for 15 seconds
- high temperature treatment for extended shelf life milk products (UHT - Ultra High Temperature) 143°C for 4 seconds
- batch pasteurisation for yoghurt mix, 90°C for 15 minutes.

The chemical and microbial stability of the milk and yoghurt type products with added phytosterol esters have been found to be similar to standard products[5].

Specifications

Free sterols are obtained from the vegetable oil refining process where they are recovered from the steam distillate in the deodorisation process. All commercially available vegetable oil sterols are obtained by similar methods, and the esterification process is standard throughout the industry.

The specification for phytosterol esters derived from vegetable oils is the same as that given in the earlier application A410 and which is contained in Standard 1.3.4 – Identity and Purity of the *Australia New Zealand Food Standards Code* is as follows:

Specification for phytosterol esters derived from vegetable oils

Phytosterol esters are phytosterols derived from edible vegetable oils esterified with long-chain fatty acids derived from edible vegetable oils.

Phytosterol esters + free phytosterols (%)	min. 94	
Free phytosterols (%)	max. 10	
Steradienes (%)	max. 0.3	
Fatty acid methylester (%)	max. 0.5	
Iron, Fe (ppm)	max. 1.0	
Copper, Cu (ppm)	max. 0.5	
Moisture (%)	max. 0.1	
Trans fatty acids (%)	max. 1.0	
Sterol profile (%) as below:		
Cholesterol	min. 0.0	max. 2.0
Brassicasterol	min. 0.0	max. 6.0
Campesterol	min. 20.0	max. 29.0
Campestanol	min. 0.0	max. 6.0
Stigmasterol	min. 12.0	max. 23.0
β-Sitosterol	min. 42.0	max. 55.0
β-Sitostanol	min. 0.0	max. 2.5
D5-Avenasterol	min. 0.0	max. 4.0
D7-Stigmastenol	min. 0.0	max. 2.0
D7-Avenasterol	min. 0.0	max. 2.0
Other	min. 0.0	max. 6.0

References

1. Phytosterol Esters (Plant Sterol And Stanol Esters) The Institute of Food Science & Technology UK , Information Statement, June 2000.

2. Food and Drug Administration 21 CFR Part 101, Food Labeling: Health Claims; Plant Sterol/Stanol Esters and Coronary Heart Disease; Interim Final Rule, September 8 2000.

3. Ferrari R A, Esteves W, Mukherjee K D, Schulte E (1997) Alterations of sterols and steryl esters in vegetable oils during industrial refining. Journal of Agricultural and Food Chemistry, 45, 4753-4757.

4. Hicks, K.B. and Moreau, R.A. (2001) Phytosterols and Phytostanols: Functional Food Cholesterol Busters. Food Technology, 55, 63-67.

5. Lea, L. (July 2002) Phytosterol-Esters: Use in a Range of Food Products Volume 1 of 3. Unilever UK document D02-018 (application to the UK Food Standards Agency to include phytosterol esters to 'milk' and 'yoghurt' type products).

6. Colebank, S. (31/3/03) The Rising Stock of Sterols & Stanols. www.naturalproductsinsider.com/articles/341FunctionalFood.html

7. European Commission, Scientific Committee on Food. General view on the long-term effects of the intake of elevated levels of phytosterols from multiple dietary sources, with particular attention to the effects on ß-carotene. SCF/CS/NF/DOS/20 ADD 1 Final (3 October 2002).

8. European Commission, Scientific Committee on Food. Opinion on an application from ADM for approval of plant sterol-enriched foods. European SCF/CS/NF/DOS/23 ADD2 Final (7 April 2003).

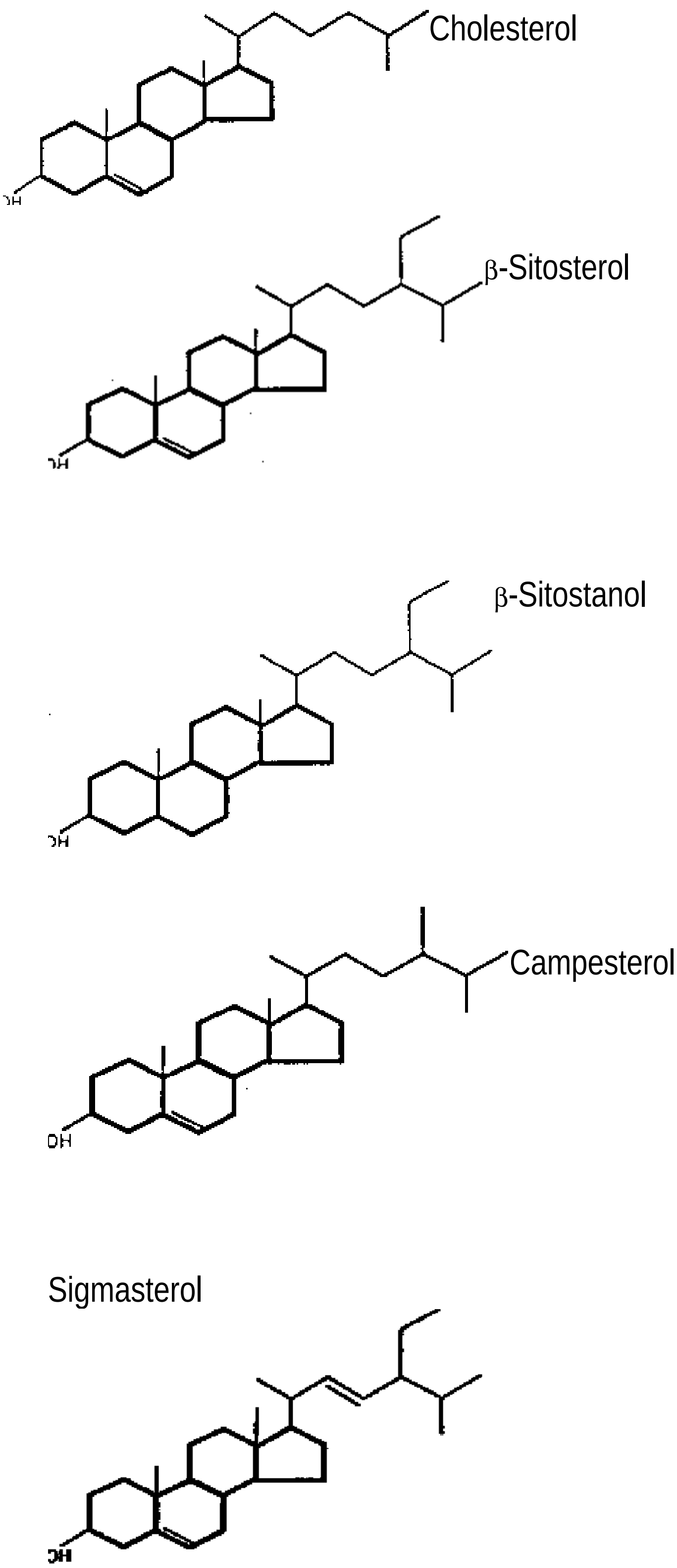

Fig. 1
Structure of cholesterol and some common phytosterols and phytostanols (taken from ref 1).

ATTACHMENT 3

SAFETY ASSESSMENT REPORT

APPLICATION A433 – PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN LOW-FAT MILK & YOGHURT

1. Introduction

Dairy Farmers are seeking a variation to Standard 1.5.1 – Novel Foods, to permit the use of phytosterol esters derived from vegetable oils as novel food ingredients in low-fat milk and a low-fat yoghurt.

2. Previous safety consideration

Phytosterol esters are a novel food ingredient currently permitted for use in edible oil spreads and margarine up to a level of 13.7% (w/w). This is equivalent to 8% (w/w) free phytosterols. Phytosterols are naturally occurring plant compounds that have been reported to reduce blood cholesterol levels by inhibiting the absorption of dietary cholesterol. Phytosterols are naturally found in common vegetable oils and spreads at a level of 0.1 – 0.9% (w/w).

The permission to use phytosterol esters in table spreads and margarine was based on data and information on the safety of phytosterol esters assessed in 2001 within Application A410. The conclusions of the safety assessment report were:

1. The studies presented provide no evidence of adverse toxicological effects associated with consumption of phytosterol esters up to a level of 1.6 g free phytosterol/day over a l-year period, although the data do indicate a potential for phytosterols to reduce plasma levels of carotenoids in humans.

2. The data available do not allow the potential risk of carotenoid deficiency that may be associated with consumption of high levels of phytosterols to be assessed. Reduced carotenoid uptake is a potential risk for children and lactating women.

3. The available data indicate that plasma cholesterol levels are reduced by approximately 5% and LDL cholesterol levels by 7-8% when phytosterol esters are consumed in edible oil spreads at a level equivalent to 1.6 g free phytosterols/day over a 1-year period. There are no data available in relation to their effectiveness in this regard when present in other foods.

4. The data available to address the potential long-term effects of phytosterols in humans are limited. While there are 3-4 week studies at several dose levels, the 1-year human study has been conducted at only one dose level. Further studies at higher dose levels would provide more confidence in both the safety of this product and in its capacity to maintain long-term reductions in plasma cholesterol levels.

3. Cholesterol metabolism

Cholesterol is a natural component of animal cell membranes as well as being a precursor for the synthesis of the steroid hormones and bile acids.

Both dietary cholesterol (mostly contained in egg yolks and animal fat) and that synthesized in the body (*de novo*) are transported through the circulation in lipoprotein particles, and stored in cells as cholesteryl esters. Both the synthesis and use of cholesterol is tightly regulated in order to prevent over-accumulation and abnormal deposition within the body. Deposition of cholesterol and cholesterol-rich lipoproteins in the coronary arteries is a major risk factor for disease, in particular atherosclerosis.

3.1 Biosynthesis of cholesterol

Slightly less than half of the cholesterol in the body derives from *de novo* biosynthesis. The liver accounts for approximately 10% and the intestine approximately 15% of the amount synthesized on a daily basis. Cholesterol is synthesized from acetyl-CoA, which is mainly produced in the mitochondria from fatty acid oxidation or from pyruvate and then transported to the cytoplasm. The biosynthetic pathway consists of four major steps to form squalene which then undergoes a two-step cyclisation to yield lanosterol which, in turn, is ultimately converted to cholesterol through a series of additional reactions.

3.2 Regulating cholesterol synthesis

The greatest proportion of cholesterol is used in bile acid synthesis. A relatively constant level of cholesterol in the body (150-200 mg/dL) is maintained by controlling the level of *de novo* synthesis. Normal healthy adults synthesise cholesterol at a rate of approximately 1 g/day and consume approximately 0.3 g/day. The level of cholesterol synthesis is regulated in part by the dietary intake of cholesterol and feedback inhibition of biosynthetic pathways. When dietary intake of cholesterol is high, hepatic cholesterol synthesis is decreased, and vice versa. However, the feedback compensation is incomplete, because a diet low in cholesterol and saturated fat leads to a modest decline in circulating blood cholesterol. The cellular supply of cholesterol is maintained at steady levels by several distinct mechanisms including the regulation of plasma cholesterol levels via LDL receptor-mediated uptake and HDL-mediated reverse transport.

3.3 Transport of cholesterol

Dietary cholesterol is transported from the small intestine via lymphatic ducts to the liver as chylomicrons. Cholesterol is transported in the plasma predominantly as cholesteryl esters associated with lipoproteins. Most of the cholesterol synthesized by the liver as well as any surplus dietary cholesterol in the liver is incorporated into very low density lipoprotein (VLDL) which eventually becomes low-density lipoprotein (LDL) in the circulation. LDLs provide cholesterol to the tissues to be utilized as an essential constituent in cell membranes and by gland cells to make steroid hormones. Cholesterol acquired from peripheral tissues is absorbed and transported as high-density lipoprotein (HDL).

3.4 Absorption of cholesterol

On a moderate fat intake, 95% or more of the ingested fat is absorbed. Cholesterol is readily absorbed from the small intestine if bile, fatty acids and pancreatic juice are present. Closely related sterols of plant origin are poorly absorbed. Almost all the absorbed cholesterol is incorporated into chylomicrons that enter the circulation through the lymphatics. Poorly absorbable plant sterols such as those found in soybeans reduce the absorption of cholesterol, probably by competing with cholesterol for esterification with fatty acids.

3.5 Cholesterol and bile metabolism

One of the predominant mechanisms for excretion of cholesterol is in the bile as free cholesterol, or as bile salts following conversion of excess amounts to bile acids in the liver. However, the excretion of cholesterol in the form of bile acids is insufficient to compensate for an excess of dietary intake of cholesterol. Bile acids are carried from the liver through the bile ducts to the gallbladder, where they are stored for future use. The ultimate fate of the bile acids is secretion into the intestine where they aid in the emulsification of dietary lipids by rendering fats accessible to pancreatic lipases, and facilitate the intestinal absorption of fat-soluble vitamins (vitamins A, D, E and K). Once in the gut, they undergo chemical modification and are either excreted in small amounts or reabsorbed by the gut and returned to the liver for recycling in the bile (enterohepatic circulation). The synthesis, and subsequent excretion of bile acids through the faeces represent the only significant mechanism for the elimination of excess cholesterol.

The entire bile salt pool of approximately 3.5 g recycles repeatedly via the enterohepatic circulation; it has been calculated that the entire pool recycles twice per meal and 6-8 times per day.

3.6 Fat digestion and absorption

Dietary fats are finely emulsified in the small intestine by the detergent action of the bile salts, lecithin and monoglycerides. When the concentration of bile salts in the intestine is high, as it is after contraction of the gall bladder, lipids and bile salts interact spontaneously to form micelles. Micellar formation further solubilises lipids and provides a mechanism for their transport to the enterocytes. Within the enterocytes, the lipids are rapidly esterified, maintaining a favourable concentration gradient from the intestinal lumen into the cells.

The fate of the fatty acids in enterocytes depends on their size. Fatty acids with less than 10-12 carbon atoms pass from the mucosal cells directly into the portal blood, where they are transported as free (unesterified) fatty acids. The fatty acids with more than 10-12 carbon atoms are re-esterified to triglycerides in the mucosal cells. In addition, some of the absorbed cholesterol is esterified. The triglycerides and cholesteryl esters are then coated with protein, cholesterol and phospholipids to form the chylomicrons which leave the cell and are transported to the liver.

3.7 Relation to atherosclerosis

Cholesterol is a major factor in the development of atherosclerosis which in turn predisposes to heart attack, cerebral thrombosis, and other major diseases. In individuals with elevated plasma cholesterol levels, there is an increased incidence of atherosclerosis and associated complications.

The normal range for plasma cholesterol is reportedly 120-220 mg/dL, but in men there is a clear, tight, positive correlation between the death rate from ischemic heart disease and plasma cholesterol levels above 180 mg/dL. There is now a consensus view that lowering plasma cholesterol slows the progression of atherosclerosis and may also inhibit thromboses, by reducing the risk of rupture of atherosclerotic plaques. Individuals with elevated LDL cholesterol have a higher than normal incidence of cardiovascular disease, whereas individuals with elevated HDL cholesterol have a lower incidence.

In general, HDL cholesterol levels are higher in those who exercise or drink 1-2 alcoholic drinks per day, whereas they are decreased in those who smoke, are obese, or live sedentary lives.

4. Phytosterols in other foods

4.1 General safety issues

4.1.1 Effects of dietary phytosterols on blood cholesterol levels

Studies submitted:
P.M. Clifton, P.J. Nestel and D.R. Sullivan. . CSIRO Health Sciences and Nutrition (South Australia), Baker Medical Research Unit (Melbourne) and Royal Prince Alfred Hospital (Sydney), June 2002.
LDL Cholesterol Lowering with Phytosterol Ester-enriched Bread, Cereal, Milk and Yoghurt in a Multi-centre Trial (Study 1) and The Effect of Consuming Higher Dietary Intakes of Phytosterol Esters Over an Extended Period in Mildly Hypercholesterolaemic People (Study 2).
Study audits carried out by NHMRC Clinical Trials Centre, 14 November 2002.

Study 1 – LDL cholesterol lowering with phytosterol ester-enriched bread, cereal, milk and yoghurt in a multi-centre trial

The objective of this study was to investigate whether consumption of certain phytosterol ester-enriched low fat foods leads to a reduction in serum cholesterol in mildly hypercholesterolaemic adults. The study was conducted at three centres, Melbourne, Adelaide and Sydney, and involved both women and men with slightly raised cholesterol levels. The subjects consumed specially prepared trial foods (bread, breakfast cereal, milk and yoghurt) containing specified amounts of phytosterols, and control foods not enriched with phytosterols, over a twelve week period. The trial foods provided the equivalent of 1.6 g per day of free phytosterols (equivalent to 2.6 g/day phytosterol esters).

Fifty-eight (35 females and 23 males) volunteer subjects were allocated to a diet in a randomized, incomplete crossover, single blind study consisting of four treatment periods of three weeks each, one of which was a control period. The subjects were selected on the basis of certain health criteria including

- Age 20-75 years
- Body Mass Index (BMI) < 31
- Total serum cholesterol >5.0 mmol/L and <7.5 mmol/L
- No lipid lowering medication
- No diabetes
- Normal thyroid status and no metabolic disorder other than hyperlipidaemia
- Not taking medications likely to affect lipid metabolism and no clinical requirement for such medication
- No history of metabolic disease
- Serum triglycerides <4.5 mmol/L
- No strong aversion and no known allergies/intolerances to the foods involved.

The study provided three active periods, in which one of the four phytosterol-enriched foods was tested per period, and one control period in which none of the four foods were enriched with phytosterol esters. During the three active periods all other test foods were supplied in their non-enriched form.

An outline of the dietary regime managed by each study centre over the duration of the study is presented in Table 1.

Table 1. Arrangement of test and control diets in each study centre.

	Adelaide (n = 22)	**Melbourne** (n = 18)	**Sydney** (n = 18)
Baseline (2 weeks)	Each subject's usual diet (baseline)		
Period 1 (3 weeks)	**Sterol – Yoghurt** Control – cereal, milk, bread	**Sterol – Milk** Control – cereal, bread, yoghurt	**Sterol – Yoghurt** Control – cereal, bread, milk
Period 2 (3 weeks)	**Control – All 4 foods**	**Sterol – Bread** Control – milk, cereal, yoghurt	**Sterol – Bread** Control – cereal, yoghurt, milk
Period 3 (3 weeks)	**Sterol – Cereal** Control – milk, yoghurt, bread	**Sterol – Cereal** Control – milk, bread, yoghurt	**Sterol – Cereal** Control – yoghurt, bread, milk
Period 4 (3 weeks)	**Sterol – Milk** Control – cereal, yoghurt, bread	**Control – All 4 foods**	**Control – All 4 foods**

Thus by food type, phytosterol-enriched yoghurt was tested twice (n=40), phytosterol-enriched milk was tested twice (n=40), phytosterol-enriched bread was tested twice (n=36), and phytosterol-enriched cereal was tested three times (n=58).

Food requirements

Serve sizes per day for each subject were yoghurt 200g, bread (white) 2 slices, cereal (muesli style) 45g, milk (2% fat, extended shelf life) 500 ml. The phytosterol enrichment of the test foods was such that each serve contained 1.6 g phytosterols. All subjects were requested to consume one serve of each food per day.

Food composition

Each of the control foods was analysed for relevant nutrient composition including energy, protein, fat (total, saturated, monounsaturated, polyunsaturated), carbohydrate (total and sugars), dietary fibre, calcium, sodium and potassium. The nutrient composition data presented for the test (phytosterol-enriched) foods were estimations based on calculations using the values for the control foods or other available data. The phytosterol content of the test foods was adjusted so that the equivalent of 1.6 g free phytosterols were available per serve per day.

The major sterol composition was beta-sitosterol, campesterol and stigmasterol, in descending order of abundance. All of the test foods were enriched with phytosterol esters, with levels expressed as the free sterol equivalent.

Monitoring and measurements

Serum lipids (total cholesterol, HDL cholesterol, triglycerides) were determined on two consecutive days at the end of each period (week 2, 5, 8, 11, 14) from venous blood samples taken after subjects fasted overnight (12 h). Plasma phytosterols were measured at the end of each period for the control, bread and milk periods in Melbourne, control and bread periods in Sydney and all periods in Adelaide. In addition, subjects were requested to complete a daily checklist of foods to monitor compliance during the periods and assess micronutrient intakes. Subjects were also provided the opportunity to report any adverse events throughout the course of the study.

Analyses

At the end of the study, all samples from each subject were analysed within the same experimental run in order to reduce reagent and instrument variation. Total cholesterol and triacylglycerols were measured using enzymatic kits and standard control sera, while plasma HDL cholesterol concentrations were measured using standard techniques. The LDL cholesterol concentration (mmol/L) in each sample was calculated from the values for total cholesterol, triacylglycerols and HDL cholesterol obtained in the laboratory analyses.

Plasma phytosterols were determined by gas chromatography and concentrations were calculated using an internal standard and reference samples of lathosterol, campesterol and sitosterol.

Results

The average age of the 58 subjects who completed the trial was 54 years. The average weight was 74 kg and there was an average gain of 0.9 kg ($p<0.01$) over the 12 weeks of the study. The food checklists indicated that dietary compliance averaged 96%, 94% and 99% respectively across the three study centres.

The effect of the phytosterol-enriched test foods on total cholesterol for each study period and centre is summarised in Table 2. The analytical results indicate that serum total cholesterol levels were lowered by phytosterol consumption in milk by 0.53 mmol/L (9.7%), and in yoghurt by 0.42 mmol/L (5.6%). Similarly, LDL cholesterol levels were lowered by phytosterol consumption in milk by 0.53 mmol/L (15.9%), and in yoghurt by 0.42 mmol/L (8.6%).

Table 2. Effect of test foods containing 1.6 g/day of phytosterols – Total cholesterol (mmol/L) at the end of each study period and at baseline (expressed as mean)

Centre	Baseline	Milk	Bread	Control	Cereal	Yoghurt
Melbourne (n=18)	6.16 (4.8-7.8)	5.90 (5.0-8.0)	6.38 (5.2-8.6)	6.50 (5.5-8.8)	6.36 (5.3-8.4)	ND
SD	± 0.83	± 0.74	± 0.81	± 0.86	± 0.80	
% change from control		-9.2	-1.8		-2.2	
Adelaide (n=22)	6.46 (4.8-8.2)	5.90 (4.7-8.0)	ND	6.60 (5.3-8.4)	6.29 (5.0-8.8)	6.23 (4.9-7.2)
SD	± 0.78	± 0.71		± 0.67	± 0.65	± 0.66
% change from control		-10.6			-4.7	-5.6
Sydney (n=18)	6.05 (5.3-7.2)	ND	5.78 (4.8-7.1)	6.14 (5.3-7.2)	6.00 (5.4-7.6)	5.80 (4.9-6.8)
SD	± 0.52		± 0.65	± 0.59	± 0.66	± 0.57
% change from control			-5.9		-2.3	-5.5
Combined	6.24	**5.90***	**6.08***	**6.43**	**6.23***	**6.04***
Total	58	40	36	58	58	40
SD	± 0.74	± 0.71	± 0.79	± 0.71	± 0.71	± 0.65
% change from control		-9.7	-3.9		-3.2	-5.6

* p<0.05 compared with control period
% change refers to the relevant control period in the 2 or 3 centres
ND = not done

The changes in serum lipids when phytosterol-containing cereal foods were consumed were similar, with LDL cholesterol levels reduced by 6.5% for bread and 5.4% for breakfast cereal. The changes in LDL cholesterol associated with phytosterol-enriched bread differed by a factor of two between study centres (i.e. 4.3% reduction in Melbourne vs. 9.6% reduction in Sydney), although the differences are not statistically significant. In the Adelaide and Sydney groups, there was no statistically significant difference between phytosterol-enriched bread, cereal and yoghurt in terms of lowering cholesterol.

Serum HDL cholesterol levels fell from baseline (established at the beginning of the study) to the control period by 0.05 mmol/L ($p<0.01$) which the study authors relate to the small mean weight gain (0.9 kg) observed over the duration of the study. HDL cholesterol levels rose significantly by 4.7% in the phytosterol-enriched bread period compared with control periods. When data from all study centres was combined, serum triglyceride levels did not change during the study. These results are summarised in Table 3.

Table 3. Effect of test foods containing 1.6 g/day of phytosterols – mean LDL cholesterol (mmol/L), HDL cholesterol (mmol/L) and Triglycerides (mmol/L), combined data from all centres

Combined	Baseline N=58	Milk N=40	Bread N=36	Control N=58	Cereal N=58	Yoghurt N=40
LDL cholesterol	4.03	**3.74***	**3.85***	4.27	**4.03***	**3.85***
SD	± 0.71	± 0.69	± 0.74	± 0.73	± 0.66	± 0.61
% change from control		- 15.9	- 6.5		- 5.4	- 8.6
HDL cholesterol	**1.50***	1.43	**1.50***	1.46	1.44	1.46
SD	± 0.41	± 0.32	± 0.40	± 0.37	± 0.42	± 0.41
% change from control		- 0.7	+ 4.7		+2.4	+1.2
Triglycerides	1.58	1.60	1.63	1.64	1.58	1.62
SD	± 0.73	± 0.63	± 0.87	± 0.77	± 0.85	± 0.83
% change from control		-9.7	-3.9		-3.2	-5.6

* $p<0.05$ compared with control period
% change refers to the relevant control period in the 2 or 3 centres

Absorption of phytosterols

The levels of phytosterols (campesterol and sitosterol) were measured in plasma for selected food periods in all three centers. Periods utilizing milk and bread as the active foods were selected due to their varying cholesterol-lowering effects. Measurement of plasma phytosterols indicates the availability for absorption of the phytosterols, without implying any correlation with their effects on serum lipids. Plasma lathosterol was also measured as an indicator of cholesterol synthesis.

Combining the information from all study centres, the results of these analyses show that plasma lathosterol levels did not change irrespective of the food period, whether active or control. At all centers, there were highly significant increases in the plasma levels of both campesterol (range of 24-52%) and sitosterol (range of 16-32%). Some data suggest that milk and bread apparently delivered similar amounts of phytosterols to the blood, but there was insufficient data to observe a pattern across all of the study centres. However, there was no relationship between the change in cholesterol levels and the change in levels of sitosterol and campesterol. Subjects who absorbed phytosterols well, did not appear to have a correspondingly better response to phytosterols than those who absorbed phytosterols poorly and/or had higher cholesterol synthesis (as assessed by lathosterol levels).

There are no findings reported in the study in relation to the monitoring of any adverse effects in any of the participants during the test-food periods.

Study 2 – The effect of consuming higher dietary intakes of phytosterol esters over an extended period in mildly hypercholesterolaemic people

The objective of this study was to measure the effects on serum lipids, fat-soluble vitamins (vitamins A, D and E only), plasma phytosterols, plasma carotenoids and other physiological/biochemical parameters in humans of diets comprising a maximum of 6.6 g/day free phytosterols, when compared to a corresponding diet without phytosterol-enriched foods. The three test foods used in this study were phytosterol ester-enriched bread, breakfast cereal and table spread. The study also aimed to quantitatively investigate the effect on plasma carotenoids of additional dietary fruits and vegetables when co-consumed with foods delivering 6.6 g/day free phytosterols (equivalent to 10.7 g/day phytosterol esters).

Thirty-five mildly hypercholesterolaemic women and men were recruited into this study which was conducted over 16 weeks at two clinical research centres, one in Adelaide and one in Melbourne. As in the first study, subjects were required to comply with a specified list of health criteria. Ten subjects from the first study (Melbourne centre) continued into Study 2 after completing a control period and a 1-week gap between studies.

All subjects undertook dietary regimens in a non-randomised manner and were instructed not to consume self-purchased phytosterol-enriched products during the course of the study. The study was single blind and foods were appropriately coded. The dietary periods of the study are presented in Table 4.

Food requirements

Test and control foods were supplied by Goodman Fielder. Full compliance with the study diet was designed to contribute a total of approximately 6.6 g/day of phytosterols as follows:

- 3 x 5 g (15 g) reduced fat spread – 2.1 g/day
- 3 slices of white bread – 2.4 g/day, and
- 1 serve (60 g) of cereal (muesli) – 2.1 g/day

Table 4. Dietary regimes

Time period	Description
Weeks 1 & 2 - **Baseline** Control (2 weeks)	Usual diet plus **phytosterol-free** forms of test foods (bread, breakfast cereal and spread) at the same quantities as the next two periods.
Weeks 2-8 **Period 1** Sterol-enriched food (6 weeks)	Usual diet plus **phytosterol-enriched** bread, breakfast cereal and spread contributing 6.6 g/day phytosterols.
Weeks 9-14 **Period 2** Sterol-enriched food plus additional fruit and vegetables (6 weeks)	Usual diet plus **phytosterol-enriched** foods (as above) with **additional vegetable and/or fruit** intake.*
Weeks 15-16 **Period 3** Free living (sterol wash-out) (2 weeks)	Usual diet plus **phytosterol-free** forms of test foods at the same quantities as the previous two periods.

* Dietary advice was given to consume at least 5 serves of fruit/vegetables every day, with at least 1 serve of either pumpkin, sweet potato, carrot, tomato, apricot, broccoli, spinach (1 serve = half a cup).

In determining the food requirements for the study, the authors based the calculations on dietary intake estimates (DIAMOND program, FSANZ) from the 1995 Australian National Nutrition Survey and using the food categories of liquid milks, yoghurts, table spreads, breakfast cereals and plain breads, based on the fortification level of 0.8 g free phytosterols per serve. The mean Australian phytosterol intake from these categories was calculated to be 3.0 g/day, while the estimated intake at the 95th percentile was 6.8 g/day. For compliance reasons, the authors restricted the scope of the study to three phytosterol-enriched foods providing a daily free phytosterol intake of 6.6 g/day.

Food composition

The major nutrient composition of the three foods (bread, cereal and spread) and the phytosterol-enriched counterpart was determined either by analysis, calculation or from other sources of available data. It was noted that the control spread supplied only trace amounts of phytosterols per day (based on normal dietary intakes) that are naturally present in the oil. All test foods were enriched with phytosterol esters with the major sterols beta-sitosterol, campesterol, and stigmasterol in descending order of abundance.

Monitoring and measurements

Serum lipids (total cholesterol, HDL cholesterol, triglycerides) were determined on two consecutive days at the end of each period (week 2, 8, 14, 16). LDL cholesterol levels were calculated. Plasma carotenoids, plasma fat-soluble vitamins (A, D and E) and plasma phytosterols were measured at the end of each period (as above).

A range of physiological parameters were also measured as biochemical safety indicators of the higher daily phytosterol intake. These measurements included:

- full blood count
- routine biochemistry (electrolytes, glucose, urea and creatinine, calcium, phosphate, liver function test, clotting tests-prothrombin, partial thromboplastin test
- routine urinalysis (protein, blood, white cells, pH, bilirubin and glucose)

In addition, as in Study 1, subjects were requested to complete a daily checklist of foods to monitor compliance during the periods and assess micronutrient intakes. Weight and height of subjects were determined at entry to the study and weights were measured at each visit to the clinic. As before, subjects were also provided the opportunity to report any adverse events throughout the course of the study.

Analyses

Venous blood samples were collected from subjects that had fasted overnight (12 hrs). Total cholesterol, triacylglycerols, HDL and LDL cholesterol were all determined as previously described (see page 21).

Vitamins and carotenoids were extracted and analysed using HPLC techniques according to published methods. All samples from each subject were extracted in duplicate and analysed in one run to minimize experimental variation. Reference standards were trans α- and β-carotene, lycopene, lutein, retinal, α-tocopherol and α-tocopherol acetate.

As in the first study, plasma phytosterols were determined by gas chromatography and concentrations were calculated using an internal standard and reference samples of lathosterol, campesterol and sitosterol.

Results

All 35 subjects (23 females and 12 males) completed the 16 weeks of the study. The average age of the subjects in Adelaide was 53.3 years and there was a mean increase in weight of 0.36 kg over the duration of the study. In Melbourne, the average age was 59.7 years and weight fell by a mean 0.09 kg over the 16 weeks period.

The authors report that compliance with the dietary regimes was above 95% for all periods, except for the washout period (Period 3) at one study centre, where it fell to around 70%. Compliance with the additional fruit and vegetable intake (total of 5 per day) in Period 2 at the two study centers was 83% and 86% respectively.

There were no significant changes in total dietary fat, saturated fat, or energy between the periods in the study. Beta-carotene intake increased by 41% in Melbourne (p=0.001) and fibre intake also increased by 2 g/day (p=0.04) from period 1 to period 2. Similarly, in the Adelaide group, β-carotene intake increased by 23% (p=0.023) and fibre intake increased by 3.3 g/day (p=0.002) from period 1 to period 2.

The effects of higher daily consumption of phytosterol-enriched foods (containing 6.6 g/day in this study compared to 1.6 g/day in Study 1) on serum lipids (total cholesterol, triglycerides, HDL and LDL cholesterol) are presented in Table 5.

Table 5. Effect of diets containing 6.6 g/day phytosterols on serum lipids (mmol/L), combined data from both study centres (Mean ±SD)

	Baseline period (2 weeks)	**Period 1** (6 weeks)	**Period 2** (6 weeks)	**Period 3** (washout-2 weeks)
Total cholesterol	6.59 ± 1.01	6.04 ± 0.73*	6.03 ± 0.84*	6.42 ± 0.97
% change		**–8.3**	**–8.5**	
HDL cholesterol	1.35 ± 0.38	1.38 ± 0.38	1.40 ± 0.40	1.39 ± 0.41
Triglycerides	1.81 ± 0.96	1.71 ± 0.87	1.67 ± 0.93	1.62 ± 0.99
LDL cholesterol	4.46 ± 0.91	3.95 ± 0.80*	3.88 ± 0.70*	4.31 ± 0.91
% change		**–11.4**	**–13.0**	

* Values are significantly different from relevant baseline and washout values (p<0.05)

The (combined) serum lipids results in this study indicate a reduction in total cholesterol (down approximately 8%) and LDL cholesterol (down approximately 12%) following consumption of foods containing 6.6 g/day of phytosterols over a period of 12 weeks.

This level of cholesterol reduction was measured at the end of period 1, after 6 weeks of consuming phytosterol-enriched bread, cereal and table spread on a daily basis, and was maintained for the test period. At the conclusion of the study, after a 2 weeks washout period in which no phytosterol-enriched products were consumed, serum lipids were not significantly different from the baseline measurements at the beginning of the study, indicating that the cholesterol lowering effects are not maintained in the absence of the phytosterol-enriched foods.

Effects of food matrix

The magnitude of the cholesterol-lowering effect from consumption of 6.6 g/day phytosterols in enriched bread, cereal and table spread, is similar to the observed effect in Study 1 when subjects consumed 1.6 g/day phytosterols in low-fat milk. In addition, as the authors note, the magnitude of the effect is also similar to that reported in the literature in which intakes of 3.2 g/day of phytosterol or phytostanol esters were consumed in margarines (Westrate & Meijer, 1998). These results and those from other published studies suggest that there is an upper limit for efficacy in terms of the potential to lower serum cholesterol that is related to the food matrix in which the phytosterols are consumed. For example, where the food matrix is bread and cereal only, more than 1.6 g/day of phytosterols may be required to achieve a reduction in serum lipids similar to that which can be achieved when milk is used as the vehicle. However, data demonstrating that bread and cereal alone can achieve the effectiveness of low-fat milk (at 1.6 g/day) or margarine (at 3.2 g/day) are not presented here.

Plasma phytosterol levels

At both study centers, the increase in levels of campesterol and sitosterol in the blood after periods 1 and 2 when compared to baseline levels was highly significant. For campesterol, the increase was approximately 99% after period 1 and rose to approximately 110% at the end of period 2. Sitosterol levels also increased by approximately 40% at period 1 and by approximately 50% at period 2 compared to baseline levels. Plasma campesterol remained higher than baseline after two weeks of washout in both study centers, suggesting that the kinetics of the two compounds are different.

These changes in the levels of circulating phytosterols are similar to those reported in several other studies using phytosterol-enriched foods, and generally show a linear relationship to the levels of phytosterols in the diet. However, the absorption of phytosterols from the gut is still very low compared to the absorption of cholesterol.

The plasma lathosterol levels showed a significant increase (13%, $p=0.002$) after period 1 and approximately 16% increase after period 2 when compared to the starting levels, but fell significantly back to baseline in the washout period. A high lathosterol level is an index of high cholesterol synthesis and concomitantly low cholesterol absorption so that phytosterols would be expected to be less effective at lowering cholesterol absorption in subjects with both low cholesterol absorption and high cholesterol synthesis. The dynamics of the total cholesterol response therefore is dependent on numerous physical and physiological factors and subject to individual variation.

Biochemical analyses

Full routine biochemistry covering urea, creatinine, electrolytes, calcium and liver function tests were performed at all visits corresponding to the end of each period in the study. Changes in enzymes such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT) can indicate liver stress and are expected to occur in a small number of subjects (about 3%) in large-scale trials using cholesterol-lowering statin drugs. A comparison was therefore considered of particular interest in this study.

Measured haematology parameters included: haemoglobin, red cell count, packed cell volume, mean cell volume, mean cell haemoglobin, mean cell haemoglobin concentration, red blood cell distribution width, platelet count, mean platelet volume, white cell count, neutrophils (%), absolute neutrophil count, lymphocytes (%), absolute lymphocyte count, monocytes (%), absolute monocyte count, eosinophils (%), absolute eosinophil count, basophils (%), absolute basophil count.

Coagulation parameters included: prothrombin time, ratio, activated kaolin partial thromboplastin time.

Biochemical parameters included: sodium, potassium, chloride, bicarbonate, glucose, urea, creatinine (blood), urate, phosphate, calcium, ionised calcium, albumin (blood), total protein (albumins and globulins), total bilirubin, gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), alanine aminotransferase (ALT), L-aspartate aminotransferase (AST), lactate dehydrogenase (LD), creatine kinase (CK), magnesium, and 25-hydroxy vitamin D (the major circulating form of vitamin D).

Results

On combined haematological data from both centres (maximum number of 35 subjects), there were no changes in full blood count or clotting profile observed from baseline (after week 2) to the end of period 1 (at week 8), the end of period 2 (at week 14) and the end of period 3 (washout). The number of subjects that were outside of the normal range for any particular parameter was also recorded. These data indicate that generally a small number (1-3) of measurements were outside the expected range, but these were randomly spread across parameters and across the study periods and therefore no pattern of change was detected.

In the biochemical analyses, an increase in ALT values was noted in one subject for whom normal levels were initially recorded at baseline. The rise to double normal levels was only detected at 12 weeks, and disappeared upon withdrawal of phytosterols. In another subject, there was an increase in GGT and ALP levels, for whom abnormal levels were initially recorded at baseline. The authors note that GGT is not normally measured in drug trials, as the levels are very sensitive and are prone to change for no apparent reason. Furthermore, the change in ALT levels was considered inconsequential and did not occur at a frequency greater than expected from chance alone. There were no other changes in plasma biochemistry recorded at any period in the study.

Four subjects (out of 35) were found at baseline with vitamin D deficiency. However, no significant changes with ingestion of phytosterol-enriched foods were observed for the duration of the study.

Urine was tested with dipsticks in the 23 subjects at the Adelaide study centre. Seven subjects were found to have abnormal results at baseline. In general, there were a variety of abnormalities that appeared and disappeared throughout the study but none of these changes could be statistically related to phytosterol intake.

Plasma carotenoids and fat-soluble vitamins

Plasma carotenoids and plasma fat-soluble vitamins (A, D and E) were measured at the end of each study period at week 2, 8, 14 and 16. The combined results from both study centres for measurements of lutein, retinol, α-tocopherol, vitamin D, lycopene and α and β-carotene are presented in the Nutrition Safety Assessment at **Attachment 4**.

Conclusions from the clinical studies

The results of these studies indicate that consumption of any of the four test foods providing approximately 2.6 g/day phytosterol esters, can result in a measurable decrease in total cholesterol and LDL cholesterol in mildly hypercholesterolaemic people. The greatest cholesterol-lowering effect was measured when the test food vehicle was milk, followed by phytosterol-enriched yoghurt, with bread and cereal exhibiting the smallest effect. The results therefore suggest that phytosterol-enriched bread and breakfast cereals are less effective food vehicles for achieving a lower blood cholesterol level than phytosterol-enriched milk.

Consumption of all phytosterol-enriched foods tested in this study resulted in a statistically significant increase in the absorption of phytosterols compared to the control period, although the levels in plasma remained very low. These results are consistent with other published studies. The authors suggest that the results obtained in Adelaide, where plasma phytosterol levels increased more when milk was used as the vehicle, may indicate that milk-delivered phytosterols are more bioavailable.

As no treatment-related changes in biochemical parameters were detected, the results of the CSIRO studies indicate that phytosterol esters may be consumed safely in amounts up to approximately 10.7 g/day, when incorporated into foods such as low-fat milk, low-fat yoghurt, fibre-increased bread and breakfast cereal.

ATTACHMENT 4

NUTRITION ASSESSMENT REPORT

APPLICATION A433 – PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN BREAKFAST CEREALS
APPLICATION A434 – PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN LOW-FAT MILK & YOGHURT

1. Introduction

The aim of this review is to evaluate information on the potential nutritional effects of phytosterols in the diet arising from the proposed fortification of breakfast cereals and low-fat dairy products. This review forms part of the assessment of two applications submitted to Food Standards Australia New Zealand (FSANZ) requesting permission to add 1.3 g of phytosterol esters per serve to breakfast cereal bars, low-fat milk and low-fat yoghurt products.

Currently, only phytosterol-enriched edible oil spreads are available in both New Zealand and Australia, and are being promoted as foods that can lower cholesterol absorption.

This review considers data from recently conducted studies and other currently available information on the nutritional safety of plant sterols if consumed in a broader range of products such as the proposed low-fat milk, low-fat yoghurt and breakfast cereal. Unless otherwise stated, this report refers to phytosterol amounts in their esterified form.

2. Potential effect of phytosterols on antioxidant absorption

2.1 Sources and roles of antioxidants

Antioxidants are defined as substances that, when present at low concentrations compared with those of an oxidisable substrate, significantly prevent or delay oxidation of the substrate. This may mean that the presence of an antioxidant can inhibit or slow down a biological process involving an oxidation reaction. Dietary antioxidants may inhibit oxidative damage to proteins, lipids, carbohydrates and DNA *in vivo* which are of major interest in nutritional research.

Food-derived antioxidants, mostly from dietary plants, can exert a range of possible beneficial effects. This has been demonstrated clearly for α-tocopherol and vitamin C (Handbook of Antioxidants, Eds. E. Cadensas and L. Packer, 2002). Many hundreds of compounds present in food may act as antioxidants, in a variety of different ways depending on their particular physico-chemical properties. It is possible for an antioxidant to protect (against oxidation) in one biological or food system, but to fail to protect or even sometimes promote oxidative damage in others.

As well as some of the vitamins, a class of plant compounds known as the carotenoids (including α- and β-carotene, lycopene, β-cryptoxanthin, zeaxanthin, lutein) may function as antioxidants, although in most instances their antioxidant roles are not well-defined. Some of the carotenoids, α- and β-carotene and β-cryptoxanthin, are precursors of vitamin A.

As carotenoids are essentially hydrophobic molecules, the uptake of carotenoids in the intestinal mucosal cells is aided by the formation of bile acid micelles in the lumen of the small intestine. Plant sterols lower blood cholesterol by reducing the absorption of dietary and biliary cholesterol, and therefore might be associated with reduced absorption of some fat-soluble vitamins (such as vitamin E), and the lipophilic carotenoids (such as β-carotene). The assessment of the potential nutritional effects of phytosterol-enriched foods therefore focuses on the effects of plant sterols on the circulating levels of carotenoids and fat-soluble vitamins.

2.2 Vitamin A - Retinol

Vitamin A is a fat-soluble vitamin important for vision, immunity, growth and as an antioxidant. Vitamin A activity can be obtained from two classes of compounds – retinol and some carotenoids. The adult recommended dietary intake (RDI) of vitamin A is 750μg of retinol equivalents per day. The estimated average requirements (EAR) for vitamin A is 500μg for men and 400μg for women. Although plasma retinol concentrations are used as an indicator for vitamin A status, due to a homeostatic mechanism, they are insensitive and fall only in the later stages of deficiency. Vitamin A deficiency is common in developing countries, affecting vision with xerophthalmia and night blindness.

2.3 β-Carotene and other carotenoids

Carotenoids are the basic source of yellow, orange and red plant pigments, and are most commonly consumed as components of fruit and vegetables (Basu 2001). β-Carotene and other carotenoids are classified as either provitamin A or nonprovitamin A carotenoids. The provitamin A carotenoids (α-carotene, β-carotene and β-cryptoxanthin) can be converted into retinol. The function of these carotenoids includes antioxidant activity.

Non-provitamin A carotenoids such as lycopene, lutein and zeaxanthin have been suggested through observational studies to be inversely associated with some chronic diseases such as heart disease and cancer (Basu 2001).

2.3.1 Sources

The predominate dietary sources of carotenoids are fruits and vegetables. Sources of β-carotene include dark green leafy vegetables and yellow or orange fruits and vegetables including carrots, kale, silver beet, spinach, pumpkin/squash, sweet potato, apricots, mango and watermelon (Lister 2003).

2.3.2 Absorption

The carotenes are normally ingested in a food matrix, which is critical to their absorption. Their chemical structure, with a hydrocarbon backbone, renders them insoluble in water and they must be in the form of micelles in order to be absorbed in the intestinal tract.

The presence of fat in the small intestine stimulates the secretion of bile from the gall bladder and increases the size of micelles, in turn facilitating the uptake of carotenes into the intestinal mucosa. Once in the mucosal cells, the carotenes are incorporated into chylomicrons for transport in the lymphatic system. The uptake of carotenes through the mucosal cells is via passive diffusion.

2.3.3 Bioavailability

The bioavailability of dietary carotenes depends on

i) digestion of the food matrix;
ii) formation of lipid micelles in the gastrointestinal tract;
iii) uptake of carotenoids by mucosal cells; and
iv) transport of carotenoids and their products to the lymph or portal circulation.

The source of carotenoids is also a factor in their bioavailability. Synthetic carotenoids (as dietary supplements) are absorbed far more readily than those that occur naturally in foods. Studies have indicated that up to 70% of synthetic carotenoids are absorbed compared with only 5% of naturally-occurring ingested carotenoids.

Bioavailability is optimized when dietary fat is consumed during the same period as the carotenoid. The processing and cooking of fruits and vegetables also affect bioavailability. Carotenoids are less available from raw than cooked fruits and vegetables, and processing techniques such as mechanical homogenization have also been shown to enhance the bioavailability of β-carotene (Cadenas 2002).

2.3.4 Contribution of β-carotene to Vitamin A intake

There are no known adverse health effects from consuming a diet low in carotenes provided that there is adequate retinol in the diet. The contribution from consumption of β-carotene equivalents[7] to vitamin A is about 50% in both Australia and New Zealand according to National Nutrition Surveys in both countries.

2.3.5 Seasonal variation

Fruits and vegetables are the main source of carotenoids in the diet. As might be expected from the seasonal nature of many fruits and vegetables, it has been observed that there is a concomitant seasonal variation in serum carotenoids (and thus retinol) levels in humans. This was confirmed in a study investigating seasonal variation in serum nutrient levels in 111 healthy individuals. The study reported significant differences ($p<0.05$) in serum concentrations of α-carotene, β-carotene and β-cryptoxanthin across a seasonal time scale, with both α and β-carotene levels higher in summer and β-cryptoxanthin levels higher in winter. Plasma β-carotene levels could vary naturally up to 50% between seasons (Omedilla 1994).

[7] β-carotene equivalents = µg β-carotene + (0.5 µg other provitamin A carotenoids)

In addition to seasonal variation in β-carotene levels, weekly variation has also been observed in individuals. In a 12-week Australian study where consecutive blood samples were collected from 12 subjects, the intra-individual and inter-individual variation was 39 and 36% respectively (Lux 1994). Following the initial study period, blood samples were taken monthly for the following six months showing a peak of plasma β-carotene in the months of spring.

2.3.6 Carotenoids and chronic disease

Epidemiological studies have indicated that people with higher intakes of fruits and vegetables may have a reduced risk of heart disease, stroke or some cancers compared with those with lower intakes. With such apparent broad health benefits, research has focussed on the antioxidant components and properties of such diets. Recently, a study into the health benefits of citrus fruit[8] reported that many of the major diseases of concern in Australia and New Zealand have a dietary component. These include cardiovascular conditions such as atherosclerosis, heart disease and stroke, cancers, obesity, dental caries, asthma, periodontal disease, type-2 diabetes, osteoporosis, cataracts and many others. Reductions in the incidence of chronic disease associated with the consumption of citrus fruits for example are thought to be attributable to an array of biologically active substances in fruits including vitamin C, folic acid, carotenoids, dietary fibre, potassium, selenium and a range of other phytochemicals.

Despite the epidemiological evidence regarding the benefits of fruits and vegetables, randomised controlled trials indicate that β-carotene and vitamin E when taken as food supplements have no beneficial effects in the prevention of heart disease, and may result in a small increase in the incidence of lung cancer in the group supplemented with β-carotene (Lee 1999, Eichholzer 2001, Asplund 2002).

In general, due to the complexity of nutrients and non-nutrients in fruits and vegetables, it has not been possible to attribute the protective effects to any single nutrient or class of nutrients. Rather, and notwithstanding genetic diversity in the population, any health benefits are associated with consuming a diet that is rich in fruits and vegetables, possibly in combination with a range of other 'healthy' lifestyle choices, such as avoiding smoking and engaging in regular exercise. Nevertheless, plant compounds with antioxidant activity, such as β-carotene, are currently the focus of further scientific attention to more broadly examine potential physiological effects.

2.4 Vitamin E

There are eight naturally occurring forms of vitamin E in plants: four tocopherol and four tocotrienols. The abundance and bioavailability of each form of natural vitamin E varies considerably. Vitamin E can also be synthesised chemically. Vitamin E is a powerful antioxidant; it plays an essential role in the protection of cell membranes and plasma lipoproteins from free radical damage.

[8] The Health Benefits of Citrus Fruits, Report to Horticulture Australia Ltd Project No: CT01037, Dr. Katrine Baghurst, Consumer Science Program, CSIRO Health Sciences & Nutrition, June 2003.

2.4.1 Sources

The major food sources of vitamin E include broccoli, dark leafy vegetables, avocado, kiwi fruit along with cold pressed vegetable oils, nuts, seeds, soy beans, wheatgerm and wholegrains (Lister 2003).

2.4.2 Bioavailability

Vitamin E is a fat-soluble vitamin. Its absorption in the small intestine is enhanced by the presence of fat, causing an increase in the formation of micelles required to absorb vitamin E into the mucosal cells lining the small intestine. Once in the mucosal cells, Vitamin E is incorporated into chylomicrons and enters the circulation via the lymphatic system.

2.4.3 Deficiency

Vitamin E deficiency is rare in humans, as is toxicity (Institute of Medicine 2000). Due to the protective effect on LDL oxidation, a serum tocopherol/cholesterol ratio of 2.25µmol/mmol is thought to be the lowest satisfactory serum value for oxidative protection. The RDIs for vitamin E of 10 mg/day and 7 mg/day tocopherol equivalents for men and women respectively are based on this ratio.

3. The nutritional effects of phytosterol ingestion in the target consumer group

3.1 Recommended serum cholesterol levels

The National Heart Foundations of both Australia and New Zealand recommend that people attempt to keep their individual total serum cholesterol level below 4 mmol/L to reduce the risk of heart disease. The Australian Institute of Health and Welfare (AIHW) state that individual total blood cholesterol levels above 5.5 mmol/L are an indication of a greatly increased risk of developing heart disease and that levels above 6.5 mmol/L are considered to indicate extremely high risk.

It is suggested by the New Zealand Guidelines Group that doctors classify individuals by risk according to age, blood pressure, smoking and diabetes status. Those classified as high-risk, with a total serum cholesterol level greater than 5.5 mmol/L, be recommended for 6-12 weeks of dietary intervention, before being considered for treatment with appropriate medication: dietary intervention should be continued indefinitely[9].

Phytosterol ester-enriched foods are primarily targeted to consumers over 40 years of age with concerns about a mildly elevated blood cholesterol measurement. Due to the direct link with diet, mild hypercholesterolaemia may be adequately addressed by strategic changes to the diet such as selectively choosing low-fat versions of staple foods, by using products containing plant sterols (currently edible oil spreads and margarines), and/or by increasing relative consumption of fruits and vegetables.

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[9] www.nzgg.org.nz

3.2 Studies on the effects of phytosterol ester-enriched foods

The applicants have submitted two studies undertaken by CSIRO Health Sciences and Nutrition to investigate (a) the efficacy of phytosterol esters in a variety of food matrices (Study 1), and (b) the effects of high intakes (10.7 g/day phytosterol esters) on nutritional, blood lipid and biochemical parameters (Study 2). This nutritional assessment focuses primarily on the results and information provided by Study 2, together with some additional data from Study 1. A detailed assessment of the data provided by Study 1 is presented elsewhere in this report (see Attachment 3).

Submitted studies

Study 1 LDL Cholesterol Lowering with Phytosterol Ester-Enriched Bread, Cereal, Milk and Yoghurt in a Multi-Centre Trial. P.M. Clifton, P.J. Nestel and D.R. Sullivan, CSIRO Health Sciences & Nutrition, 2002.

Study 2 The Effect of Consuming Higher Dietary Intakes of Phytosterol-esters Over an Extended Period in Mildly Hypercholesterolaemic People. P.M. Clifton, P.J. Nestel and D.R. Sullivan, CSIRO Health Sciences & Nutrition, 2002.

3.2.1 Objective and methodology

The objective of Study 2 was to measure effects on serum lipids, fat-soluble vitamins (vitamins A, D and E only), plasma carotenoids, plasma phytosterols, and other physiological/biochemical parameters in free living humans provided with specific phytosterol-fortified foods providing 6.6 g/day free phytosterols (equivalent to 10.7 g/day phytosterol esters). Three test foods were used in this study: phytosterol ester-enriched bread, breakfast cereal and table spread, as well as a matched diet with no added phytosterols (as a control). The study also aimed to investigate any nutritional effects, particularly on plasma carotenoid levels, of additional dietary fruits and vegetables when co-consumed with the test foods.

Thirty-five mildly hypercholesterolaemic (cholesterol levels 5.0 – 7.5 mmol/l) women and men were recruited into this study which was conducted over 16 weeks at two clinical research centres, one in Adelaide and one in Melbourne. All subjects undertook dietary regimens in a non-randomised manner and were instructed not to consume self-purchased phytosterol-enriched products during the course of the study. The study was single blind and foods were appropriately coded. The dietary periods of the study are presented in Table 1.

Table 1. Dietary regimen (Study 2)

Time period	Description
Weeks 1 & 2 **Baseline** Control (2 weeks)	Usual diet plus **phytosterol-free** forms of test foods (bread, breakfast cereal and spread) at the same quantities as the next two periods.
Weeks 2-8 **Period 1** Sterol-enriched food (6 weeks)	Usual diet plus **phytosterol-enriched** bread, breakfast cereal and spread contributing 6.6 g/day free phytosterols.

Weeks 9-14 **Period 2** Sterol-enriched food plus additional fruit and vegetables (6 weeks)	Usual diet plus **phytosterol-enriched** foods (as above) with **additional vegetable and/or fruit** intake.*
Weeks 15-16 **Period 3** Free living (sterol wash-out) (2 weeks)	Usual diet plus **phytosterol-free** forms of test foods in the same quantities as the previous two periods.

* Dietary advice was given to consume at least 5 serves of fruit/vegetables every day, with at least 1 serve of either pumpkin, sweet potato, carrot, tomato, apricot, broccoli, or spinach (1 serve = half a cup).

Serum lipids (total cholesterol, HDL cholesterol, triglycerides) were determined on two consecutive days at the end of each period (weeks 2, 8, 14, 16). LDL cholesterol levels were calculated. Plasma carotenoids, plasma fat-soluble vitamins (A, D and E) and plasma phytosterols were measured at the end of each period (as above).

<u>Carotenoid levels 'adjusted' for LDL-cholesterol</u>

In the analysis of results, changes in carotenoids and fat-soluble vitamins have been provided as adjusted and non-adjusted levels, on the assumption that:

1. the carotenoids are transported in the circulation within low density lipoprotein (LDL) carriers, and reduced LDL-cholesterol levels will naturally result in reduced levels of these substances; and
2. due to the antioxidant role of carotenoids in protecting LDL particles against oxidation, it is generally considered appropriate to consider the magnitude of change as a ratio to LDL-cholesterol.

3.2.2 Results

Dietary compliance was monitored using food frequency questionnaires and daily records of fruit and vegetable consumption. The authors report that compliance with the dietary regimen was above 95% for all periods, except for the washout period (Period 3) at one study centre, where it fell to around 70%. Compliance with the additional fruit and vegetable intake (total of 5 per day) in Period 2 at the two study centres was 83% and 86% respectively.

There were no significant changes in total dietary fat, saturated fat, or energy between the periods in the study. Intake of β-carotene increased by 41% in Melbourne (p=0.001) and fibre intake also increased by 2 g/day (p=0.04) from period 1 to period 2. In the Adelaide group, β-carotene intake increased by 23% (p=0.023) and fibre intake increased by 3.3 g/day (p=0.002) from period 1 to period 2.

The results of the analyses of fat soluble nutrients (adjusted for total cholesterol) from Study 2, are presented in Table 2.

Table 2. Mean levels (± SD) of plasma carotenoids and fat-soluble vitamins on a diet containing 6.6 g/day phytosterols, with and without additional dietary fruit and vegetables, combined data from both study centres (n=35). The levels are adjusted for total cholesterol (µmol/L/TC mmol/L)
FV = 5 daily serves fruits and vegetables

Period	Lutein	α-tocopherol	Lycopene	α-carotene	β-carotene
Baseline	0.077[1] ±0.034	6.03[1] ±0.99	0.13[1] ±0.06	0.024[1] ±0.025	0.105[1,3] ±0.091
Period 1 (Phytosterol)	0.067[2] ±0.03	5.85[1] ±0.97	0.12[1,2] ±0.06	0.020[2] ±0.014	0.082[2] ±0.057
% change	**-14%**	**-3%**	**-11%**	**-23%**	**-26%**
Period 2 (Phytosterol + FV)	0.073[1,2] ±0.031	5.68[2] ±0.84	0.11[2] ±0.05	0.023[1] ±0.013	0.083[2,3] ±0.051
% change	**-6%**	**-6%**	**-22%**	**-5%**	**-21%**
Period 3 Washout	0.075[1] ±0.034	6.07[1] ±1.22	0.12[1,2] ±0.05	0.023[1] ±0.013	0.092[1] ±0.059
% change	**-3%**	**0%**	**-11%**	**-4%**	**-13%**

Values with different superscripts within each column are significantly different ($p<0.05$) from each other.

There was a significant fall in plasma carotenoid levels measured during the first study period ($p<0.05$), with α-carotene and β-carotene reduced by 23% and 26% respectively across the combined data for all participants. At the end of the second study period, following consumption of additional fruit and vegetables, plasma α-carotene levels had increased significantly back to baseline values. Beta-carotene levels increased again only during the washout period when all phytosterol fortified foods were removed from the diet. Plasma lutein levels decreased by 14% during period 1, and increased again during period 2 with the daily consumption of additional fruits and vegetables, to levels consistent with the baseline and washout period. Plasma α-tocopherol levels were not affected by consumption of phytosterols, with measurements lower than baseline and washout only during the high fruit and vegetable intake period. Plasma lycopene levels were decreased by 11% during the first period which extended to 22% following the period of added fruit and vegetable consumption, with some recovery during the two-week washout period. Levels of plasma vitamin D did not change significantly during any of the study periods (data not shown).

3.2.3 Additional analyses from Study 1

The results of similar nutritional and biochemical investigations were also provided from Study 1 in which the daily consumption of phytosterol esters was 2.6 g/day from 3 different phytosterol enriched foods (either bread, breakfast cereal, low-fat milk or yoghurt) tested sequentially over a period of twelve weeks. As in the previous experimental design, plasma carotenoids and two fat-soluble vitamins (A and E only) were measured.

When data from both the Melbourne and Adelaide centres were combined (Table 3), only β-carotene levels were significantly decreased (by approximately 10%) by milk providing 1.6 g/day free phytosterols (equivalent to 2.6 g/day phytosterol esters). The reduction in α-carotene levels when adjusted for cholesterol was approximately 6%, which was not statistically significant. There was no change of nutritional significance in levels of lutein, retinol, vitamin E or lycopene.

Table 3. Effect of diets containing 1.6 g/d of phytosterols on absolute and adjusted plasma carotenoids (μmol/L) and fat-soluble vitamins (μmol/L) from Melbourne and Adelaide study centres combined (n=40), milk data versus the control only. (Mean ± SD, TC = total cholesterol)

Period	Lutein	Retinol	α-tocopherol	Lycopene	α-carotene	β-carotene
Control (TC 6.56)	0.44 ±0.23	2.34 ±0.43	37.4 ±9.6	0.65 ±0.37	0.13 ±0.08	0.56 ±0.44
Milk (TC 5.90)	0.41 ±0.21	2.35 ±0.39	34.5** ±5.9	0.62 ±0.37	0.11** ±0.06	0.45** ±0.30
% change	**-6.6%**	**+0.6%**	**-7.7%**	**-4.9%**	**-16.1%**	**-19.4%**
Adjusted control	0.067 ±0.035	0.36 ±0.08	5.71 ±1.37	0.10 ±0.05	0.02 ±0.012	0.084 ±0.066
Adjusted milk	0.070 ±0.037	0.40 ±0.08	5.88 ±0.99	0.10 ±0.06	0.019 ±0.010	0.076* ±0.053
% change	**+4%**	**+33.3%**	**+2.9%**	**+4.9%**	**-5.7%**	**-9.3%**

*p<0.05, **p<0.01

The additional results from Study 1 allow a comparison of data from one type of phytosterol-enriched test food separately and therefore provides some further insights into the physiological effects of phytosterol ingestion according to the food delivery matrix. The consumption of phytosterols in both milk and bread significantly lowered adjusted β-carotene levels by 14% and 8% respectively, despite the phytosterol-enriched bread failing to show a significant reduction in cholesterol (Melbourne data). This suggests that phytosterols in milk are more effective in the gut at interfering with both cholesterol and β-carotene absorption. However, the milk data obtained from the Adelaide centre does not show the same pattern. Adjusted β-carotene levels were not significantly lower than the controls, despite a decrease in LDL-c (14.4%) and total cholesterol. The authors conclude that it is therefore not inevitable that β-carotene levels will fall in combination with a cholesterol-lowering effect.

Effects of phytosterol intake

All measures of plasma carotenoids following free phytosterol intakes of 1.6 g/day and 6.6 g/day regardless of food source are compared in Table 4. With the exception of lycopene, where the adjusted level was not significantly different (p=0.07) from the control, all measurements showed a statistically significant reduction in carotenoids at the higher level of phytosterol intake (6.6 g/day). In addition, the data indicate that the reduction in plasma carotenoids is more pronounced at higher intakes of phytosterols. There was no effect of phytosterol intake level on the change in plasma α-tocopherol level (data not shown).

Table 4. Comparison of low (1.6 g/d) and high (6.6 g/d) phytosterol intakes on plasma carotenoids (μmol/L), combined from all test periods: milk and bread in Melbourne, bread in Sydney, milk in Adelaide (Mean ± SD)

Period	Lutein Low PS intake (n=76)	Lutein High PS intake (n=35)	Lycopene Low PS intake (n=76)	Lycopene High PS intake (n=35)	α-carotene Low PS intake (n=76)	α-carotene High PS intake (n=35)	β-carotene Low PS intake (n=76)	β-carotene High PS intake (n=35)
Baseline /Control	0.43[1] ±0.22	0.50[1] ±0.21	0.67 ±0.35	0.87 ±0.40	0.13[1] ±0.09	0.15[1] ±0.15	0.53[1] ±0.41	0.69[1] ±0.58
Phytosterol	0.41 ±0.21	0.40[2] ±0.18	0.61 ±0.36	0.71 ±0.35	0.12[2] ±0.08	0.12[1] ±0.08	0.47[2] ±0.36	0.49[2] ±0.34
% change	**-4%**	**-22%**	**-7%**	**-19%**	**-7%**	**-23%**	**-13%**	**-30%**
Adjusted control	0.068 ±0.035	0.077[1] ±0.034	0.10 ±0.05	0.13[1] ±0.06	0.021 ±0.014	0.024[1] ±0.025	0.083[1] ±0.062	0.11[1] ±0.09
Adjusted phytosterol	0.070 ±0.036	0.067[2] ±0.030	0.10[1] ±0.05	0.12[1] ±0.06	0.020 ±0.015	0.020[2] ±0.014	0.078[2] ±0.062	0.082[2] ±0.057
% change	**+3%**	**-14%**	**-1%**	**-11%**	**-1%**	**-17%**	**-7%**	**-26%**

Values with different superscripts are significantly different (p<0.05) from each other.

3.2.4 Results across both studies

Ten of the subjects participated in both Study 1 and Study 2 allowing a comparison of low intakes of phytosterols (1.6 g/day in milk and bread) with higher intakes (6.6 g/day in bread, cereal and spread) on plasma carotenoid levels in the same individuals (data not shown). The authors note that although the number of subjects was small, the results indicate that the reduction in β-carotene was approximately the same at both levels of phytosterol consumption, being in the order of 20% (adjusted for cholesterol).

These results also provide some indication of the effect of the food matrix on plasma cholesterol and carotenoid measurements, observing that 6.6 g/day of phytosterols in bread, cereal and margarine did not reduce adjusted plasma β-carotene any more than 1.6 g/day of phytosterols in milk, which was highly effective in lowering serum cholesterol.

3.2.5 Discussion of results

The decreases in plasma carotenoid levels recorded in Study 2 were consistent with the decreases observed from additional biochemical analyses in Study 1, in general showing some relationship with levels of intake of phytosterols and the nature of the food matrix. Thus, while phytosterol-enriched milk showed the greatest reduction in cholesterol absorption, it also resulted in lower plasma carotenoid levels. The reduction in plasma carotenoid levels with 6.6 g/day phytosterols (in bread, cereal and spread) was not different to that reported in the literature for lower levels (1.6 – 3.2 g/day) phytosterol consumption. Even 1 g/day of phytostanols has been reported to lower lipid-standardised (adjusted) β-carotene levels by 14.4% (Mensink, 2002). In general, a comparison of the data from the different study centres highlights the great variability in plasma β-carotene levels. The authors comment that carotenoid absorption is not a well-regulated process in humans and levels can fluctuate widely according to a variety of physiological and environmental factors.

Fruit and vegetable intake

The results from Study 2, where subjects were asked in the second period to consume 5 servings per day of fruits and vegetables, suggest that increased consumption of some carotenoid-rich fruit and vegetables does not completely restore plasma levels to baseline for all of the carotenoids examined. Lutein and α-carotene levels appeared to respond positively to additional fruits and vegetables in the diet in the presence of phytosterol-enriched foods. Lutein and lycopene were reduced with higher levels of phytosterol intake (6.6 g/day) but were not affected at lower intake (1.6 g/day) levels (Tables 3 & 4).

The results also indicate that the reduction in β-carotene levels with consumption of phytosterol-enriched foods in general was not compensated by additional fruits and vegetables in the diet. The authors noted a maximum fall in β-carotene of approximately 30% (unadjusted for cholesterol) in all groups regardless of the level of phytosterol intake. However, despite this effect, after 12 weeks of consumption of phytosterol-enriched foods, plasma β-carotene levels were still at levels associated with the lowest risk of all-cause mortality in US adults, according to epidemiological studies cited in the Institute of Medicine Dietary Reference Intakes (2). Furthermore, retinol levels remained constant at all study centres irrespective of the amount of phytosterol consumption.

Study 2 did not attempt to examine the reduction in carotenoids at different time points and therefore does not provide any information on a pattern of reduction with ongoing phytosterol intakes. Nevertheless, as the effects were detectable early in the study and carotenoid levels returned almost completely to baseline in the two-week washout period when phytosterol-enriched foods were removed from the diet, it is likely that the reduction in carotenoid absorption had stabilised, along with the reduction in cholesterol absorption, due to the physiological linkage. Data with respect to carotenoid levels after long-term use (years rather than months) of phytosterol-enriched foods has not been presented.

3.2.6 Nutritional issues

The results from both CSIRO studies provide evidence that the effects of phytosterol ester consumption up to 10.7 g/day have no significant impact on the general nutritional status of adults over the medium-term. The data also suggest that this level of consumption may be safe over longer periods of time.

Comparisons between Study 1 and Study 2 suggest that a higher intake of phytosterols has a greater potential to compromise levels of certain carotenoids, most significantly β-carotene, without any concomitant benefit in terms of a reduction in LDL-cholesterol. The nature of the food matrix in which the phytosterols are presented is a factor in the cholesterol-lowering effects and therefore also in the secondary nutritional effects.

However, there is no evidence in the literature that the observed reduction in β-carotene, with consumption of phytosterol-enriched foods, will result in adverse health outcomes. Epidemiological studies show unequivocally that fruit and vegetable consumption is inversely associated with cardiovascular disease and some cancers (eg gastric cancer), but to date it has not been possible to elucidate the role of individual plant components with any certainty. Clinical intervention trials using β-carotene supplements in the diet either had no benefit or caused harm, leading to speculation that a host of other compounds (or a synergistic mix) in fruits and vegetables contribute to the beneficial effects, or that an increased intake of β-carotene may merely be a marker of a 'healthy' lifestyle which in itself has been associated with a lower risk of some chronic diseases.

Increasing the intake of fruit and vegetables when consuming phytosterol-enriched foods resulted in a modest improvement in the levels of some carotenoids and therefore validates the use of advisory statements on the packaging of these products. In addition, additional consumption of fruits and vegetables is consistent with other public health messages in relation to the prevention of a range of common diseases with a dietary component.

The authors claim that the cholesterol lowering effect of phytosterol-enriched spreads can conservatively be translated to an estimated reduction of 15-20% in the risk of developing cardiovascular disease. Epidemiological studies suggest that a similar reduction in the risk of heart disease can apply to high consumers of fruits and vegetables (at the 90th percentile) compared to low consumers (at the 10th percentile). For the same reduction in cardiovascular disease risk, the authors claim that use of phytosterol-enriched products represents a smaller dietary change for consumers when compared to the magnitude of the dietary changes required to convert from a low to a high consumer of fruits and vegetables.

In assessing the overall risk that can be attributed to a reduction in plasma β-carotene levels resulting from consumption of phytosterol-enriched foods, the authors cite European studies (Westrate and Meijer, 1998 & Hendriks *et al*, 1999) that claim α- and β-carotene levels measured in the Dutch population are 20% lower that the baseline levels in the submitted CSIRO studies. In addition, the plasma lycopene levels are reported to vary between 26-60% of Australian mean levels. A broad natural variation therefore already exists in different geographical populations, and significant fluctuations in carotenoid levels may also arise from adherence to a low-fat diet, seasonal variation and a variety of other environmental variables.

One environmental variable is in the nature of the diet itself. A short-term study measuring the effects of fibre and fibre sources on plasma carotenoids (Nutrition Epidemiology Group, Nuffield Institute for Health, UK – 2001) reported that both plasma α- and β-carotene are negatively affected by the consumption of cereal and cereal products. In a free-living population consuming their usual diet, fibre from cereals had a negative effect particularly on α- and β-carotene (8.4% and 6.6% reduction in plasma levels respectively for a doubling of fibre intake). These results are consistent with other reports indicating that high intakes of dietary fibre impair the bioavailability of carotenoids[10].

3.3 Published studies

Table 5 summarises results from the CSIRO studies and other studies published in the scientific literature investigating the nutritional effects of phytosterol-enriched foods. Taken together, these studies provide evidence that consumption of phytosterol esters up to 3 g/day by mildly hypercholesterolemic adults would have no significant nutritional effects on fat-soluble vitamin or carotenoid status. Although most studies do show a reduction in plasma β-carotene and α-carotene levels, only some have shown the reduction to be statistically significant (CSIRO 2002, Gylling 1999, Davidson 2001, Mensink 2002, Hendriks 2003, Raeini-Sarjaz 2002).

Two studies have investigated the effects of phytosterol intakes higher than 3 g/day, however the majority of studies are not long-term. In addition, because of differences in experimental design and in some cases the absence of specific dietary information, the majority of results show effects of dietary phytosterols only in terms of the cholesterol:β-carotene ratio, and do not record changes in any other fat-soluble nutrients.

3.3.1 Studies with higher intakes of phytosterols

Davidson *et al* (2001) studied three test groups of 23 subjects each, who consumed 0, 3, 6, or 9 g/day of phytosterol esters in reduced fat spreads for eight weeks. Blood concentrations of measured fat-soluble vitamins (vitamins A, D and E) remained within normal reference ranges. There was no statistical difference in serum vitamin response for these nutrients in those subjects who consumed 9 g/day phytosterols compared with the two groups consuming 3 g/day and 6 g/day respectively.

Pair wise comparisons of β-carotene levels after the intervention period indicated significant differences between the 9 g/day group compared to the control and the 3 g/day group ($p<0.05$). Only the control group and 9 g/day group also differed significantly with respect to serum α-carotene levels. The authors concluded that consumption of phytosterols at a level of 9 g/day was safe and well tolerated.

It should be noted that the reduced-fat spread and salad dressing used as phytosterol-ester delivery vehicles in this study did not produce the expected magnitude of reduction in LDL-cholesterol levels. Despite this, reductions in levels of fat-soluble vitamins and serum carotenoids were recorded. In addition, all groups receiving phytosterols showed a relatively small increase in corresponding serum phytosterol levels indicating that the significance of the results from a nutritional perspective may be limited.

[10] Reidl, J. *et al*. Some dietary fibers reduce the absorption of carotenoids in women. J. Nutr. 129, 2170-6, 1999.

3.3.2 Research with controlled diets

Although there are two published studies investigating the nutritional effects of phytosterol consumption in the context of a controlled diet, only one provides information that is relevant to this assessment.

Raeini-Sarjaz *et al*. (2002) reported no effect of consumption of esterified plant sterols (or stanols) on serum fat-soluble vitamins or carotenoid concentrations when consumed in conjunction with a diet adequate in fruit and vegetables, compared to baseline diets. The study involved 15 hypercholesterolemic males administered a daily amount of 1.92 g/70 kg body weight of plant sterol esters in a metabolic kitchen setting in the context of a diet formulated to meet the Canadian Recommended Nutrient Intakes. Measurements for serum retinol, α- and γ-tocopherol, vitamins D and K, lycopene, lutein, α- and β-cryptoxanthin, and α- and γ-carotene were conducted. The authors concluded from their results that moderate consumption of plant sterol and stanol esters would not be expected to affect fat-soluble vitamin and carotenoid concentrations in conjunction with a healthy diet.

3.3.3 Fruit and vegetable consumption

A study by Noakes *et al.* (2002) specifically examined whether consuming daily amounts of foods high in carotenoids prevents a reduction in plasma carotenoid concentrations in subjects who consume plant sterol (or stanol) esters. Forty-six hypercholesterolemic subjects completed a three way, double blind, crossover comparison in which 25 g/day of one of the following 3 spreads were consumed for 3 weeks: control (placebo/sterol free), sterol–ester (2.3 g/day plant sterol esters) or stanol-ester (2.5 g/day plant stanol esters). During the study period, subjects were advised to eat five or more servings per day of fruits and/or vegetables, of which at least one serving was to be carrots, sweet potatoes, pumpkin, tomatoes, apricots, spinach or broccoli.

As expected, there was a reduction in total cholesterol with consumption of sterol esters (-6.1%) and stanol esters (-7.3%), compared with the control spread. The decrease in the LDL-cholesterol concentration was 7.7% with consumption of sterol ester-enriched spread and 9.5% with consumption of stanol ester-enriched spread. There were no significant changes in HDL-cholesterol or triacylglycerol concentrations.

Consumption of the different spreads did not significantly change the concentrations of retinol and lutein, which the authors note is consistent with their transport by retinol binding protein, and HDL (40%) respectively. Similarly, α-tocopherol concentrations were not significantly different among the spread periods or between the spread periods and baseline period. After standardising for lipids, there were no significant differences in plasma carotenoid concentrations between the experimental groups and the control. However, before lipid adjustment, both the sterol and stanol periods significantly lowered the β-carotene concentration by 9% compared to the control period, but not compared with the baseline period. When the 1-week baseline and control periods were analysed separately, the levels of lutein, α-carotene and β-carotene increased by 11%, 29% and 13% respectively, demonstrating the effects of increasing dietary intake of the specified fruits and vegetables, in the absence of plant sterols. Interestingly, the concentration of plasma lycopene did not change significantly during the study.

The authors concluded that daily consumption of an average of one extra daily serving of high-carotenoid fruit or vegetables, compensates plasma concentrations of α- and β-carotene and maintained concentrations of lipid-standardised plasma carotenoids in subjects consuming sterol or stanol-enriched spreads. The conclusions of this study suggest that compliance with dietary advice to consume specified fruits and vegetables, in conjunction with phytosterol-enriched foods, is likely to compensate for a decrease in carotenoid levels.

3.3.4 Long-term studies

There are few long-term studies investigating the nutritional effects of phytosterol consumption. Gylling (1999) investigated the effects on carotenoids and fat-soluble vitamins of ingestion of 2-3 g/day phytosterols over 12 months. Serum cholesterol and vitamin concentrations were measured at 0 and 12 months. The levels for serum α-tocopherol, α-carotene, β-carotene and cholesterol were all significantly lower in experimental subjects compared with controls after 12 months. However, when levels were adjusted for LDL concentration, β-carotene was the only nutrient significantly lower than the controls.

A one-year study by Hendriks *et al*. (2003) involved 185 volunteers randomised into either a control or experimental group who consumed 1.6 g/day of phytosterol esters in a margarine-type spread. Carotenoids were measured at both 26 and 52 weeks and compared to baseline and to the control group. In absolute terms, serum β-carotene levels were reduced by 22% at 26 weeks and by 25% at 52 weeks in the experimental group compared to baseline. Serum α-carotene levels were reduced by 11% at 26 weeks and by 15% at 52 weeks in the experimental group compared to baseline. When the results were corrected for LDL concentration, only α-carotene was reduced in the experimental group who consumed the phytosterol-fortified spread.

The study reported no change in LDL and cholesterol concentration (a plateau effect) in the second half of the study period between 26-52 weeks, and the researchers concluded that the nutritional effects had reached a plateau by the mid-time point.

3.3.5 Studies in hypercholesterolaemic children

Five studies investigated the effects of phytosterol esters in children (Gylling 1995, Tammi 2000, 2001 & 2002, Amundsen 2002), however only two of these investigated nutritional parameters. All children in these studies were either hypercholesterolaemic, or were genetically susceptible to high cholesterol levels.

One study of 38 children (each of whom had a parent with hypercholesterolemia) who were supplemented with 1.6 g/day phytosterol esters, showed significant decreases in serum concentrations of β-carotene and lycopene, with the difference in β-carotene disappearing after statistical adjustment for cholesterol. Twenty-one of the 38 children took either fish oil, or vitamin A, D or E supplements (Amundsen 2002).

Another study that measured the serum antioxidant levels of 72 six-year old children consuming 1.5 g/day plant stanols over a three-month intervention period showed that serum β–carotene and β-carotene/LDL concentration was significantly lowered as a result of treatment. α-Carotene and lycopene were not measured (Tammi 2000).

The results of these studies confirm that consumption of phytosterols can result in a reduction in carotenoid levels in all consumers irrespective of age, where there is a concomitant reduction in cholesterol absorption.

3.3.6 Normocholesterolemic children

Studies examining the effects of phytosterol-enriched foods in children with normal cholesterol levels are not available. This is because the primary research interest in the cholesterol-lowering effects apply to adult consumers with slightly raised cholesterol levels that are not high enough to require therapeutic intervention, but are above recommended levels for reducing risk factors associated with the development of cardiovascular disease. Given the target consumer group, it is unlikely that data in children other than with genetic/familial hypercholesterolaemia will become available.

3.3.7 Older adults

The NHMRC Dietary Guidelines for Older Australians (1999) and other papers (for example, Heseker 1994) suggest that older adults (over 65 years) generally have changing nutrient requirements because of age-related changes in body composition and physiological function. The changing nutrient requirements could include a higher dietary requirement for carotenoids (eg β-carotene), and vitamins C and E due to increased oxidative stress. At the same time, due to a general decline in physical activity and subsequent energy intake, and reductions in the bioavailability of certain nutrients with increasing age, it is recognised that meeting any increased nutritional requirements depends on varying factors affecting diet, eating habits and lifestyle.

Despite these variables, according to data from the Australian National Nutrition Survey (1995-96), the mean nutrient intakes for both males and females in the over 65 age-group of vitamin A as retinol equivalents is almost double the RDI for males and approximately 1.5 times the RDI for females. The New Zealand National Nutrition Survey (1996-97) also indicated the average intake of vitamin A as retinol equivalents was approximately 1.5 times the RDI for men and women over 65 years of age. These data indicate that in terms of retinol equivalents, the current levels of intake by elderly consumers in Australia and New Zealand are generally well above daily requirements.

While there are no studies currently available that specifically examine the nutritional effects of phytosterol-enriched foods in older-age consumers, the NHMRC guidelines stress the importance of variety in the diet in order to provide a more complete profile of nutrients and non-nutrients. This recognises the importance of whole foods, particularly fruits and vegetables, as beneficial in reducing the risk of developing chronic diet-associated diseases. Health benefits to be derived from a diet rich in fruits and vegetables are likely to be attributable to the synergistic effects of a complex mix of phytochemicals including carotenoids, flavonoids and isoflavonoids, polyphenols, isothiocyanates, indoles, sulphoraphane, monoterpenes, xanthin, and non-digestible polysaccharides.

Given this information, the significance of a reduced level of one carotenoid, β-carotene (a pro-vitamin), with consumption of phytosterol-enriched foods should be considered in the context of the significant increase in the incidence of peripheral vascular disease, cerebrovascular disease and arteriosclerosis in the older adult population, and the measurable health benefits provided by a lower blood cholesterol level in this age group.

In the context of a changing physiology, older consumers may need to adapt dietary habits and eating patterns to compensate for a variety of changing nutrient requirements, in order to maintain optimal health. The dietary advice to consume greater amounts of fruits and vegetables when consuming phytosterol-enriched foods is therefore consistent with broad public health messages to this population group.

3.3.8 Pregnant and lactating women

Currently there is no research specifically investigating the nutritional effects of consumption of phytosterol-enriched foods by pregnant and lactating women. On the contrary, pregnant and lactating women have been excluded as subjects on nutritional grounds. The Scientific Committee on Food (SCF, 2003) considers that use of phytosterol-enriched foods by pregnant and lactating women is inappropriate because of the resultant lowered absorption of both dietary cholesterol and β-carotene, and the lack of information on whether this would have an adverse nutritional impact on women with increased physiological load.

Currently in Australia and New Zealand, phytosterol-enriched edible oil spreads and margarines are required to carry a mandatory advisory statement to ensure that pregnant and lactating women do not consume these products. This cautionary approach is therefore consistent with the views expressed by other independent scientific committees.

3.3.9 Phytosterolaemia

Sitosterolaemia is a rare genetic (autosomal recessive) disorder in which affected individuals hyper-absorb and retain both cholesterol and other (plant, fish) sterols. The effects of this genetic condition are tendon and tuber xanthomas, arthralgias and arthritis, accelerated atherosclerosis and premature coronary artery disease (SCF 2003). The potential impact of phytosterol-enriched foods on patients with this disorder is discussed in more detail in the safety assessment at Attachment 3.

3.3.10 Phytosterols as antioxidants

The oxidation of biological molecules is known to be associated with the development of numerous disorders and pathological events such as atherosclerosis, cancer and various age-dependent processes. Chemical compounds and substances such as vitamin E that suppress oxidation have therefore become a focus of study over recent times to explore more fully their potential *in-vivo* antioxidant properties. As well as vitamins and other nutrients, plant substances such as polyphenols (rich in red wine and tea) act to protect biological molecules and tissues from oxidative damage, thereby contributing to the antioxidant pool in the body.

A recent paper (Yoshida and Niki, 2003) explored the antioxidant properties of plant sterols (campesterol, β-sitosterol, stigmasterol) and reported that phytosterols themselves can act as an antioxidant *in-vitro*, a modest radical scavenger in solution, and physically as a stabiliser in liposomal membranes. The possible antioxidant role of phytosterols *in-vivo* remains as a future subject for study.

3.4 Summary of nutritional effects of phytosterol esters

Plant sterols (phytosterol-esters in this assessment) have been shown in a large number of studies to lower the absorption of dietary and biliary cholesterol thereby decreasing the levels of LDL-cholesterol in the circulation. As cholesterol absorption is reduced, there is a concomitant effect on the absorption of some lipophilic nutrients. When these secondary physiological effects were examined in further studies, reductions in α- and β- carotene, lycopene, lutein and cryptoxanthin were observed, while the levels of vitamins A, D and E remained unaffected. Additional carotenoid-rich fruits and vegetables in the diet, when co-consumed with the phytosterol-enriched foods, partially compensated for the lower bioavailability of carotenoids in the presence of phytosterols.

With some variability, consumption of phytosterol-enriched foods generally results in a reduction in β-carotene levels of approximately 20-25%. This reduction does not translate into an overt nutritional deficiency as absolute levels remain within a broad natural range and there is no measurable effect on retinol or vitamin A levels. The nutritional significance of a reduction in β-carotene levels therefore cannot be directly measured or assessed. In terms of antioxidant status, other nutrients such as vitamin C and vitamin E are not affected by consumption of phytosterols and other phytochemicals present in fruits and vegetables contribute to the complexity of the diet and overall health.

In light of the nutritional effects, consumption of phytosterol-enriched foods is not appropriate for children, or pregnant or lactating women on the general assumption that there is no direct necessity to lower absorption of dietary cholesterol in these groups. Given their requirements for optimal nutrition, these population groups would therefore derive no particular immediate health benefit from increasing their intake of phytosterols. In contrast, consumers over the age of 40 years, and particularly those with slightly elevated cholesterol levels, can make simple dietary changes that may effectively reduce one of the known risk factors in the development of atherosclerosis and cardiovascular disease.

The data submitted with these applications indicate that consumption of phytosterol-enriched foods providing up to approximately 10.7 g/day phytosterol-esters is safe from a nutritional perspective. Furthermore, other information from published studies suggests that intake of phytosterol esters at these higher levels (up to approximately 9 g/day) is not associated with adverse effects arising from a reduction in some carotenoids. The effects of phytosterol ester consumption above 10.7 g/day on nutritional parameters, or over the long-term, have not been extensively researched, and there is therefore a lack of detailed information in this area. As there is no additional cholesterol lowering effect with increased phytosterol ester intake above approximately 4 g/day, there is no additional benefit in consuming unlimited amounts of phytosterol-enriched foods.

The results of several studies suggest daily consumption of 5 serves of fruits and vegetables, particularly those high in β-carotene, when choosing phytosterol-enriched foods, may assist in maintaining the levels of some carotenoids. The European SCF recommends that consumers be made aware of the potential β-carotene lowering effect of phytosterol-enriched products by the provision of appropriate dietary advice relating to the regular consumption of fruits and vegetables.

4. International reviews on the nutritional aspects of phytosterols in foods

4.1 European assessment

Foods containing added phytosterols have been available in Europe since the mid 1990's. As part of the process of assessment, the Scientific Committee on Food (SCF) of the European Commission has considered various safety aspects of phytosterol esters and has produced several opinion reports (2000a, 2002a, 2002b, 2003) reviewing in particular the nutritional effects of phytosterols, and the long-term effects of elevated levels of phytosterols from multiple dietary sources.

Previously, the Committee concluded that yellow fat spreads containing up to 8% of free phytosterols are safe for human consumption. It was noted that ingestion of approximately 20g of phytosterol-enriched spread per day for one year reduced β-carotene concentration by 20%. The Committee considered that although this reduction was within the normal range and within normal seasonal variation, it may become of greater nutritional relevance for individuals with a sub-optimal vitamin A status.

On the basis of results from several different trials using plant sterols or stanols, decreases in blood carotenoids plateau at consumption levels of 2.2 g/day (Plat et al. 2000). Apart from the carotenoid lowering effect, the Committee found that no other nutritionally relevant changes were evident when considering the results of several randomised trials of plant sterol or stanol margarines in humans, some of which lasted for one year.

The SCF considers that the greatest nutritional effect of phytosterol esters appears to be upon β-carotene, with only minimal effects on fat-soluble vitamins and other carotenoids. Based on the general acceptance that consumption of up to 10 mg/day of β-carotene from carotenoid-rich fruits and vegetables confers non-specific health benefits, the Committee has recommended the consumption of carotenoid rich fruit and vegetables to counterbalance the expected reduction of blood β-carotene arising from long-term consumption of phytosterol enriched foods.

The Committee concluded that, due to the lack of evidence of benefits from phytosterols at higher levels of intake, consumption of free phytosterols exceeding a range of 1-3 g/day (equivalent to 1.6 – 4.8 g/day phytosterol esters) was inadvisable. They also considered that with an ever-increasing number of potential foods as candidates for phytosterol enrichment, additional measures may be required to manage potentially excessive intakes (SCF 2003).

4.2 Review by the Mayo Clinic

In 2003 the Mayo clinic published a paper summarizing the deliberations of 32 experts on the safety of sterols and stanols (Katan 2003). The paper was a meta-analysis of 41 trials aimed at determining the safety of phytosterol intake at a level of 2 g of free stanols or sterols per day in relation to heart disease. The authors suggest that reduction of LDL cholesterol levels by 10% could be expected to reduce the incidence of ischaemic heart disease by between 12 and 20 % over 5 years.

The meta-analysis of 18 trials investigating the effects of sterol and stanols intake on plasma concentrations of fat-soluble vitamins showed statistically significant reductions in α-carotene (9%), β-carotene (28%) and lycopene (7%). On statistical correction for total cholesterol, only the decrease in β-carotene remained significant. The authors considered that the decrease in β-carotene could be prevented by the addition of 'adequate' fruit and vegetables to the diet.

This review noted that plasma β-carotene levels are affected by a variety of dietary factors. Olestra and wheat bran have been shown to significantly decrease β-carotene levels, as have some lipid lowering drugs (probucol and cholestyramine). Therefore, based on currently available information, there is no evidence that decreased levels of β-carotene are associated with increased health risks.

Table 5. Studies of the Effect of Phytosterol Consumption on Plasma Fat-soluble Vitamins and Carotenoids: Details of the studies

Author	Number of Subjects	Cholesterol status at baseline	Dietary intake	Smokers/non smokers	Mean Age	Weight at baseline	Fruit and vegetable intake
CSIRO, 2002	Adelaide 13 women 10 men	Combined centres: TC 6.59 ±1.01 mmol/l HDL 1.35±0.38 mmol/l LDL 4.46±0.91 mmol/l	8281 kJ/day Fat 24% TE SAFA 10.3% TE	Not discussed	53.3 yrs	BMI 27.9	phase 1 not discussed, phase 2-83% compliance with 5 serves / day
	Melbourne 10 men 2 women	Combined centres: TC 6.59 ±1.01 mmol/l HDL 1.35±0.38 mmol/l LDL 4.46±0.91 mmol/l	6853 kJ/day Fat 33% TE SAFA 12.5% TE	Not discussed	59.7 yrs	BMI 27.6	phase 1 not discussed, phase 2- 86% compliance with 5 serves /day
Gylling, 1999	102 active subjects 49 controls	TC >5.58 mmol/l	Fat 85g/day SAFA 34g MUFA 32 g PUFA 15g	Not discussed – not in exclusion criteria	50±1 yrs	BMI 26	not discussed
Davidson 2001	0 g/day n=21 3.0 g/day n=21 6.0 g/day n = 19 9.0 g/day n=23	mildly hypercholesterolemic	TE 2019 Kcal/day Fat 33% TE SAFA 11%TE MUFA 12.6% TE PUFA 6.4%TE	74 smokers 10 non- smokers	46 yrs	79 kg	not discussed
Nestel P 2001	22 subjects 4 men 18 women	mildly hypercholesterolemic TC >5.5 mmol/l	Fat 34%TE SAFA 11.5%TE	non smokers	60±9 yrs (34-70 yrs)	BMI 24±1 (18.3-26.9)	not discussed
Raeini-Sarjaz 2002	15 men	hypercholesterolemic TC 6-10 mmol/l	All food prepared in metabolic unit. Fat 35% TE SAFA 15% MUFA 10% PUFA 10%	not discussed	37-64 yrs	not discussed	not discussed

Mensink 2002	30 subjects 30 controls 16 men 44 women	TC 5.14±0.78 mmol/l men TC 5.12±0.80 mmol/l women	Energy/day S 9.5 MJ, C 11.3 MJ Fat % TE S 29.1%, C 31.7% SAFA S 10.8%, C 11.4% MUFA S 10.9%, C 12.2% PUFA S 5.3%, C 5.9%	7 smokers	36±14 yrs	BMI 23.3±2.7	not discussed
Westrate 1998	95 subjects	TC 5.35±1.06 mmol/l	FAT 41% TE SAFA 15.5% MUFA 14% PUFA 10%	not discussed	45±12.8 yrs	24.2±2.16	not discussed
Hendricks 1999	100 subjects 42 men 58 women	TC 5.10±0.97 mmol/l (2.71-7.42 mmol/l)	Fat 33% TE SAFA 13.5% MUFA 11.6% PUFA 6.0%	not discussed	37±10 yrs	22.8 ± 2.5 (17.7-28.6)	not discussed
Hallikainen 2000	22 subjects 14 women 8 men	TC 6.87±1.28 mmol/l	Standardised background diet designed for 8 different levels of energy requirement Fat 34% TE SAFA <12% MUFA 14% PUFA 8%	not discussed	50±11 yrs	26 ± 3.4	no information on fruit and vegetable intake
Hendricks 2003	190 subjects Experimental 44 men, 45 women Controls 46 men, 50 women	TC 5.9 ± 0.98 mmol/l		6 smokers control 11 smokers exp.	48±8 yrs	24.9 ± 3.2	no information

ns No significant difference
TC Total Cholesterol

Table 6. Studies of the Effect of Phytosterol Consumption on Plasma Fat-soluble Vitamins and Carotenoids: Results

Study	Level of intake	Food source	Length of study	Cholesterol	α-Tocopherol	α -Carotene	β -Carotene	Retinol	Lutein	Lycopen e
CSIRO	6.6 g/day	bread, breakfast cereal, table spread	total 12 weeks 2 phases-6 weeks each 2nd phase with extra F&V		P1 –10% p<0.05 P2 - 13% p<0.05	ns	cf baseline P1 -28% p<0.05 P2 –28% p<0.05	ns	P1 –23% p<0.05 P2 –15% p<0.05	P1 –18% p<0.05 P2 –30% p<0.05
					P1 –15% p<0.05 P2 –7% p<0.05	ns	ns	ns	P1 -15% p<0.05 P2 –7% p<0.05	P1 - 18% p<0.05 P2 –23% p<0.05
			Adelaide and Melbourne combined	TC –8.5% LDL –13% (p<0.05)	ns	P1 –31% p<0.05 P2 ns p<0.05	P1 –30% p<0.05 P2 –26% p<0.05	ns	ns	ns
Gylling 1999	3 g/day for 6 months, then either 2 or 3 g/day for 6 mths	Margarine	52 weeks	TC -9% (P<0.001)	-10±1% (P<0.05) Proportion to cholesterol unchanged	ns	sig ↓ (p<0.05)	ns	-	-
Davidson 2001	0 g/day 3 g/day 6 g/day 9 g/day	Reduced fat spread and salad dressing	8 week treatment period	ns between groups	ns	ns	ns	ns	ns	ns
				ns between groups	ns	ns	ns	ns	ns	ns
				Total:HDL -9.6±14.9% p<0.008	ns	Significantly lower than 0 and 3g/day p<0.004	Significantly lower than 0 and 3g/day p<0.001	ns	ns	ns
Nestel P 2001	2.4 g/day	breads and breakfast cereal	12 weeks	LDL –13.6% P<0.001	ns	ns	ns	ns	-	ns

Raeini-Sarjaz 2002	sterols 1.92 g/70 kg bw/day	margarine (controlled diet)	3 weeks		ns	increased P<0.01	ns	ns	ns	ns
Mensink 2002	3 g/day	low fat yoghurt 450 ml/day	4 week double blind, placebo controlled	control vs. ex groups: TC –8.7% (P<0.001) LDL –13.7% (P<0.001)	ns	not measured	β-C:LDL -12.9 ±21.2% cf. control P=0.038	ns	ns	-
Westrate 1998	1.5-3.3 g/day	Margarine sterols - soybean sheanut rice-bran sitostanol ester 5.0 mg/kg carotene	3.5x 4 weeks	control vs. ex groups: TC – 8-13%	-	α and β-carotene combined decreased from av 220μg/l in first period to 168μg/l in fourth.		-	-	↓ from period 1 – 4 85μg/l to 63μg/l
Hendricks 1999	0.83, 1.61, 3.24 g/day	Margarine	3.5x 4 weeks	Sig ↓ TC in all phases HDL ↓ after 1.61 &3.2g cf baseline	-6% 1.61g -8% 3.2g α-toc/TC ns	Combined α and β-carotene concentrations -11% w/ 0.83g/day -19% w/ 3.24g/day		-	-	lyco/TC ns
Hallikainen 2000	5x4 weeks in the order: 2.4, 2, 1.6, 0, 0.8 g/day	Rapeseed oil Margarine 25g/day	20 weeks	1.6,2.4&3.2g TC sig lowered LDL sig lowered	ns	ns	ns	-	-	-
Hendricks 2003	1.6 g/day	Margarine 5.7 mg/kg carotenoids	1 year	TC ↓4% LDL ↓ 6%	ns	sig ↓ cf with controls after 26 and 52 weeks but no sig diff for /TC	sig ↓ cf with controls after 52 weeks	ns	sig ↓ cf with controls after 26 and 52 weeks	ns

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ATTACHMENT 5

DIETARY EXPOSURE ASSESSMENT REPORT

Application A434 – Phytosterol esters derived from vegetable oils in low fat milks& yoghurts

Summary

The application under assessment seeks permission to use phytosterol esters derived from vegetable oils as a novel food ingredient, under Standard 1.5.1 – Novel Foods, in low fat milk (fat content < 1.5%) and low fat yoghurt (fat content < 1.5%).

A dietary exposure assessment was undertaken to determine the impact of allowing phytosterol esters to be added to the above foods. The assessment took into account the existing permission under Standard 1.5.1 to add phytosterol esters to edible oil spreads (the 'baseline' scenario) as well as the proposed addition of phytosterol esters to low fat milks and low fat yoghurts (the 'low fat milks and low fat yoghurts only' scenario) and a combination of theses products (the 'low fat milks and low fat yoghurts plus baseline' scenario). In each scenario, the modeling was based on the addition of phytosterol esters at the level of 0.8 g free phytosterols per serve. The analysis also assumed that all foods considered (edible oil spreads, low fat milks and low fat yoghurts) contained added phytosterol esters. Intrinsic levels of phytosterols in foods were not taken into consideration.

Modeling was conducted assuming that consumers do not change the amounts and general types of foods that they eat, simply substituting phytosterol containing edible oil spreads, low fat milks or low fat yoghurts for their non-phytosterol counterparts. Food consumption data from the most recent Australian and New Zealand National Nutrition Surveys (NNSs) were used – the 1995 Australian NNS of those aged 2 years and above, and the 1997 New Zealand NNS of those aged 15 years and above were used. Exposure was estimated for the target populations (40-64 years and 65 years and above), and for the general population, as well as for two specific non-target groups – children aged 2-12 years (Australia only) and women of childbearing age (16-44 years), as a proxy for pregnant and lactating women.

Assuming that consumers maintain their existing eating patterns, and simply substituting phytosterol containing spreads, low fat milks, and low fat yoghurts for their non-phytosterol counterparts, the estimated mean dietary exposure (expressed as free phytosterols) did not exceed 1.9 grams per day (g/day) in any population group under any of the scenarios considered in this assessment. At the 95th percentile of exposure, no population group exceeded 4.7 g free phytosterols per day for any of the scenarios. The analysis shows that, for the target population group (40 years and above) in particular, edible oil spreads contribute more to dietary exposure to added free phytosterols (78-83% of exposure) than low fat milks and low fat yoghurts, according to the available data on food consumption patterns.

1. Introduction

1.1 Information supplied by the applicant

The applicant is seeking approval to use phytosterol esters in foods at levels formulated to provide between approximately 2 g/day and 3 g/day of free phytosterols specifically to consumers in the target group (through 2-3 serves of products). Target consumers are adults over the age of 40 years with concerns about their blood cholesterol level. However, casual consumption by other non-target population groups, including children, must also be considered.

The applicant did not provide new data relating to dietary exposures to phytosterol esters in Australia or New Zealand. Instead, the applicant referred to a previous assessment (Application A410) which concluded that an 'average' consumer would not exceed the level of intake of phytosterols shown to be safe by the available data at that time, and that the 95th percentile exposures[11] would marginally exceed this level.

However, the dietary exposure assessment provided by the applicants was not sufficiently detailed to draw conclusions on projected exposure to phytosterols among specific population subgroups of particular interest. FSANZ has therefore conducted a dietary exposure assessment to estimate potential exposure to phytosterols if these are permitted in low-fat milks and low-fat yoghurts.

1.2 Existing phytosterol enriched products

There are a small number of edible oil spreads currently on the market that contain phytosterols. These products carry statements to the effect that plant sterols assist in lowering cholesterol absorption. Permissions for the use of phytosterol esters at no more than 137 g/kg of food (equivalent to 1.37 g per 10 g serve of spread) is under Standards 1.5.1 and 2.4.2 of the Code.

1.3 Natural presence of phytosterols

Major sources of naturally occurring phytosterols are vegetable fats and oils, nuts and seeds (Food Standards Agency, 2002). Reported average intakes of phytosterols from unfortified foods vary in the range of 160 to 500 mg per day (Thurnham, 1999). These levels are therefore 5–10 fold lower than would result from addition of phytosterols to foods.

1.4 Post launch monitoring in Europe

The Unilever Company conducted post launch monitoring in Europe of the use of yellow fat spreads containing added phytosterol esters, following approval to add the esters by the European Commission. For regular users of phytosterol enriched spreads, median household consumption of spread was between 15 g/day and 18 g/day, which represents slightly less than 2 x 10 g serves per day. Surveys suggested that these amounts represent consumption by a single person in the household and are lower than predicted at the time of approval of the products, when consumption of the spreads was predicted to be 20–30 g per person per day.

[11] The exposure level that is equalled or exceeded by only 5% of the population.

The ninety-fifth percentile consumption did not exceed 45g of spread (4.5 serves) per day. Of particular note, the survey information indicated that the majority of households where these spreads were used did not include children and between 87% and 91% of regular purchasers of these spreads had no children living at home (Scientific Committee on Food, 2002).

2. Dietary modelling

The dietary exposure assessment was conducted using dietary modelling techniques that combine food consumption data with food chemical concentration data to estimate the exposure to the food chemical from the diet. The dietary exposure assessment was conducted using FSANZ's dietary modelling computer program, DIAMOND.

Dietary exposure = food chemical concentration x food consumption

The exposure was estimated by combining usual patterns of food consumption, as derived from national nutrition survey (NNS) data, with proposed levels of use of phytosterol esters in foods.

2.1 Dietary Survey Data

DIAMOND contains dietary survey data for both Australia and New Zealand: the 1995 NNS from Australia that surveyed 13 858 people aged 2 years and above, and the 1997 New Zealand NNS that surveyed 4 636 people aged 15 years and above. Both of the NNSs used a 24-hour food recall methodology.

The dietary exposure assessment was conducted for both Australian and New Zealand populations. For the Australian population, the following groups were included in the exposure assessment: the whole population aged 2 years and above; the target groups of people aged 40 – 64 years and those aged 65 years and above; and specific non target groups of special interest including children aged 2–12 years and females of child bearing age, aged 16–44 years. For the New Zealand population, the sub-groups included: the whole population aged 15 years and above; the target groups of people aged 40 – 64 years and 65 years and above; and non target group of females of child bearing age, aged 16–44 years. No New Zealand survey data are available for children aged 2-12 years in a form suitable for modelling data.

The target group for phytosterol-containing products is identified as people aged 40 years and above because it is this age group who are likely to have increasing concerns about their general health and who are likely to be interested in reducing a slightly elevated blood cholesterol level through dietary means. People aged 65 years and above were assessed separately because of the potential for some people in this target group to experience inadequate diets or reduced nutrient bioavailability.

Children generally can experience higher dietary exposures due to their smaller body weight, and higher consumption of food per kilogram of body weight compared to adults. An exposure assessment was therefore also conducted on younger non-target age groups because of a possibility that children could consume these products on a casual basis if available in the household. However, the Unilever post-launch monitoring of households in Europe using phytosterol-enriched products suggests this is not particularly likely.

In addition, to estimate the exposure of pregnant and lactating women to phytosterols from enriched products, exposure was estimated in a proxy group, women of childbearing age (16-44 years).

2.2 Additional Food Consumption Data or Other Relevant Data

No further information was required or identified for the purpose of refining the dietary exposure estimates for this application.

2.3 Concentration levels and serving sizes

The levels of free phytosterols in low fat milks and low fat yoghurts used in the exposure assessment were derived from the application. Levels of free phytosterols per serve were converted to concentrations in mg/kg to enable them to be entered into DIAMOND. Serve sizes are based on average product serve sizes from food packages - including 1 serve of edible oil spreads (10 g), 1 glass of milk (250 mL) and 1 small punnet of low fat yoghurt (140 g). The foods and proposed levels of use are summarised below in Table 1.

Table 1. Proposed levels of use of free phytosterols in foods

Food Code	Food Name	Serve size (g)	Proposed level of free phytosterol per serve (g/serve)	Concentration Level used in modelling (mg/kg)
1.1.1.2	Low fat milks (<1.5% fat), unflavoured	250	0.8	3 200
1.2.2.2	Low fat flavoured yoghurts (<1.5% fat content), including low fat fruit yoghurts	140	0.8	5 714
2.2	Edible oil spreads including reduced fat spreads	10	0.8	80 000

In estimating dietary exposure using DIAMOND, the whole category for each food was assumed to contain phytosterol as neither NNS has specific consumption data for phytosterol containing foods since such foods were not available at the time of the surveys.

2.4 Estimating risk

Estimated dietary exposures are normally compared to a reference health standard in order to determine any potential risk to health of the population or sub-groups. As novel food ingredients, free phytosterols do not have an established reference health standard and therefore estimated exposures were simply reported in gram amounts per day.

Intakes of free phytosterols up to 4.2 g/day have been associated with reductions in LDL cholesterol and have been used in recent clinical trials to study safety and efficacy in different food matrices.

2.5 How were the estimated dietary exposures calculated?

The DIAMOND program allows free phytosterols concentrations to be assigned to food groups. All foods in each of these groups included in this assessment were assigned the concentration of free phytosterols shown in Table 1. Estimated dietary exposures were calculated for the following three scenarios:

- edible oil spreads including margarines (baseline scenario);
- low fat unflavoured milks and low fat flavoured and fruit yoghurts (low fat milks and low fat yoghurts scenario); and
- edible oil spreads, low fat milks and low fat yoghurts combined (low fat milks and low fat yoghurts + baseline scenario).

An individual's exposure to free phytosterols was calculated using their individual food records from the dietary survey. The DIAMOND program multiplies the specified concentration of free phytosterols by the amount, if any, of edible oil spread, low fat milk or low fat yoghurt that an individual consumed in order to estimate the exposure to each of these foods. Once this has been completed for the foods specified to contain phytosterols, the total amount of free phytosterols consumed from all foods is summed for each individual. Population statistics (mean and high percentile exposures) are then derived from the ranked exposures of individuals who consumed added phytosterols.

The consumer populations differ in each of the three scenarios assessed. Consumers who choose to eat edible oil spreads do not necessarily also choose low fat milks and low fat yoghurts. In the baseline plus low fat milks and low fat yoghurts scenario, the consumer population includes those who consume only edible oil spreads, those who consume only low fat milks, and those who consume only low fat yoghurts as well as those who consume any combination of these foods. Therefore mean consumer exposure in the baseline + low fat milks and low fat yoghurts scenario does not represent the result of simply summing mean consumer exposure from the baseline scenario and from the low fat milks and low fat yoghurts scenario, as the consumer population is not exactly the same.

Percentage contributions of each food group to total estimated exposures are calculated by summing the exposures for a food group from each individual in the population group who consumed from that food group, and dividing by the sum of the exposures of all individuals from all food groups containing free phytosterols, and multiplying by 100.

Food consumption amounts for each individual take into account where each food in a classification code is consumed alone and where it was used as an ingredient in other foods prepared by the consumer (for example, margarine used in cooking).

2.6 Assumptions in the dietary modelling

Assumptions made in the dietary modelling include:

1. food consumption amounts are those reported in the NNSs, as it is assumed people will not change eating habits but simply substitute one product type for another;
2. where a permission is given to a food group classification, all foods in that group contain phytosterols at the concentration specified in Table 1; and

3. there is no contribution to phytosterols exposure through the use of complementary medicines (Australia) or dietary supplements (New Zealand).

The second assumption leads to a conservative estimate of dietary exposure to phytosterols, as it is highly unlikely that all foods within a group, such as all available brands of margarine, would contain added phytosterols.

2.7 Limitations of the dietary modelling

A limitation of estimating dietary exposure using 24-hour recall data is that it may not be an accurate reflection of typical exposure over a lifetime. Hence, estimated dietary exposure for high consumers is likely to be an overestimate.

While the results of national nutrition surveys can be used to describe the usual intake of groups of people, they cannot be used to describe the usual intake of an individual (Rutishauser, 2000). In particular, they cannot be used to predict how consumers will change their eating patterns as a result of an external influence such as the availability of a new type of food.

3. Results

3.1 Estimated dietary exposures to phytosterols assuming food selection patterns do not alter

The estimated dietary exposures to free phytosterols for the different food groups for the mean and 95th percentile, consumers only, are shown below in Figures 1 and 2 respectively (baseline scenario, 'low fat milks and low fat yoghurts only' scenario and 'low fat milks and low fat yoghurts plus baseline' scenario) for Australia and Figures 3 and 4 (baseline scenario, 'low fat milks and low fat yoghurts' scenario and 'low fat milks and low fat yoghurts plus baseline' scenario) for New Zealand mean and 95th percentile exposure. Numerical data are also provided for New Zealand and Australia in Table 2 (edible oil spreads), Table 3 (low fat milks and low fat yoghurts) and Table 4 (edible oil spreads, low fat milks and low fat yoghurts). Results for consumers only (eaters of foods containing free phytosterols) are presented rather than data from the whole survey population because the purpose of the risk assessment is to consider the potential impact of phytosterol addition to a variety of foods on people who report eating these foods. All values reported are expressed as free phytosterols and are reported in grams/day.

Figure 1: Estimated mean dietary exposure to free phytosterols for different population groups and scenarios for Australia

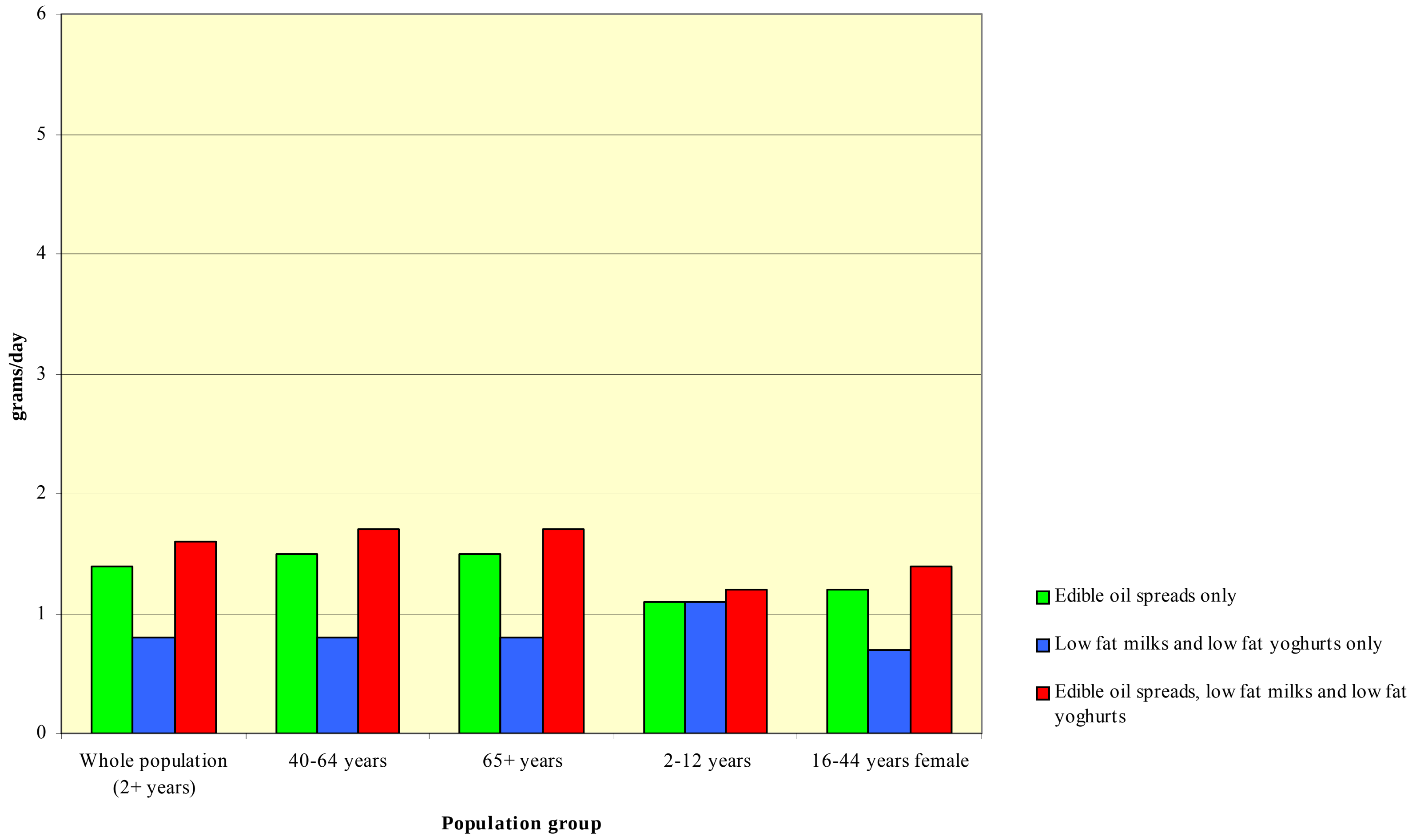


Figure 2: Estimated 95th percentile dietary exposure to free phytosterols for different population groups and scenarios for Australia

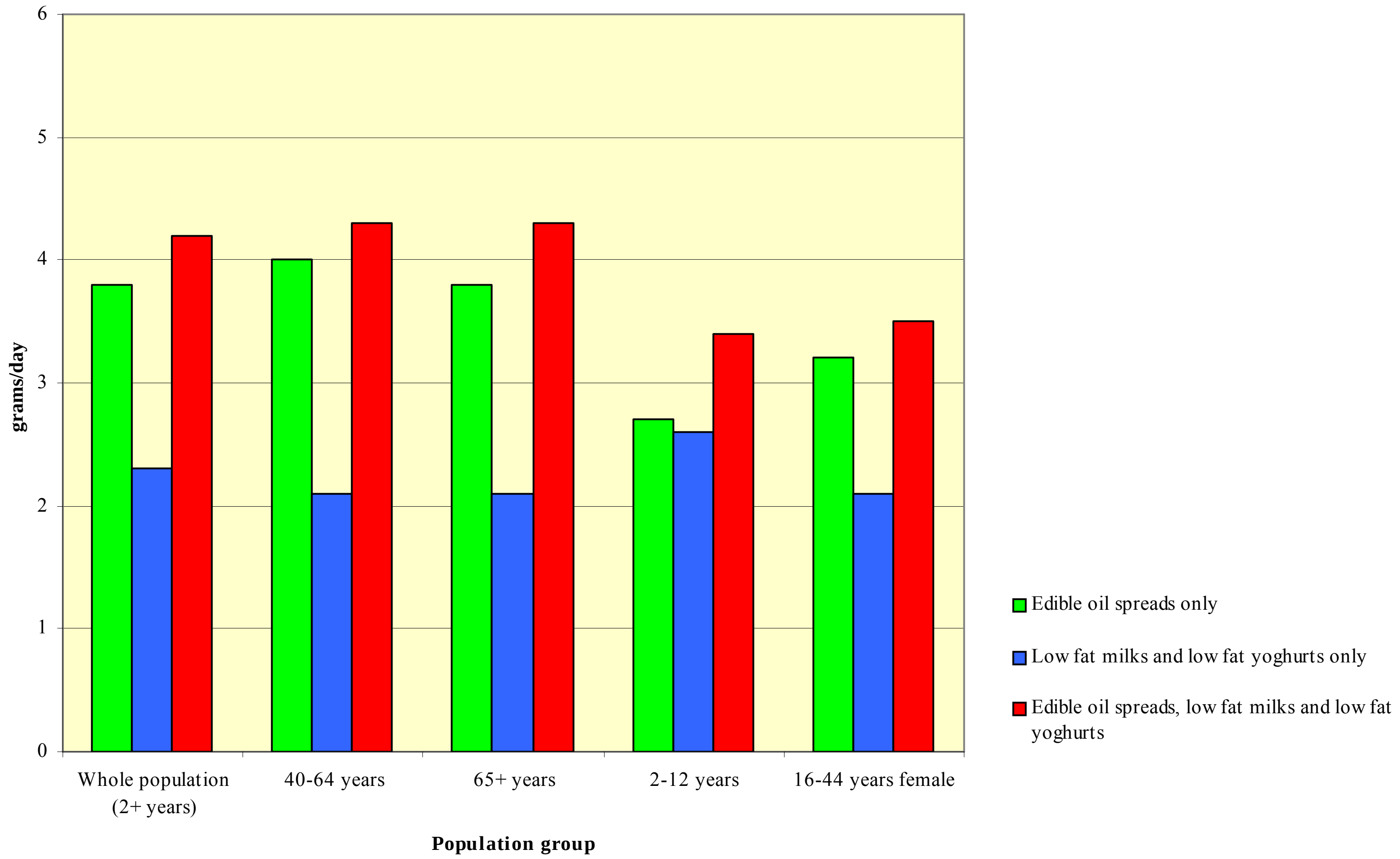


Figure 3: Estimated mean dietary exposure to free phytosterols for different population groups and scenarios for New Zealand

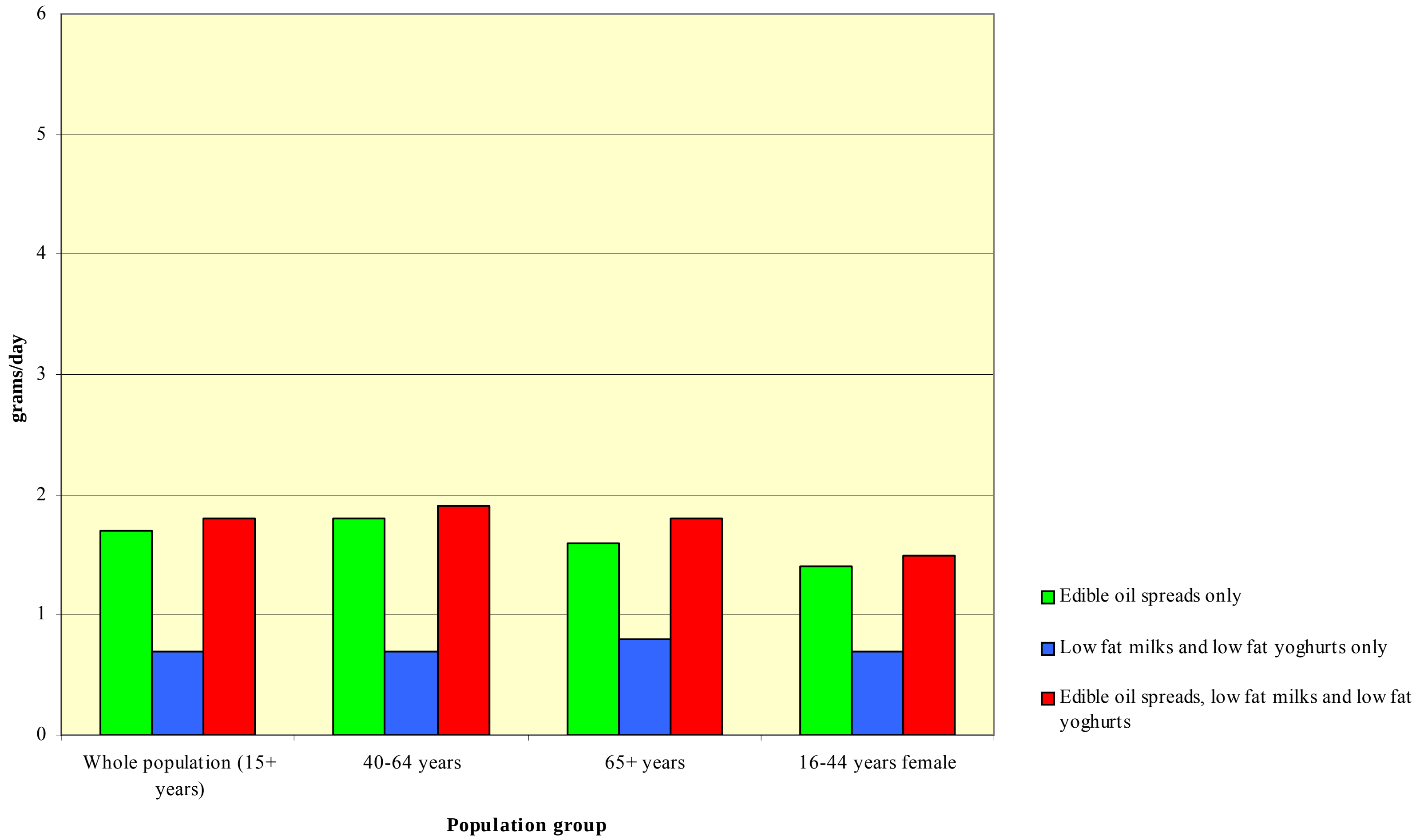


Figure 4: Estimated 95th percentile dietary exposure to free phytosterols for different population groups and scenarios for New Zealand

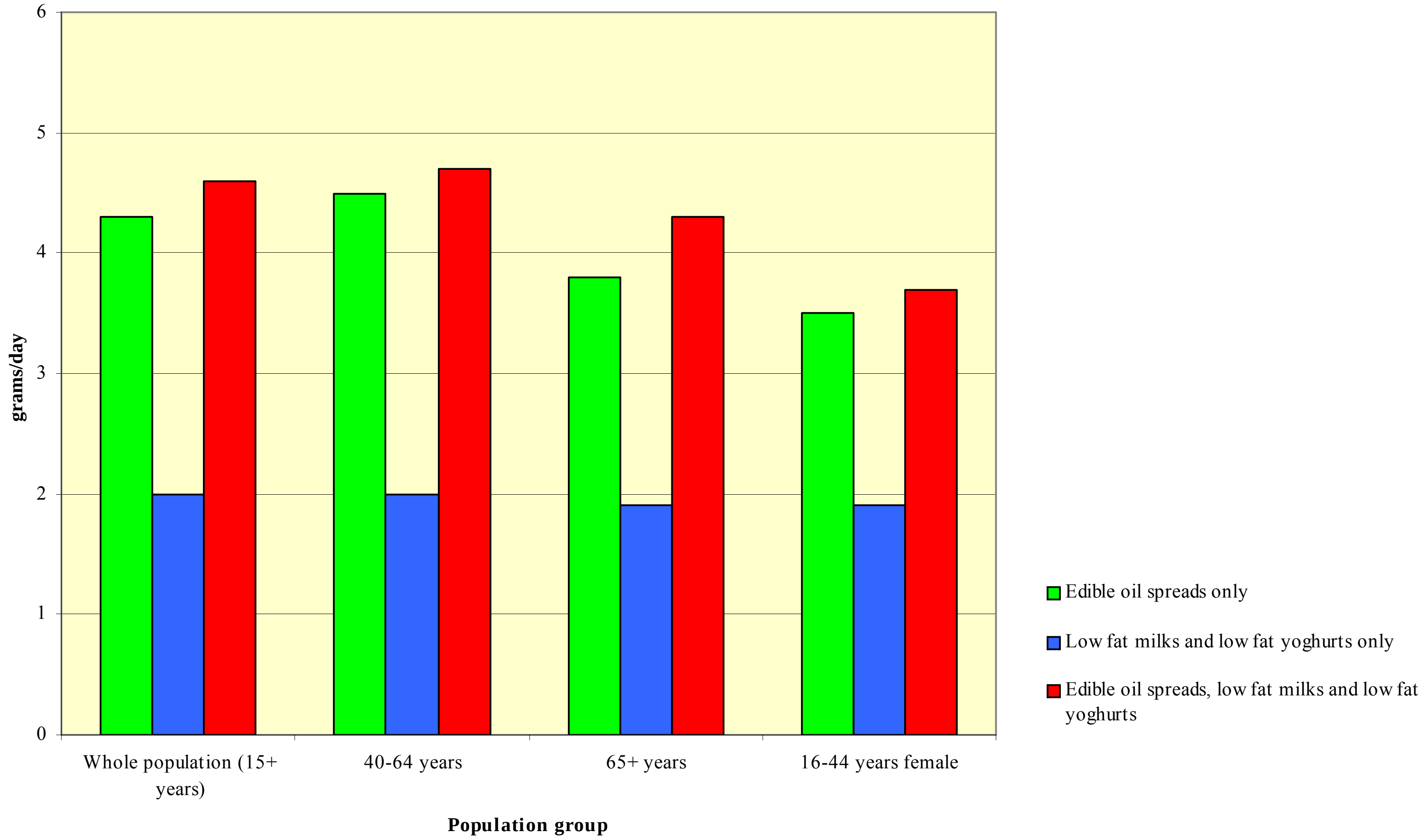


Table 2. Estimated dietary exposure to free phytosterols from edible oil spreads, for different population groups for Australia and New Zealand

Country	Population group	Number of consumers of phytosterols	Consumers as a % of total respondents#	Mean consumer exposure g/day	95th percentile consumer exposure g/day
Australia	Whole population (2 years+)	11 002	79	1.4	3.8
	40-64 years	3 372	78	1.5	4.0
	65+ years	1 557	79	1.5	3.8
	2-12 years	1 754	84	1.1	2.7
	16-44 years female	2 428	76	1.2	3.2
New Zealand	Whole population (15 years+)	3 093	67	1.7	4.3
	40-64 years	1 184	69	1.8	4.5
	65+ years	606	74	1.6	3.8
	16-44 years female	946	63	1.4	3.5

Total number of respondents for Australia: whole population (2 years and above) = 13 858, 2-12 years = 2 079, 40-64 years = 4 318, 65+ years = 1 960, 16-44 years female = 3 178; New Zealand: whole population (15 years and above) = 4 636, 40-64 years = 1 725, 65+ years = 817, 16-44 years female = 1 509;

(1) Estimated baseline dietary exposure to free phytosterols from edible oil spreads

Estimated mean dietary exposure to free phytosterols among consumers of edible oil spreads does not exceed 1.8 g/day (see Table 2 above), equivalent to slightly more than 2 serves of phytosterol-containing spreads per day. The highest mean exposure in both countries is for those aged 40-64 years (a sub-set of the target group for these products), and also the whole population (aged 15+ years) for New Zealand and those aged 65+ years for Australia. High consumers (95th percentile) of spreads have estimated dietary exposures to phytosterols up to 4.5 g/day, equivalent to 5½ serves of phytosterol-containing spreads per day. Again the group with the highest 95th percentile exposure is the 40-64 year age group for both countries, and also the whole population (aged 15+ years) for New Zealand.

These data show that the mean consumers of edible oil spreads in all population groups consume more than one serve of edible oil spreads per day, with the maximum mean consumer intake being 1.8 g (or 2.25 serves) per day for New Zealanders aged 40-64 years.

Table 3. Estimated dietary exposure to free phytosterols from low fat milks and low fat yoghurts, for different population groups for Australia and New Zealand

Country	Population group	Number of consumers of phytosterols	Consumers as a % of total respondents#	Mean consumer exposure g/day	95th percentile consumer exposure g/day
Australia	Whole population (2 years+)	4 510	33	0.8	2.3
	40-64 years	1 785	41	0.8	2.1
	65+ years	727	37	0.8	2.1
	2-12 years	348	17	1.1	2.6
	16-44 years female	1 166	37	0.7	2.1
New Zealand	Whole population (15 years+)	1 632	35	0.7	2.0
	40-64 years	689	40	0.7	2.0
	65+ years	341	42	0.8	1.9
	16-44 years female	469	31	0.7	1.9

Total number of respondents for Australia: whole population (2 years and above) = 13 858, 2-12 years = 2 079, 40-64 years = 4 318, 65+ years = 1 960, 16-44 years female = 3 178; New Zealand: whole population (15 years and above) = 4 636, 40-64 years = 1 725, 65+ years = 817, 16-44 years female = 1 509;

(2) Estimated ('low fat milks and low fat yoghurts') scenario dietary exposure to free phytosterols from low fat milks and low fat yoghurts

Estimated mean dietary exposure to free phytosterols among consumers of low fat milks and low fat yoghurts does not exceed 1.1 g/day (see Table 3 above), reflecting the smaller number of serves consumed per day of these foods than of edible oil spreads except in the 2-12 years age group. The highest mean exposure is for Australians aged 2-12 years. High consumers (95^{th} percentile) of free phytosterols from low fat milks and low fat yoghurts have estimated dietary exposures up to 2.6 g/day, equivalent to more than 3 serves of low fat milk and low fat yoghurt per day.

These data show that the mean Australian consumers of low fat milks and low fat yoghurts from all population groups assessed consume equal to about one serve per day of phytosterol enriched low-fat milk/low-fat yoghurt with the highest mean consumer intake being 1.3 serves of low-fat milk/low-fat yoghurt per day for Australian children aged 2-12 years. For the New Zealand population, the highest mean consumer of low-fat milk/low-fat yoghurt has an estimated exposure to these products of 1.0 serve per day.

Table 4. Estimated dietary exposure to free phytosterols from edible oil spreads, low fat milks and low fat yoghurts, for different population groups for Australia and New Zealand

Country	Population group	Number of consumers of phytosterols	Consumers as a % of total respondents#	Mean consumer exposure g/day	95th percentile consumer exposure g/day
Australia	Whole population (2 years+)	11 941	86	1.6	4.2
	40-64 years	3 757	87	1.7	4.3
	65+ years	1 691	86	1.7	4.3
	2-12 years	1 809	87	1.2	3.4
	16-44 years female	2 704	85	1.4	3.5
New Zealand	Whole population (15 years+)	3 570	77	1.8	4.6
	40-64 years	1 376	80	1.9	4.7
	65+ years	681	83	1.8	4.3
	16-44 years female	1 114	74	1.5	3.7

Total number of respondents for Australia: whole population (2 years and above) = 13 858, 2-12 years = 2 079, 40-64 years = 4 318, 65+ years = 1 960, 16-44 years female = 3 178; New Zealand: whole population (15 years and above) = 4 636, 40-64 years = 1 725, 65+ years = 817, 16-44 years female = 1 509;

(3) Estimated ('low fat milks and low fat yoghurts plus baseline') scenario dietary exposure to free phytosterols from edible oil spreads, low fat milks and low fat yoghurts

When free phytosterols are added to low fat milks and low fat yoghurts as well as edible oil spreads, estimated mean exposure to free phytosterols increases slightly from 1.4 g to 1.6 g/day for the Australian population, and from 1.8 g/day to 1.9 g/day for the New Zealand population (see Table 4 above). Estimated mean dietary exposure does not exceed 1.9 g/day for any population group and is highest for those aged 40-64 years in New Zealand. High consumers of free phytosterols (95th percentile) from edible oil spreads, margarines and low fat milks and low fat yoghurts have estimated dietary exposures of between 4.3 g/day to 4.7 g/day for all population groups assessed. Again, the group with the highest 95th percentile exposure is the New Zealand population group 40-64 years.

Discussion

At first inspection, it may appear surprising that the addition of phytosterols to low fat milk and low fat yoghurt, as well as to edible oil spreads, indicates only a slight increase in predicted mean intakes of phytosterols compared to baseline exposure; an increase of 0.2 g/day for all Australians and New Zealanders.

These findings reflect both the greater number of serves of edible oil spreads consumed on average and the much larger number of consumers of edible oil spreads than of low fat milks or low fat yoghurts in the low fat milks and low fat yoghurts + baseline scenario. The proportion of Australians and New Zealanders who consume low fat milks and low fat yoghurts (33% and 35%, respectively) is substantially lower than the proportion who consume edible oil spreads (79% and 67%, respectively). As noted earlier, the DIAMOND program derives results from each individual's food consumption patterns.

Major contributing foods to total estimated dietary exposures

The relative contributions of edible oil spreads, low fat milks and low fat yoghurts to estimated exposures to free phytosterols are displayed in Figures 5 and 6. More detailed results are presented in Appendix 1.

Foods may be high contributors to phytosterol exposure when they have a high concentration of free phytosterols, when they are consumed in large quantities and/or are consumed by a large proportion of the survey population.

Edible oil spreads are more important contributors to dietary exposure to free phytosterols than are low fat milks and low fat yoghurts, on a population basis, assuming that eating patterns recorded in 1995 have been maintained.

Figure 5: Percent contribution of each food group to free phytosterols dietary exposure for Australia

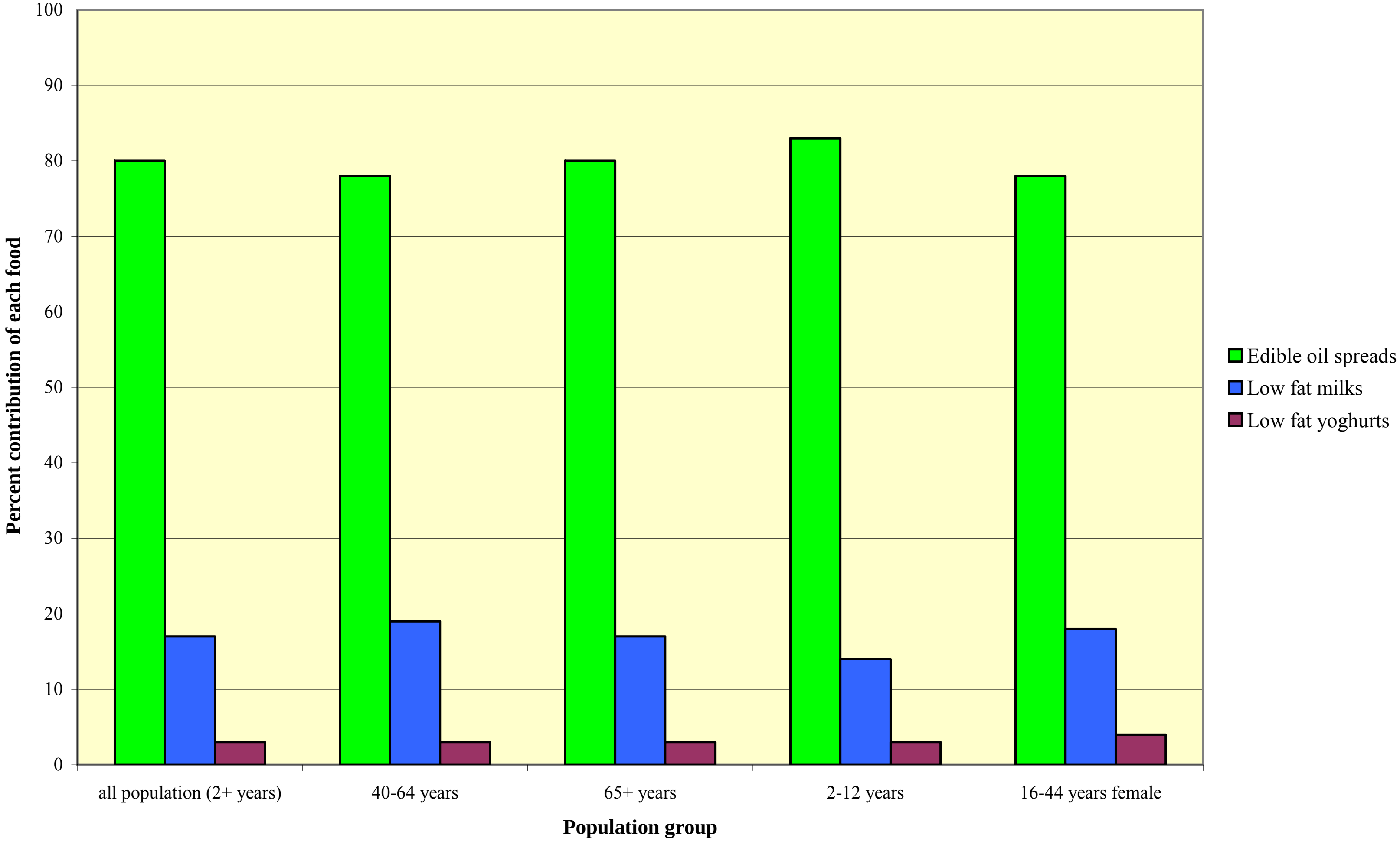
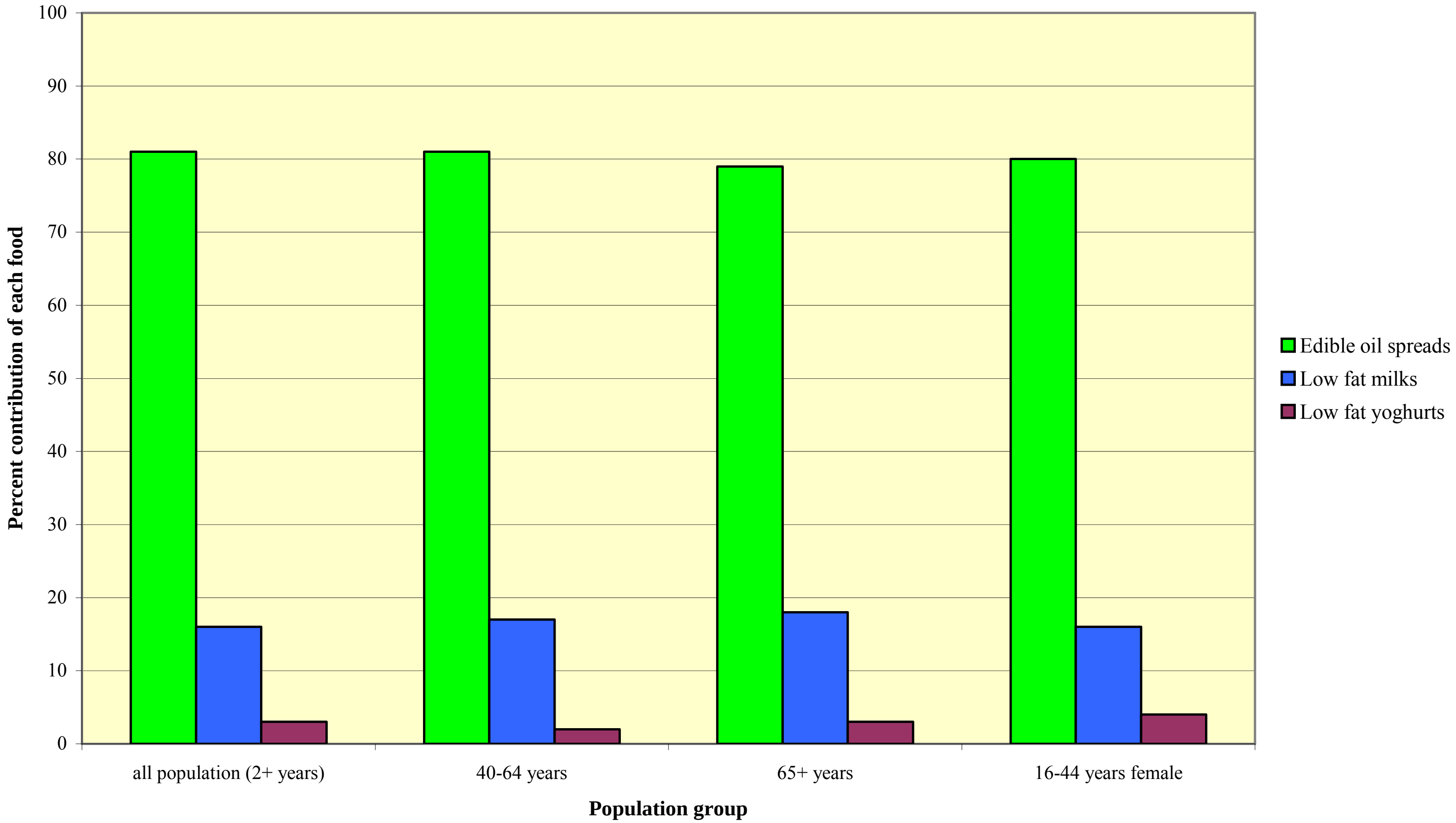


Figure 6: Percent contribution of each food group to free phytosterols dietary exposure for New Zealand



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Appendix 1

Major contributors to free phytosterols from edible oil spreads, low fat milks and low fat yoghurts for Australia and New Zealand.

Table A1.1. Major contributing foods to total free phytosterols dietary exposure for Australia and New Zealand, for different population groups

Country	Population group	Major contributing foods and percent of projected total free phytosterols intake
Australia	Whole population (2+ years)	Edible oils and margarines (80%) Low and milks (17%) Low fat yoghurts (3%)
	40- 64 years	Edible oils and margarines (78%) Low and milks (19%) Low fat yoghurts (3%)
	65+ years	Edible oils and margarines (80%) Low and milks (17%) Low fat yoghurts (3%)
	2 - 12 years	Edible oils and margarines (83%) Low and milks (14%) Low fat yoghurts (3%)
	16 – 44 years female	Edible oils and margarines (78%) Low and milks (18%) Low fat yoghurts (4%)
New Zealand	Whole population (15+ years)	Edible oils and margarines (81%) Low and milks (16%) Low fat yoghurts (3%)
	40- 64 years	Edible oils and margarines (81%) Low and milks (17%) Low fat yoghurts (2%)
	65+ years	Edible oils and margarines (79%) Low and milks (18%) Low fat yoghurts (3%)
	16-44 years female	Edible oils and margarines (80%) Low and milks (16%) Low fat yoghurts (4%)

ATTACHMENT 6

COMBINED DIETARY EXPOSURE ASSESSMENT REPORT

Applications A433 & A434 – Phytosterol esters derived from vegetable oils in breakfast cereals, low fat milk and low fat yoghurt

Summary

FSANZ is currently considering two separate applications seeking permission to use phytosterol esters derived from vegetable oils as a novel food ingredient under Standard 1.5.1, in 'healthy' (i.e. high-fibre, low-sugar) breakfast cereals (A433) and in low fat milk and low fat yoghurt (A434). This dietary exposure assessment was undertaken to determine the combined impact of allowing phytosterol esters to be added to all of the above foods, and incorporates the results of the dietary exposure assessment at **Attachment 5** to this report. The results therefore are an indication of likely exposures to phytosterol esters should both applications be approved.

This report provides a detailed dietary assessment of baseline plus all proposed foods (edible oil spreads, healthy breakfast cereals, low fat milk and low fat yoghurts). Assessments were conducted for the general Australian and New Zealand populations (2 years and above and 15 years and above, respectively), for two target populations for phytosterol products (those aged 40-64 years and 65 years and above) and for two non-target populations - women of childbearing age (16-44 years) and children (2-12 years, Australia only). Food consumption data were derived from the 1995 Australian National Nutrition Survey (NNS) and the 1997 New Zealand NNS. Food chemical concentration data were derived from levels proposed in both applications and from the maximum level of use already permitted in edible oil spreads and margarines in the Code.

Estimated mean dietary exposure from all foods, expressed as free phytosterols, did not exceed 1.9 grams per day (g/day) in any population group assessed. At the 95th percentile of exposure, no population group exceeded 4.7 g free phytosterols per day. The major source of dietary exposure to added phytosterols was edible oil spreads for all population groups assessed. It should be noted that the modelling approach was conservative as it assumed all requested foods contained phytosterols at the maximum concentration, and therefore dietary exposure is overestimated.

1. Introduction

This dietary exposure assessment combines the results of separate dietary exposure estimates for each of the applications A433 and A434 (at Attachment 5 to each Draft Assessment Report), to provide an estimate of overall phytosterol ester intake, if all foods under assessment contained phytosterols (a worst-case scenario).

2. Methodology

The dietary exposure assessment took into account the existing permission under Standard 1.5.1 which allows the addition of phytosterol esters to reduced fat edible oil spreads and margarine, but not the intrinsic levels of phytosterols in foods.

Both Applicants propose to add phytosterol esters in amounts equivalent to 0.8 g free phytosterols per serve (1.3 g phytosterol esters). All values reported are expressed as free phytosterols.

As indicated in the individual dietary exposure assessment for each application, there are a number of assumptions and limitations in the dietary modelling process and therefore each dietary exposure assessment should be used only as a guide for risk management decisions regarding food regulation.

3. Concentration levels and serving sizes

The levels of free phytosterols in healthy breakfast cereals used in the exposure assessment were derived from Application A433, while the levels of use for low fat milk and low fat yoghurt were derived from Application A434. Levels of free phytosterols per serve were converted to concentrations in mg/kg to enable them to be entered into DIAMOND. Serve sizes are based on average product serve sizes from food packages - including 1 serve of edible oil spreads (10 g), 1 serve of healthy breakfast cereal (45 g), 1 glass of milk (250 mL) and 1 small punnet of low fat yoghurt (140g). The foods and proposed levels of use are summarised below in Table 1.

Table 1: Proposed levels of use of free phytosterols in foods

DIAMOND Food Code	Food Name	Serve size (g)	Proposed level of free phytosterol per serve (g/serve)	Concentration Level used in modelling (mg/kg)
1.1.1.2	Low fat milks (<1.5% fat), unflavoured	250	0.8	3 200
1.2.2.2	Low fat flavoured yoghurts (<1.5% fat content), including low fat fruit yoghurts	140	0.8	5 714
2.2	Edible oil spreads including reduced fat spreads	10	0.8	80 000
6.3.4	Healthy Breakfast cereals	45	0.8	17 778

4. Results

Estimated dietary exposures to added phytosterols

The estimated exposures to phytosterols from all foods encompassed by A433 and A434 combined were calculated and are presented in Figure 1 (means) and Figure 2 (95^{th} percentile) for Australia, and Figure 3 (means) and Figure 4 (95^{th} percentile) for New Zealand. For comparative purposes the following are presented:

- estimated exposure baseline (edible oil spreads only);
- estimated exposure A433 (edible oil spreads plus healthy breakfast cereals);
- estimated exposure A434 (edible oil spreads plus low fat milk and low fat yoghurt); and
- estimated exposure all foods combined

A complete set of numerical results are provided for Australia and New Zealand in Appendix 1, Table A1.1 (all proposed foods). Results for consumers only (eaters of foods containing phytosterols) are presented, rather than results based on all respondents. This is because the purpose of the risk assessment is to consider the potential impact of phytosterol addition to a variety of foods on people who report eating these foods.

Estimated mean exposure to phytosterols among consumers of any phytosterol containing food does not exceed 1.9 g/day (see Appendix 1). The highest mean exposure is for those aged 40-64 years in New Zealand, which is one of the target groups for phytosterol-containing products. High consumers (95^{th} percentile) of the specified foods have estimated dietary exposures to phytosterol esters up to 4.7 g/day. Again, the group with the highest 95^{th} percentile exposure is the 40-64 year age group in the New Zealand population.

Figure 1: Estimated mean dietary exposure to free phytosterols for different population groups and scenarios for Australia

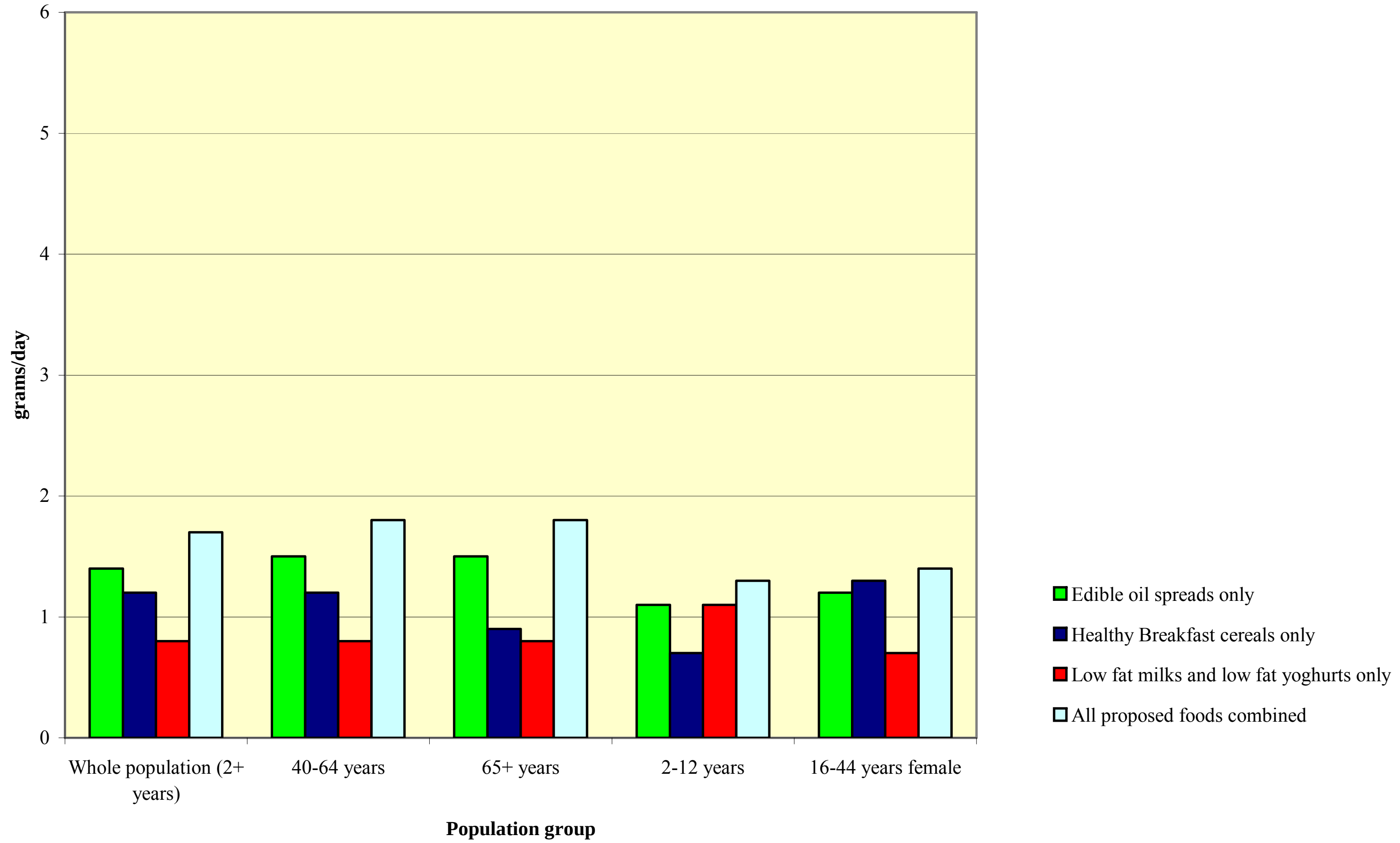


Figure 2: Estimated 95th percentile dietary exposure to free phytosterols for different population groups and scenarios for Australia

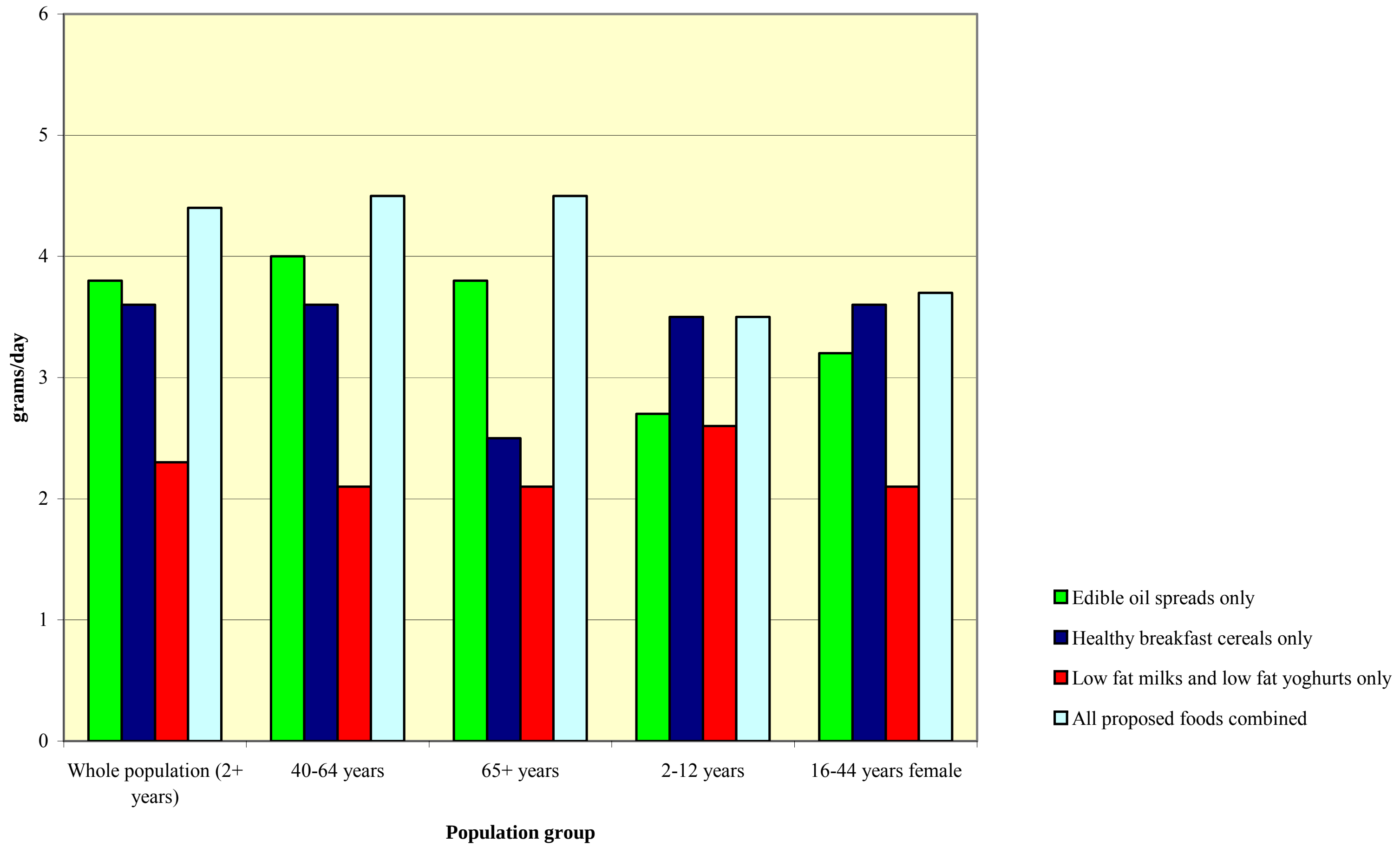


Figure 3: Estimated mean dietary exposure to free phytosterols for different population groups and scenarios for New Zealand

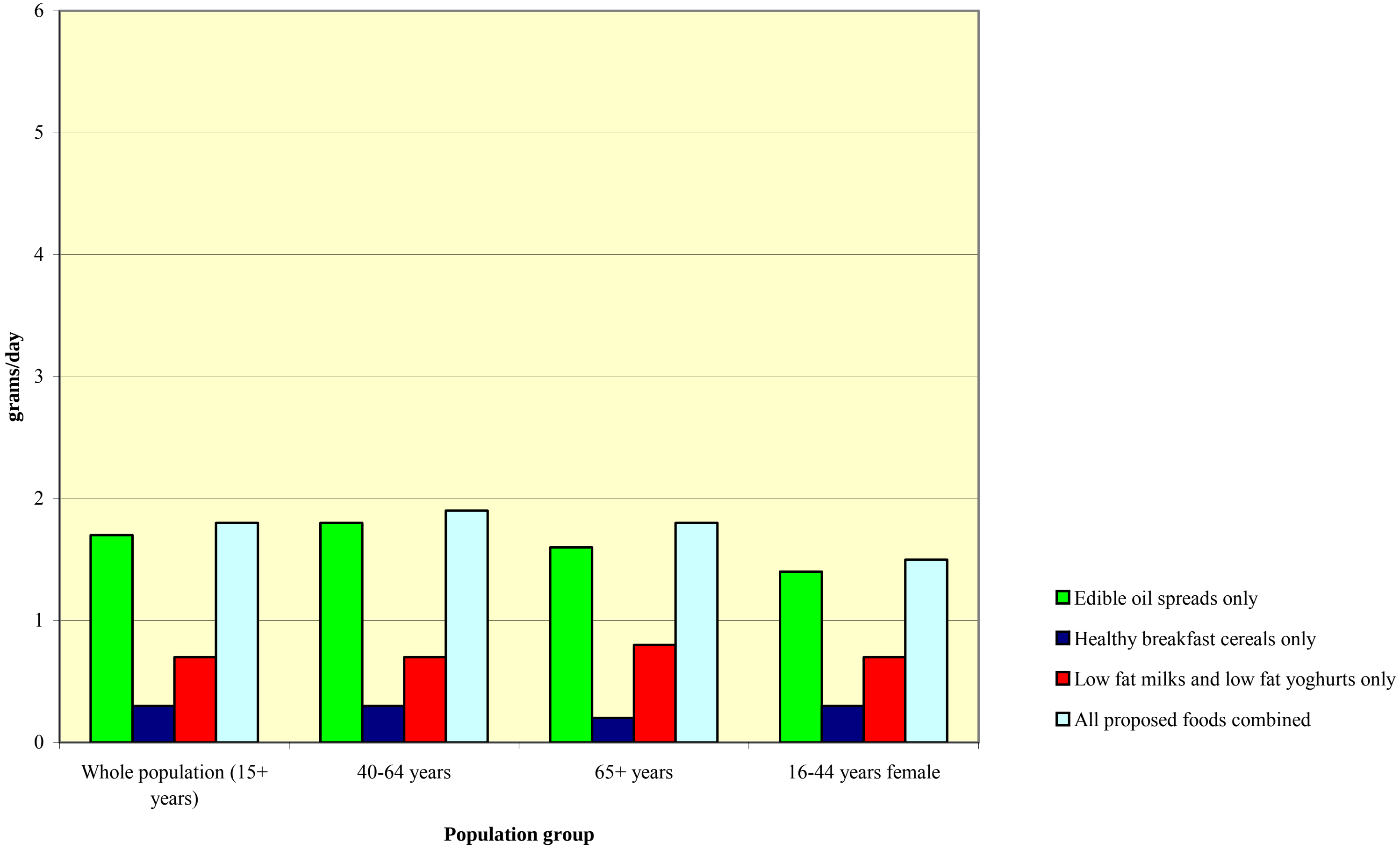
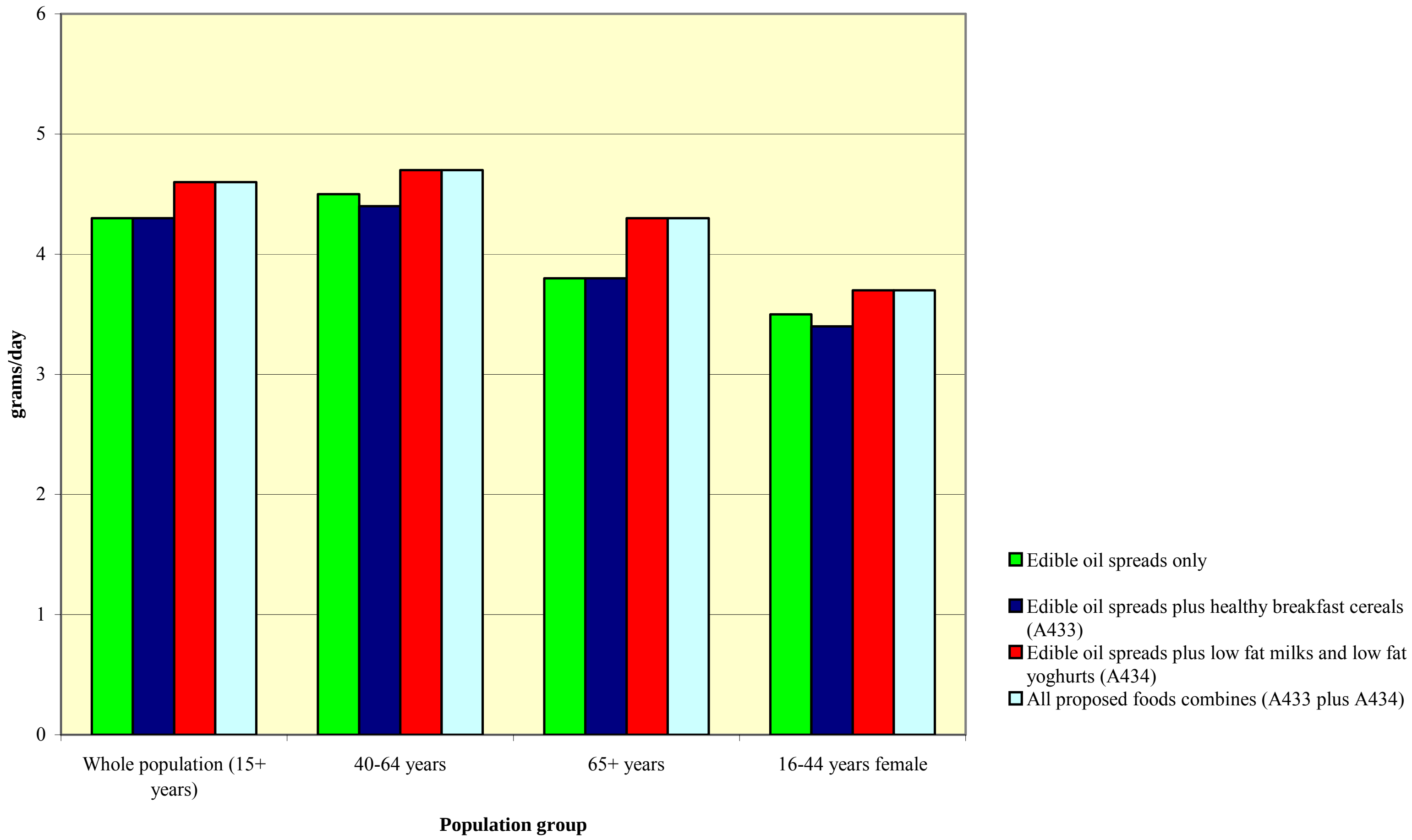


Figure 4: Estimated 95th percentile dietary exposure to free phytosterols for different population groups and scenarios for New Zealand



Major contributing foods to total estimated dietary exposures

The relative contributions of each phytosterol containing food to combined dietary exposures to free phytosterols are displayed in Figure 5 for Australia, and Figure 6 for New Zealand. More detailed results are presented in Appendix 2.

Foods may be high contributors to phytosterol exposure when they have a high concentration of free phytosterols, when they are consumed in large quantities and/or are consumed by a large proportion of the survey population.

When all foods are combined in the exposure assessments, edible oil spreads are the major contributors to dietary exposure to free phytosterols, for every population group assessed.

Figure 5: Percent contribution of each food group to free phytosterols dietary exposure for Australia

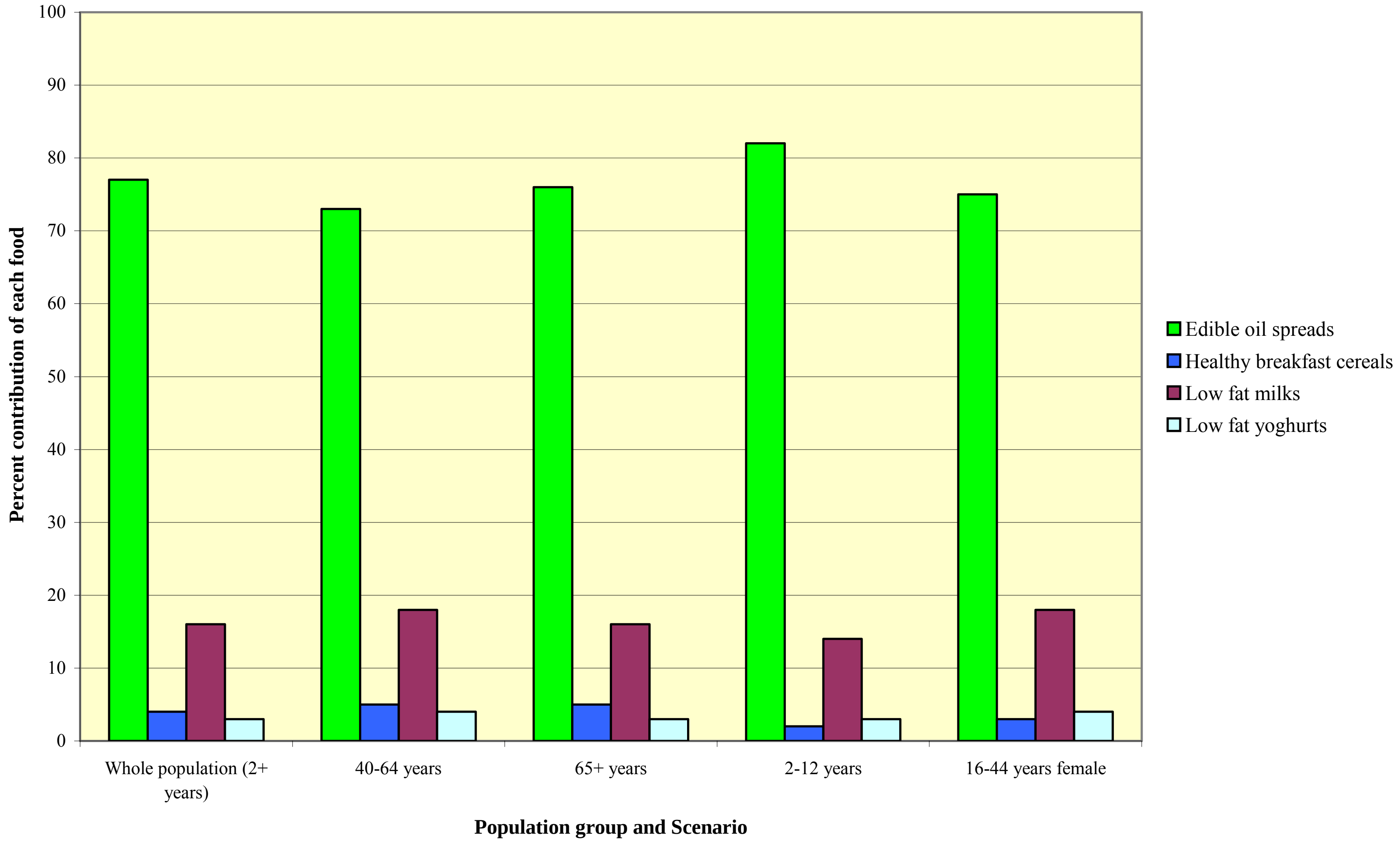
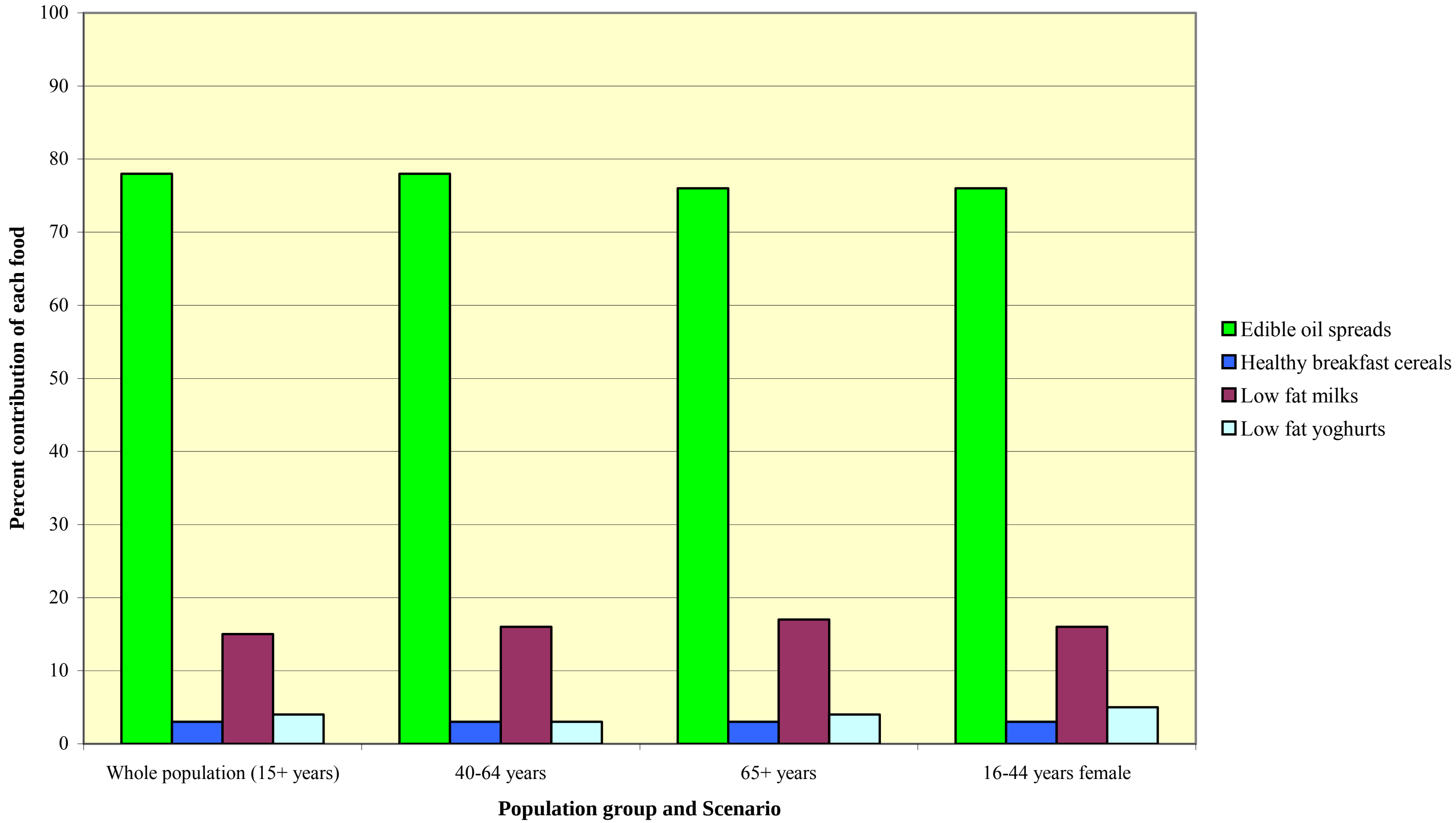


Figure 6: Percent contribution of each food group to free phytosterols dietary exposure for New Zealand



References

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Appendix 1

Estimated exposures to free phytosterols from all foods combined for Australia and New Zealand

Table A1.1. Estimated dietary exposures to free phytosterols from all foods combined (edible oil spreads, healthy breakfast cereals, low fat milk and low fat yoghurts), for different population groups for Australia and New Zealand

Country	Population group	Number of consumers of phytosterols	Consumers as a % of total respondents#	Mean consumer exposure grams/day	95th percentile consumer exposure grams/day
Australia	Whole population (2 years+)	12 016	87	1.3	4.4
	40-64 years	3 787	88	1.4	4.5
	65+ years	1 709	87	1.5	4.5
	2-12 years	1 814	87	1.3	3.5
	16-44 years female	2 720	86	1.4	3.7
New Zealand	Whole population (15 years+)	3 686	84	1.8	4.6
	40-64 years	1 420	82	1.9	4.7
	65+ years	705	86	1.8	4.3
	16-44 years female	1 148	76	1.5	3.8

Total number of respondents for Australia: whole population (2 years and above) = 13 858, 2-12 years = 2 079, 40-64 years = 4 318, 65+ years = 1 960, 16-44 years female = 3 178; New Zealand: whole population (15 years and above) = 4 636, 40-64 years = 1 725, 65+ years = 817, 16-44 years female = 1 509;

Appendix 2

Major contributors to free phytosterols from all proposed foods for Australia and New Zealand

Table A2.1. Major contributing foods to total free phytosterols dietary exposure for Australia and New Zealand, for different population groups

Country	Population group	Major contributing foods and percent of total free phytosterols exposures
Australia	Whole population (2+ years)	Edible oil spreads (77%) Low fat milk (16%) Healthy breakfast cereal (4%) Low fat yoghurt (3%)
	40- 64 years	Edible oil spreads (73%) Low fat milk (18%) Healthy breakfast cereal (5%) Low fat yoghurt (4%)
	65+ years	Edible oil spreads (76%) Low fat milk (16%) Healthy breakfast cereal (5%) Low fat yoghurt (3%)
	2 - 12 years	Edible oil spreads (82%) Low fat milk (14%) Low fat yoghurt (3%) Healthy breakfast cereal (2%)
	16 – 44 years female	Edible oil spreads (75%) Low fat milk (18%) Low fat yoghurt (4%) Healthy breakfast cereal (3%)
New Zealand	Whole population (15+ years)	Edible oil spreads (78%) Low fat milk (15%) Low fat yoghurt (4%) Healthy breakfast cereal (3%)
	40- 64 years	Edible oil spreads (78%) Low fat milk (16%) Low fat yoghurt (3%) Healthy breakfast cereal (3%)
	65+ years	Edible oil spreads (76%) Low fat milk (17%) Low fat yoghurt (4%) Healthy breakfast cereal (3%)
	16-44 years female	Edible oil spreads (76%) Low fat milk (16%) Low fat yoghurt (5%) Healthy breakfast cereal (3%)

ATTACHMENT 7

SUMMARY OF PUBLIC SUBMISSIONS – 1ST Round

The first public consultation period for this Application was conducted between 19 March 2003 and 30 April 2003. The following submissions were received:

1. Australian Dairy Corporation

- supports Option 2 – approval of phytosterol esters in low-fat milk and low-fat yoghurt, with careful consideration as to appropriate labelling of these products to provide advice to consumers.
- does not support Option 3 – a general approval for the use of phytosterol esters in foods because of concerns that a broad approval could lead to over-consumption and use of foods that are incompatible with the Australian Dietary Guidelines.
- cites the UK Advisory Committee on Novel Foods and Processes (ACNFP) judgement that increasing the product range to include milk and yoghurt-type products would not lead to over-consumption of phytosterols.
- states that research shows that phytostanols in yoghurt can lower LDL cholesterol as effectively as enriched margarines.
- considers that enrichment of specific foods with either phytostanols or phytosterol esters would benefit public health by:

  – improving access to phytosterol enriched foods;
  – improving the clarity of dietary advice to patients with risk of heart disease;
  – allowing consumers of phytosterol enriched milk and yoghurt to experience all of the benefits of these foods in terms of other nutrients that may be lacking;
  – consuming additional low-fat milk and yoghurt in conjunction with a low-fat diet rich in fruits and vegetables can also benefit other coronary heart disease risk factors such as high blood pressure and plasma homocysteine levels.

2. Joanne Dellow – University of Otago

- considers that phytosterol enrichment of low-fat dairy products such as milk and yoghurt should not be approved at this time because of insufficient evidence of efficacy and safety at higher consumption levels, despite strong evidence that phytosterols are effective in lowering cholesterol when present in edible oil spreads.
- provides detailed analysis of phytosterols in terms of their safety, efficacy in various food matrices, possible mechanisms of action, and dietary or nutritional effects.
- questions whether low-fat dairy products are appropriate foods for older adult males. Considers that it is important that the proposed products are already part of the target population's habitual diet because both dietary and lifestyle modifications are difficult to implement and long-term adherence is difficult to maintain.
- considers that the published studies so far do not unequivocally demonstrate no adverse effects in humans and that the long-term effects of phytosterols are generally unknown.
- cites studies that show that intake of phytosterols of 1.6g per day adversely affects beta-carotene levels, and therefore the proposed level of use of 2.4g per day from three servings of phytosterol enriched products will have deleterious nutritional effects.

3. So Natural Foods Australia

- supports Option 2, to approve the use of phytosterol esters in low-fat milk and yoghurt
- considers that there should be additional permissions for use of phytosterol esters in non-dairy beverages derived from legumes that are consumed as alternatives to dairy products because:

  - it is unfair to discriminate against those consumers who are intolerant to dairy products;
  - soybeans naturally contain phytosterols and the addition of the esters to soy-derived dairy alternatives will enhance the inherent health benefits;
  - soy foods are recommended by the American Heart Association for people with elevated total and LDL-cholesterol, and the addition of phytosterols to soy products will further enhance their cholesterol lowering ability. Consumers will therefore not need to change or increase their consumption of enriched foods to meet dietary recommendations;
  - in expanding the current application to include legume-derived alternatives, a greater variety of cholesterol-lowering foods will be available, allowing consumers to more easily reach the required intake; and
  - as phytosterols are found naturally in soy, they are likely to be as effective in lowering cholesterol as they are when present in other foods such as beverages, margarines, ground beef and baked goods.

- there are benefits to industry and to consumers by broadening the permission to include analogues derived from legumes. The benefits to industry include increased domestic market opportunities, increased sales and profitability, increased opportunity to impact on public health, and increased opportunity to provide information to consumers about healthy eating and lifestyle.
- there are costs to industry by not allowing the use of phytosterol esters in the corresponding non-dairy beverages by way of decreased market share in the novel foods arena, and a reduced ability to develop products which positively impact on public health.
- the benefits of adding phytosterol esters to low-fat milk and low-fat yoghurts, and their legume-derived alternatives, significantly outweigh the potential costs to business and to consumers.
- if the application is expanded to include analogues derived from legumes, industry would support a responsible approach to the marketing and labelling of the phytosterol enriched products to foster appropriate consumer usage.

4. Australian Food and Grocery Council (AFGC)

- supports Option 3 – a broad permission for the use of phytosterol esters in food, but also supports Option 2 – permission to use phytosterol esters in low-fat milk and low-fat yoghurt as the next best option. Considers that this application could at least be extended to cover all yoghurts and all milks.
- disputes FSANZ’s authority to require efficacy data in relation to labelling as the Novel Foods Standard (Standard 1.5.1) refers only to the safety of the food, and there is already sufficient prohibitions on misleading or deceptive labelling in State, Territory and New Zealand Food Acts, the Trade Practices Act, and State, Territory and New Zealand Fair Trading Acts.

- states that if a reduction in absorption of fat-soluble vitamins is demonstrated, FSANZ can require phytosterol-enriched foods to contain a minimum quantity of the vitamins either naturally-occurring or by fortification. This disadvantage should not be the basis of a rejection of the application, as the ability to reduce cholesterol offers significant health advantages and reduced absorption of fat-soluble vitamins can be overcome.
- considers that the over-use scenario by target consumers is unlikely partly because of the cost disincentive.
- states that habitual consumption by non-target groups is also unlikely and of minimal health risk.
- agrees that appropriate labelling is essential, consistent with the existing requirements for phytosterol enriched table spreads and margarines.
- FSANZ cited health risk factors such as high blood cholesterol as part of the economic argument in favour of mandatory nutrition labelling. Approval of cholesterol lowering foods would therefore be consistent with this position.
- supports FSANZ in proposing that maximum permitted levels and specifications for identity and purity may be required.
- supports the same quantity of phytosterols being required in a serve of each of the foods to which phytosterols are added,
- a broad permission would be advantageous to obviate the necessity for further applications of a similar nature. At the very least, consideration should apply to all breads, breakfast cereals and breakfast cereal bars.

5. New Zealand Dietetic Association

- opposes the Application because there is neither sufficient nor substantial evidence yet available regarding the safety of higher intakes of phytosterols and prolonged exposure to phytosterols in fortified foods.
- considers that the current permission for phytosterol-enriched table spreads enables controlled use of the products, and allows defined quantities to be recommended by health professionals to targeted people.
- considers that general use of phytosterol-enriched foods by non-target groups e.g. the young, is premature since the scientific evidence is unclear on potential effects on carotenoids, lycopene, vitamin E, eostrogenic activity, and other biological activities.
- states that the lack of long term and large scale safety studies and the potential for widespread use of the products would preclude any recommendation of use by target consumers.
- increasing the range of foods will lead to an increase in the daily intake of phytosterols to say > 3g/day, with a paucity of supporting safety studies.
- Existing evidence shows reductions in plasma antioxidants, particularly lipophilic β-carotene, α-carotene, lycopene and other carotenoids (e.g. lutein, zeaxanthin) with higher intakes of phytosterols. Consumers cannot be relied upon to increase their consumption of fruit and vegetable to offset this decrease in absorption.
- expresses particular concern for vulnerable groups such as children, adolescents and the elderly because the foods in question are favoured by these groups in large quantities and it is possible that, if available to the entire household, the foods will not be consumed exclusively by one target family member. In addition, consumer familiarity with the phytosterol-enriched foods may erode compliance with the dietary recommendations on the labels.
- considers that the high cost of purchase will not work as a limiting factor.

6. Rosemary Stanton (Aust)

- opposes the Application on the basis of concerns about the nutritional issues for both target and non-target consumers including:

  - the possibility of side effects, particularly a reduction in levels of fat-soluble vitamins, α-tocopherol, β-carotene, lycopene.
  - a paucity of studies looking at the longer term nutritional effects from higher consumption of phytosterol- enriched foods.
  - reported undesirable reduction in HDL cholesterol
  - potential for unknown effects on other carotenoids and fat-soluble compounds such as the family of tocopherols and tocotrienols that may be important nutrients.

- considers that dietary advice on the labels of phytosterol-enriched foods recommending consumption of fruits and vegetables will be ineffectual, as similar dietary advice has not been heeded by the Australian public.
- states that food manufacturers are unlikely to provide information to consumers that explains why additional fruits and vegetables are desirable.
- potential effects on children ought to be investigated because of the nature of the foods in question i.e. fibre-increased bread, breakfast cereal bars, low-fat milk and yoghurt, that are favoured foods of the young.
- considers that there are other effective measures for reducing cholesterol, namely reducing consumption of saturated fat and/or losing excess weight which have other beneficial health effects on the risks of developing diabetes or hypertension. The availability of a range of phytosterol-enriched foods may encourage a reliance only on these foods as a means of reducing cholesterol.
- medicalisation of the food supply is not the best method of dealing with health problems, as it can be misinterpreted by consumers.
- considers that the consumption levels of foods containing phytosterols will be difficult to control and there is no evidence that higher consumption is needed to achieve the desired effect. To minimise the possibility of overconsumption, messages on food labels would need to be carefully worded and it is doubtful that this would be as effective as limiting the availability of phytosterol-enriched food products.
- proposes that it would be more appropriate to market phytosterols as supplements.

7. Sanitarium Health Food Company (Aust)

- opposes the application because of a current lack of adequate information regarding the safety of higher intakes of phytosterols from fortified foods.
- states that studies are required on the effects of phytosterol esters on a wide range of antioxidants in the blood, including β-carotene and other carotenoids like lutein and zeaxanthin.
- considers that consumers may choose phytosterol-enriched products without increasing their consumption of carotenoid-rich foods such as fruits and vegetables, possibly because of a lack of advice about dietary effects.
- doubts that consumers will comply with dietary advisory statements on the label of a phytosterol-enriched product.

- advises that there could be an impact from a broader availability of phytosterol-enriched foods on people with the rare condition sitosterolaemia.

8. New Zealand Food Safety Authority

- considers that the assessments of both applications are especially important in terms of the potential impacts of phytosterol-enriched products on non-target consumer groups such as children.
- labelling information for consumers is important and should advise that consumption in excess of the recommended number of servings will not provide additional cholesterol-lowering benefit.
- the addition of phytosterol-esters to bread and cereals poses regulatory problems because the composition of these products in not prescribed in the Code. Linking permission to these product types would require product definitions in the Code.
- reinforce the importance of manufacturers being aware of the permitted claims about the benefits of phytosterols, and staying within the provisions of the Code and the New Zealand Medicines Regulations.

9. Dietitians Association of Australia

- considers that there are potential benefits for consumers and dietitians if a broader range of plant sterol containing foods is available.
- expresses concerns about the possible higher intakes of plant sterols by non-target groups particularly pregnant/lactating women, elderly people, healthy and obese children and adolescents.
- a safety assessment using relevant studies must be completed.
- nutrient criteria for any food under consideration should be applied before products qualify for the addition of plant sterols.
- supports mandatory advisory statements on labels (but none specified).
- an informed decision on the merits of the application can only be done when more information is available.

10. Unilever Australia

- supports Option 2, to approve phytosterol esters in fibre-increased bread and breakfast cereal bars, and endorses the comments of the AFGC.
- FSANZ should consider applications for like foods currently being assessed in the international arena in terms of the proposed levels of free phytosterols per serving of food. In these applications (A433 and A434), the applicants are seeking permission to use 0.8 g free sterols per serve of requested foods. The current Unilever application to the EU seeks approval to use 1 g of free sterols per serving of dairy food (milk and yoghurt). Information derived from Post Launch Monitoring of yellow fat spreads containing phytosterol esters has demonstrated that even regular users do not use the recommended quantities of spread, and this is confirmed also by data for Australian and New Zealand consumers. Therefore, permission to use 1 g of free phytosterols per serving of milk and yoghurt would enable consumers to reach the target amount of 2-3 g per day in 2-3 servings, rather than requiring a minimum of three servings.

- a common and easily understood labelling protocol ought to apply to all plant sterol containing foods to facilitate proper use by consumers. For example, the European Commission are in the process of preparing a directive on a common labelling format for all products containing phytosterols/esters/stanols. In addition to the mandatory advisory statements already required on products for sale in Australia/New Zealand, statements to this effect are suggested:

  - the product is for people who want to lower their blood cholesterol levels;
  - a declaration of the amount of phytosterols in the food eg. *one (package) of this food contains (x) g of plant sterols/stanols*; and
  - a recommendation on a suitable number of servings per day eg. *it is recommended to consume no more than 3 g sterol each day for the best cholesterol lowering effect.*

- the specifications for the phytosterol esters derived from vegetable oils in the Code are now not generic enough to apply to the phytosterols produced from the current range of available plant sources.
- submits draft specifications under consideration by Food Chemicals Codex, and questions the need for minimum limits for the typical sterol distribution.

11. Richard James (NZ)

- opposed to both Applications A433 and A434
- considers that the advisory statements currently required on the table spreads and margarines are "warning" consumers that these foods should not be eaten by infants, children, pregnant or lactating women, and that the foods proposed in the applications are most likely to be consumed by children.
- provides information on the dangers to children from diets that reduce their cholesterol.
- considers that phytosterols are estrogenic and raised this issue during the previous assessment of phytosterols in the food supply under Application A410. Considers that plant estrogens are already too prevalent in the diet with widespread adverse public health outcomes.
- expresses concerns with the medicalisation of the food supply to benefit a particular section of the population, which will inevitably lead to consumption by people who do not need to lower their cholesterol.
- lowering cholesterol levels below a normal level can have deleterious effects on health.
- if approved, the products should have mandatory warning statements because it is not known what cumulative effects may occur, or what the long-term effects of continual consumption may be.

12. Valerie James (NZ)

- opposed to both Applications A433 and A434
- provided material claiming that phytosterols can act as endocrine disrupters in fish, and exhibit a classic estrogenic effect in animals.
- phytosterol-containing products should carry conspicuous warnings to the effect that these products are unsuitable for pregnant women, infants and children.
- suggests that phytosterols have a 'drug-like' effect and consumers could actually be taking part in a large, uncontrolled human experiment.

- proposes that the benefits from lowering cholesterol are uncertain, and that there is almost no evidence that dietary cholesterol induces hypercholesterolaemia.
- suggests an association between a low serum cholesterol and the risk of lung cancer may be through lowering beta-carotene levels. Natural forms of carotenes are more beneficial than supplements.
- the Application fails to show that any benefits outweigh the potential risks.
- are associated with lung cancer and phytosterols serum cholesterol with lung cancer.

13. Nestlé Australia

- supports the general approval of the use of phytosterol-esters as ingredients in foods, including low-fat milk and low-fat yoghurt.
- considers that use of phytosterol esters in foods can assist in the reduction of diet-related conditions such as high blood cholesterol, which is a known risk factor for disease.
- approval of this Application has the potential to reduce public health costs incurred by government.

14. Environmental Health Unit, Queensland Health

- strongly opposed to this Application, on the basis of expert dietary advice.
- express a range of concerns including:

  - the long term effects and safety of consumption of phytosterols is unknown;
  - the inappropriate use of food as a medicine;
  - the potential for inequity in the marketplace, where the foods containing phytosterols are more costly than the traditional counterpart and are therefore less affordable to lower socio-economic groups who already carry a greater chronic disease burden;
  - consumption of phytosterols is reported to lower serum alpha-tocopherol and carotenoids;
  - phytosterol-esters reported to have an oestrogenic activity in animals, with unknown relevance in humans;
  - phytosterol enriched foods present particular health risks to individuals with sitosterolaemia and who are homozygous for the condition. The risks to heterozygous individuals are not known; and
  - the safety and use of these products by non-target groups (children, pregnant women, people with normal or low serum cholesterol) needs to be fully investigated.

- suggests that the results from one clinical study are unlikely to provide sufficient information to alter previous conclusions about the lack of available data to assess the safety of phytosterols in a broad range of foods. The study would need to have used a large number of participants, and other similar studies would also be required using overseas populations.
- a statement to consume 2-3 servings per day of a particular food to ensure adequate consumption of the ingredient implies a therapeutic dose, which is inappropriate.
- all consumers may be affected, not just those with health concerns about high serum cholesterol.

- a wider range of foods containing added phytosterols may lead to excess consumption of phytosterols.
- there could be significant impact on Government educational resources and capacity if either of the options to approve the use of phytosterol-esters is successful, because in general, consumers do not understand what phytosterol-esters are and the role they may play in healthy eating and chronic disease management (specifically cardiovascular disease).

15. Food Technology Association of Victoria Inc

- supports option 2 i.e. approval of the use of phytosterol-esters as ingredients in low-fat milk and low-fat yoghurt.

16. Australian Quarantine and Inspection Service (AQIS)

- AQIS will defer comment until the Draft Assessment Report is completed and released for public comment.

Issues raised in first round public submissions:

(i) Medicalisation of the food supply

The Environmental Health Unit of Queensland Health, in addition to Richard and Valerie James (NZ) and Rosemary Stanton (Aust), express concerns that a broader approval for phytosterols equates to the food supply becoming a vehicle for the delivery of a therapeutic agent not required by the whole population.

Response

Phytosterol esters derived from vegetable oils are already approved novel foods under Standard 1.5.1 in the Code. Although they occur naturally in foods such as legumes and nuts at low levels, they are regarded as novel food ingredients when used in amounts some 5-10 fold higher than normal food consumption would provide.

Several identified risk factors for major diseases such as cardiovascular disease and stroke can be correlated in varying degrees with diet. Of these, obesity, high blood cholesterol, and high blood pressure have been at the forefront of public health messages over an extended period. In Australia and New Zealand, government and non-government organisations like the National Heart Foundation as well as clinicians, nutritionists, dieticians and other health professionals have reinforced the link between dietary and lifestyle choices and improved general health.

The pursuit of a 'healthy diet' is now promoted in many countries. These messages were formulated in the early 1980s and, in the UK, were documented in a report of the National Advisory Committee on Nutrition Education (NACNE, 1983). This publication sought to establish the nature of a healthy diet in practical terms and proposed nutritional guidelines based on accumulated information. The proposed guidelines included recommendations for changes in the profile of energy and nutrient intake in the typical diet over both the short and long term. Specifically, this entailed reductions in total and saturated fat, salt and sugar intake, together with a concomitant increase in fibre intake.

In Australia, similar dietary recommendations have prevailed over many years in broad nutritional health policy developed by the National Health and Medical Research Council (NHMRC), as guidelines and in food-based regulations.

In response to nutritional messages concerning the health benefits of reducing obesity in the population as a whole, and subsequent changing consumer attitudes particularly with respect to processed foods, the food industry has engaged in continuous development of new food products that reflect the changing market conditions. Consumers also have readily demonstrated the extent to which they can alter traditional eating habits in their widespread acceptance and consumption of low or reduced fat foods, even where staple foods in the New Zealand and Australian diet, such as dairy products, are targeted.

Despite the obvious market success and broad availability of fat-modified foods, they are not suitable for all consumer groups. For example, low-fat milk is not recommended for young children because of the requirement for a full complement of dietary fats necessary for their growth and development. Similarly, low or no-fat versions of many foods are not selected by many consumers, on the basis of personal choice. In general, consumers have adapted well to the co-existence of numerous product variations that cater to individual dietary requirements and food preferences. In this regard, mandatory labelling, in combination with manufacturers' information provided on packages, are significant communication tools to assist consumers to make an informed choice with respect to their food purchases.

Foods with added phytosterol esters are intended for a specific group of consumers for whom they offer a potential benefit in terms of reducing the absorption of dietary cholesterol. At the same time, these foods offer no advantages to individuals who are not primarily interested in lowering LDL cholesterol. These purchasing criteria are not significantly different from those that can be applied to other more specialised foods targeted to particular sections of the public. Restricting package sizes of phytosterol-enriched foods further reinforces the message that these foods are not for everyone.

These marketing features of phytosterol enriched products places them in a similar retail position to low fat products which do not provide benefits to all consumers and whose unsuitability to certain subgroups within the population is managed through labelling statements. With phytosterol-enriched spreads already on the market for several years, market research has shown that consumers who are sufficiently motivated to purchase these products have demonstrated that their use of them is informed and appropriate.

(ii) Long term safety

Several submitters including the New Zealand Dietetic Association, Rosemary Stanton, Joanne Dellow and Queensland Health express concerns about the long term safety of phytosterols, particularly with respect to the nutritional effects, and where non-target population groups consume phytosterol enriched products.

<u>Response</u>

Phytosterol-esters have been assessed as safe when consumed at levels up to approximately 10 g per day. Although the presence of phytosterols in the diet affects uptake of certain fat-soluble nutrients to some extent, the most significant observed effect is a reduction in β-carotene levels (see Attachment 4).

Even for this nutrient, the reduced levels are within the normal range, which is naturally broad because of individual variation due to the influence of genetic, physiological and environmental factors. For example, the bioavailability of fat-soluble nutrients can be adversely affected by a range of variables in the diet itself, including consumption of low-fat foods, the source of the nutrient (eg. whether fruit or vegetable), and whether the food has been cooked or is eaten raw.

While there are other suggested functions for carotenoids, the only generally accepted function is that of precursors of vitamin A (retinol) for β-carotene, α-carotene and β-cryptoxanthin. However, the CSIRO clinical studies indicate that retinol levels in consumers of phytosterol esters at levels up to 10.7 g/day are unaffected, remaining within the normal range.

The concerns about long-term effects generally focus on the carotenoids and especially on the potential role of antioxidant activity in health and disease. Most hypotheses on the beneficial effects of carotenoids arose from studies in animals and epidemiological studies. Although many carotenoids exert antioxidant activity under specific conditions *in vitro*, the relevance of this activity *in vivo* to the prevention of disease is as yet unknown.

Classes of carotenoids are absorbed and metabolised differently by the body and among different animal species. The diversity in structural and geometric isomers, each with differing physicochemical properties, also makes it extremely difficult to uncover a mechanism of action for a single carotenoid *in vivo* and relate it to a potential role in disease.

The risk management strategies presented in this report are intended to minimise habitual consumption by consumers not in the target group. On the basis of the safety assessment and nutrition report, occasional consumption would be considered to have no adverse effects on the health of any consumer group, including children. Furthermore, post-launch monitoring of products in Europe (conducted by industry) indicates that consumption of phytosterol-enriched foods is predominantly as intended by the manufacturers i.e. by consumers in the target age group. This information also indicates that consumption is below the expected or anticipated levels.

(iii) Nature of phytosterol enriched foods

Richard and Valerie James contend that phytosterols in staple consumer items such as milk and yoghurt are not appropriate because these foods are consumed by a broad section of the population including children and pregnant women. There is a claim that the type of products under assessment are therefore unsuitable because there is conflict between established food consumption patterns and the mandatory statements that are required on current phytosterol enriched products (edible oil spreads) advising against consumption by children and pregnant women.

<u>Response</u>

The food industry has generated a broad and varied range of dairy products over recent times, each targeted to various sectors of consumers or a niche market. Dairy foods currently available include a range of modifications to the fat content from enrichment to almost complete removal, and calcium enriched versions. Given such a varied product range, not all of the available products are suitable or appropriate for all consumers.

For example, low-fat versions of milk and yoghurt are not suitable for young children unless on the advice of a health professional. At the other end of the spectrum, milks supplemented with additional cream are unsuitable for consumers on fat or calorie restricted diets, or those simply seeking to reduce their intake of saturated fats. Similar options are available within a range of probiotic yoghurt products.

There is no evidence that consumers are confused or overwhelmed by the variety of choices available within the dairy product category. Rather, industry data indicate that consumers have responded positively to the availability of different versions of milk, cheese and yoghurt and purchase according to their personal preferences and requirements. In the case of phytosterol-enriched table spreads and margarines, this is also considered to be the case.

FSANZ considers that with the requirement for prominent labelling, consumers will be able to readily identify and discriminate between a phytosterol-enriched milk or yoghurt and the conventional forms. The mandatory *advisory* statements will be required to reinforce the appropriate use of the food, as they are already with other foods such as milk, and beverages made from soy or rice up to 2.5% w/w fat, unpasteurised egg products, or kola beverages containing added caffeine. A mandatory *warning* statement is reserved for foods that represent a significant health risk to certain individuals or groups, and therefore would not be warranted on phytosterol-enriched foods.

(iv) Extension of use to other foods

So Natural Foods (Australia) supports permission to use phytosterol esters as ingredients in low-fat milk and low-fat yoghurt and considers that this option ought to extend to the legume-derived analogues that are consumed as alternatives to dairy products. The reasons include that as phytosterols are natural components of soy products, the addition of phytosterol esters is merely enhancing the existing nutritional profile. The company also claims that permission for use of phytosterols in certain dairy products without a corresponding permission in the non-dairy analogues would effectively discriminate against those consumers who are normally intolerant of dairy products by restricting the choices of phytosterol-containing foods. They further claim that by expanding the available range of phytosterol-containing foods, consumers should be able to reach the required level of intake for the cholesterol-lowering benefit more readily, without altering their established eating patterns.

If consideration is not extended to the legume-derived products, it is claimed that manufacturers are likely to experience decreased market share in the novel foods arena, and potentially a reduced demand for their soy based products in particular, as well as having a reduced ability to develop products with a positive public health impact.

<u>Response</u>

From the data supplied to FSANZ and other literature in the public domain, it is apparent that the nature of the food matrix has some impact on the efficacy of phytosterols. The ability of phytosterol esters to reduce cholesterol absorption when present in low fat milk and low fat yoghurt is supported by the results of the CSIRO clinical studies supplied with the current application. These results ensure that statements made by manufacturers on the packaging of phytosterol-enriched products can be shown to be truthful.

Although phytosterols occur naturally in certain soy products, no technical information has been provided to FSANZ on their efficacy in terms of lowering cholesterol absorption when present in higher amounts in soy foods. In addition, in order to consider extending the use of phytosterols into a separate category of foods such as soy based beverages and yoghurts, detailed information on proposed marketing strategies and likely consumption levels would also be required from the relevant manufacturers, to ensure that products were compatible with the target group of consumers.

Because of the existence of parallel permissions under Standard 1.3.2 Vitamins and Minerals for addition of certain vitamins and minerals to both dairy and legume-derived foods, it has been proposed that this assessment could be broadened to include both dairy and non-dairy categories of foods. This expansion would not be justified however as phytosterol esters are regarded as novel food ingredients in the Code, and are therefore subject to a specific regulatory process that is separate from the regulation of vitamins and minerals. An application for the use of phytosterol esters in legume-based beverages could be considered if supported by appropriate data.

(v) Risks to consumers in the target age group

Richard and Valerie James raise the concern of the impact on consumers in the target group (over 40's) who have normal or low cholesterol level.

Response

It is envisaged that the phytosterol-enriched products under consideration if approved, would be easily distinguished from their non-enriched counterparts. Comprehensive labelling and a price premium are expected to act synergistically to discourage consumers who do not have a specific interest in the products. The scientific evidence indicates that consumers with normal cholesterol levels would not be exposed to additional health risks if phytosterol-enriched milk and yoghurt products were consumed.

In terms of lowering cholesterol, there are no adverse health outcomes in lowering LDL cholesterol levels in humans who do not have a pre-existing high LDL cholesterol level. In general terms, with respect to cardiovascular disease risk, any reduction in LDL-cholesterol is regarded as beneficial by the medical profession. Hypocholesterolemia only arises in certain situations where there is pre-existing liver disease, malabsorption, or genetic disorders, or through prescribed pharmacological agents. In otherwise healthy individuals, a modest reduction in LDL-cholesterol levels achievable through dietary means is generally regarded as a positive outcome.

(vi) Phytosterols and oestrogenic activity

Richard and Valerie James as well as the New Zealand Dietetic Association consider that phytosterols are potentially estrogenic, that is, they contribute to similar effects in the body that generally result from the activity of the female hormone oestrogen.

Response

This issue was also raised in relation to the assessment of Application A410 in 2000, when approval was subsequently given for the use of phytosterols in edible oil spreads and margarine. The response provided at that time stated that there is no experimental evidence from *in vitro* or *in vivo* studies that phytosterol esters disrupt hormonal activity. *In vitro* oestrogen binding studies indicate that phytosterols do not bind to the rat oestrogen receptor nor do they bind or activate the human oestrogen receptor. *In vivo* uterotrophic assays in immature rats did not produce any adverse clinical changes.

The European SCF has also recently reviewed this issue in some detail[12]. The Committee reports on several studies using fish, rats and the mustelid European polecat. While some studies found that, when used at high levels or when administered subcutaneously, plant sterols (especially sitosterol) might have oestrogenic activity, these findings were not consistently reported when re-investigated. The Committee concluded that additional studies, including a two-generation reproductive study in rats, provided sufficient reassurance of the absence of endocrine effects of phytosterols via the oral route.

(vii) Validation of efficacy

The Australian Food and Grocery Council (AFGC) contends that FSANZ is not justified in requiring that efficacy data verify with labelling statements used by manufacturers on the packaging of phytosterol-enriched products, because a health claim is not being considered in relation to phytosterols.

Response

Based on examination of current packaging for phytosterol-enriched edible oil spreads and margarines, and on information supplied with this application, manufacturers intend to differentiate foods with added phytosterols with such labelling statements as ‘With natural plant sterols which reduce cholesterol uptake’ or ‘With plant-derived ingredients that lower cholesterol absorption’.

At the time of assessment of edible oil spreads, appropriate data were provided to show that phytosterol enrichment of these foods was associated with a cholesterol lowering effect. Further evidence was required to demonstrate that phytosterol esters could be similarly efficacious in lowering cholesterol absorption when they are added to other foods, such as low-fat milk and yoghurt. The availability of such evidence supports the use of the manufacturers statements concerning that food and its linkage with reduced cholesterol absorption.

These data requirements are entirely consistent with the second and third objectives set out in Section 10 of the FSANZ Act 1991. Specifically, FSANZ must ensure that *food regulatory measures provide consumers with adequate information relating to food to enable them to make informed choices* and, particularly relevant to this application, *prevent misleading or deceptive conduct*.

[12] General view of the Scientific Committee on Food on the long-term effects of the intake of elevated levels of phytosterols from multiple dietary sources, with particular attention to the effects on β-carotene. European Commission, Belgium, October 2002.

Without the appropriate scientific evidence that phytosterol esters are efficacious in a variety of food matrices, the veracity of labelling statements could not be supported.

(viii) Addition of vitamins

The AFGC suggests that, in view of the potential effects on the absorption of certain fat-soluble nutrients arising from consumption of phytosterol-enriched foods, FSANZ ought to require the foods in question to contain a minimum quantity of fat-soluble vitamins either naturally occurring or by addition.

Response

A number of published studies and the clinical studies submitted with this application confirm that plant sterols can interfere with the absorption of fat-soluble nutrients such as carotenoids, at the same time as inhibiting absorption of dietary cholesterol. The nutritional effects are almost certainly related to the mechanism of action of plant sterols in the intestine, which is thought to involve the exclusion of cholesterol from micelles. The decreased absorption of nutrients dependent on dietary fat for uptake is therefore a secondary physiological effect, the consequence of reduced cholesterol absorption.

Some studies report that increased consumption of fruits and vegetables can partially compensate for the lower absorption of fat-soluble nutrients. While levels of substances such as lycopene and α-carotene are partially restored by fruit and vegetable consumption, the studies suggest that β-carotene levels do not respond to the same extent, most likely because of the greater hydrophobicity of the β-carotene molecule compared with the other carotenoids. Consequently the physico-chemical properties of β-carotene are a barrier to its uptake in a cholesterol-depleted environment. There is no available evidence to demonstrate that additional intake through fortification is likely to restore levels of β-carotene.

In addition, FSANZ has previously assessed the issue of voluntary fortification of foods with vitamins and minerals as part of Application A424 – Fortification of foods with calcium. That assessment found the eligibility of particular vitamins or minerals to be permitted for voluntary fortification in new foods would be considered only in cases where the population group intake of that vitamin or mineral is assessed as inadequate. In the case of carotene forms of vitamin A, dietary estimate for both Australia and New Zealand indicates that the estimated mean daily intake for consumers in the target age group is approximately 1.6 times the recommended dietary intake (RDI). Of particular note, the modelling also shows that children (2 to 11 years of age) have a mean dietary intake between approximately 1.8 and 2.4 times the RDI (Australia only data). Fortification of phytosterol-enriched foods with β-carotene would therefore not be compatible with these criteria.

(ix) Relevant specifications for phytosterol esters

Unilever Australasia claims that the current specifications in Standard 1.3.4 for phytosterol esters derived from vegetable oils were submitted in 1999 for Application A410, and were restrictive. The company now suggests that the specifications be revised in line with those being considered for use as novel foods by other regulatory agencies, to ensure an international market for these products. Based on newer analytical methods, Unilever claims that more generic specifications would be preferable, which only include those components that have been demonstrated to affect the safety and/or efficacy of the foods.

Response

The applicants for the current phytosterol assessments have not requested a change to the technical specifications, but rather have indicated that they can comply with those that already exist. FSANZ compared the existing specifications with those suggested by Unilever, and found differences that would require further consideration. For example, it would need to be demonstrated that phytosterol esters matching the suggested generic specifications would be equivalent in terms of safety to those meeting the current specifications.

ATTACHMENT 8

SUMMARY OF PUBLIC SUBMISSIONS – 2nd Round

The second public consultation period for this Application was conducted between 26 May 2004 and 28 July 2004. The following submissions were received:

1. Department of Health, South Australia

- expresses concerns about the reduction in β-carotene levels associated with consumption of phytosterol enriched products, especially for consumers who may have pre-existing low levels of carotenoids, or who consume greater than 3 serves per day.
- risk management measures should strengthen the advice to consume a maximum of 3 serves per day.
- small or single serve container sizes, e.g. for yoghurt, may appeal more to children.
- addition of phytosterols to a broader range of foods is of concern and should be addressed more holistically rather than progressing applications on a case-by-case basis.

2. Dietitians Association of Australia

- supports the Application, and the cautious expansion of the range of foods permitted to contain added phytosterols.
- considers that the dietary modelling should have treated adolescents as a distinct population group because of their propensity to consume large quantities of the foods in question.
- the advisory statements should appear in a prominent place and in a prominent font on the label of foods containing added plant sterols.

3. Public Health Association of Australia

- opposes the Application because phytosterols ought to be regarded as therapeutic agents, not as food.
- there is no comparison between allowing reduced fat products in the food supply and potentially allowing the deliberate addition of plant sterols to foods, for the purposes of lowering blood cholesterol.
- there is a paucity of data on the long-term health effects of plant sterols, particularly the potential effects on levels of α-tocopherol and β-carotene, and the safety assessment did not adequately address this issue.
- the data used in the dietary exposure assessment is out of date and does not reflect major changes in the food supply over the past 10 years.
- expresses support for the recommended risk management strategies regarding labelling, etc, should the Application be approved.
- recommends that consumers be made as aware as possible of the maximum number of serves per day through labelling. However, the words '*recommended daily intake*' could easily be confused with Recommended Dietary Intake (RDI), which applies to nutrients, and therefore should not be allowed.
- post-market monitoring would be useful for phytosterol enriched products.

4. Unilever Australasia

- supports the approval of all applications seeking to use plant sterols in foods.
- post-launch monitoring information for the yellow fat spreads in Europe, demonstrates that even in regular users, there is a reluctance to consume table spreads in appropriate amounts to supply sufficient plant sterols to see a beneficial effect. The current applications provide consumers with a wider choice of foods and a better opportunity to include plant sterol enriched foods in their diet.
- the proposed regulations in terms of container sizes are too restrictive to allow flexible product development to meet consumer expectations of product range. Given the proposed restrictions as to food matrix, successive applications to FSANZ would be required each time for each new product, which would be significantly onerous on food manufacturers.
- strongly supports the provision of information to consumers to prevent confusion about consumption of phytosterol enriched products and advocates the use of labelling requirements that would be common to all products, as is being considered in the European Union.

5. Environmental Health Unit, Queensland Health

- strongly opposed to the use of phytosterol esters in breakfast cereals.
- considers that plant sterols are unnecessary for the prevention and management of chronic disease and reaffirms that a diet high in fruits and vegetables and wholegrains, moderate in lean meat and dairy foods, and low in saturated fat and sugar as providing the most effective health outcomes.
- expresses disappointment that the addition of plant sterols to a broader range of foods is being addressed on a case-by-case basis rather than as a larger issue involving government, industry and consumers.
- does not consider there is any valid comparison to be made in the availability of fat-modified foods, and the potential availability of foods containing plant sterols, as dietary interventions to address diet-related health issues.
- limiting consumption to 2-3 serves per day implies a therapeutic dose, which is inappropriate in foods.
- agrees with the rationale to restrict plant sterols to ‘healthy’ breakfast cereals only, but queries why there is reference to the fibre and sugar content, without reference to salt and saturated fat content. Suggests also that the National Heart Foundation and the National Health and Medical Research Council produce similar guidance documents for amounts of fibre and sugar in healthy foods, which does not correlate with the draft regulations produced by FSANZ.
- the manufacturer’s suggested packaging referring to *recommended daily intake* of plant sterols could be confused with the term RDI (recommended dietary intake) used for essential nutrients.
- the pictorial advice to consumers should indicate that the 2-3 serves per day is the *maximum* amount to be consumed.
- questions the ‘broad natural range’ referred to by FSANZ in the Draft Assessment Report in relation to β-carotene levels.
- provides a list of references that suggest reduced β-carotene levels of the order of 20-25% may be associated with a range of chronic diseases.

- the new CSIRO clinical trials do not address issues relating to the long-term safety of phytosterols, and involved less than 100 participants.
- the dietary exposure assessments are based on out of date dietary data.

6. New Zealand Food Safety Authority

- confirms the need for consistency in the regulatory approach for all 3 current phytosterol applications.
- the proposed permission restricts the container size for yoghurt at 140g which is not appropriate for all markets. Greater flexibility is suggested in terms of yoghurt containers up to 1 litre/1 kg.
- supports the proposed mandatory statement relating to the number of serves per day but emphasises the need for consumers to know that TOPS and phytosterol esters are all plant sterols.

7. Valerie James (New Zealand)

- opposed to the Application on the grounds that the products are neither beneficial nor safe.
- considers the interference to vitamin uptake is not counterbalanced by benefits since dietary cholesterol has no relevance to the incidence of stroke or to coronary heart disease.
- plant sterols are not potentially beneficial for all, especially women not at risk of CHD, NZ Maori in whom it has been suggested low cholesterol could be deleterious to health, nor the elderly.

8. AFGC

- supports approval of the Application to permit phytosterol esters in low-fat milk and yoghurt.
- as FSANZ has assessed the clinical data on the efficacy of foods containing plant sterols, further assessment should not be necessary in the event that a Standard for health claims is established.
- the drafting for the proposed permission in Standard 2.5.1 is overly prescriptive and does not allow for production variations.
- raises minor drafting issues including reference to the *nominal capacity* of a package, rather than to the actual size, to allow for headspace in the package.

9. New Zealand Dietetic Association

- opposed to the Application, because of insufficient evidence on the safety of higher intakes and prolonged use of phytosterol fortified foods.
- plant sterols should only be permitted in foods promoted for the prevention or treatment of CVD.
- there is a concern that consumers may overdose if further foods are approved, and the reduction in antioxidants is not fully reversed by eating additional fruits and vegetables.

10. Nestlé Australia Ltd

- supports approval for the addition of phytosterol esters to low-fat milk and low-fat yoghurt.
- considers the exclusion of drinking yoghurts is not warranted because of the compositional and nutritional similarities between low-fat yoghurt and drinking yoghurt.
- the specification of an exact amount of permitted phytosterol esters in the legal drafting for milk and yoghurt products is overly restrictive, does not allow for production variations to occur, and is inconsistent with the permission for edible oil spreads and margarines.

11. Food Technology Association of Victoria

- supports approval of the Application to permit the addition of phytosterol esters to low-fat milk and low-fat yoghurt.

12. Tasmanian Department of Health and Human Services - Community, Population and Rural Health.

- opposes the Application, on the grounds that phytosterol fortified foods are not needed for the prevention or management of chronic disease. Rather, public health nutrition evidence supports a diet high in fruits and vegetables and wholegrains, moderate in lean meat and dairy foods and low in saturated fat and sugar as providing the most effective health outcomes.
- the dietary exposure estimates generated by FSANZ use outmoded data and therefore are no longer reliable.
- FSANZ did not provide dietary modelling for all of the proposed foods combined.[13]
- the issue of medicalisation of the food supply was not adequately addressed in the Draft Assessment Report.
- although FSANZ contends that consumers use phytosterol fortified margarines appropriately, other data from FSANZ (NFO Donovan Research) indicates that there is a level of confusion relating to the meaning of labels on a range of foods.
- queries what is meant in the FSANZ report by a ‘broad natural range’ with respect to levels of β-carotene. Contends that there is evidence that lower levels of β-carotene are associated with a range of chronic diseases.
- more data are required that consider the safety of phytosterols over a long period of consumption.
- manufacturers of phytosterol enriched products referring to ‘*recommended daily intake’* is too easily confused with the term Recommended Dietary Intake (RDI).

13. National Heart Foundation of Australia

- supports approval of the Application to permit the addition of phytosterol esters to low-fat milk and low-fat yoghurt.

[13] The Combined Dietary Exposure Assessment Report was at Attachment 6 of the Draft Assessment Report for both Applications A433 & A434, and included estimates for both mean and 95th percentile consumption modelled on all foods encompassed by the current applications.

- considers that the fat content for low-fat yoghurt should be 1.5 g/100g or less, and the container size limit should be 200g to better reflect the marketplace.
- supports a case-by-case approach in the assessment of foods enriched with plant sterols to ensure an appropriate food vehicle with a nutritional composition that is consistent with healthy eating patterns.
- the mandatory advisory statements should be revised to convey the right message to consumers and to reduce the labelling burden on manufacturers. Specifically, the following are suggested:

  (i) Statement no. 2 should be reworded to reflect the fact that the caution required for the non-target groups is related to effects on blood carotene levels, and not due to any harmful effects of phytosterols; and
  (ii) Statement no. 3 should be reworded to make reference to the benefit of an additive effect with cholesterol-lowering medications and the importance of not stopping medication without medical advice.

14. New South Wales Food Authority

- supports approval of this application to permit the addition of phytosterol esters to breakfast cereals.

15. George Weston Foods Limited (Australia)

- supports approval of the Application to permit the addition of phytosterol esters to low-fat milk and yoghurt, and also supports the Application for breakfast cereals.

16. Foodwatch (Catherine Saxelby) (Australia)

- supports approval of this application to permit the addition of phytosterol esters to breakfast cereals, and also supports the applications for low-fat milk and yoghurt.
- as a dietitian with a special interest in heart disease, considers that a broader range of phytosterol enriched foods would be beneficial to consumers who are concerned about their cholesterol level. The present range of edible oil spreads is not sufficient for those people who wish to use these products effectively.

17. John Newton (Australia)

- considers that phytosterol enriched foods are not needed, and that some research indicates that low cholesterol is associated with the risk of early death.

18. Sanitarium (New Zealand and Australia)

- supports the cautionary approach adopted by FSANZ.
- considers that while FSANZ has undertaken an extensive safety evaluation of plant sterol enriched foods, the long term impact of increased sterol intakes on plasma carotenoid levels has not been adequately addressed.
- should the Applications be approved, additional risk management strategies are suggested:

(i) thorough review of the impact on people with phytosterolaemia;
(ii) mandatory advisory statements to be in a prominent place and also in advertising and promotional material;
(iii) phytosterol enriched breakfast cereal to be in restricted package size; and
(iv) long-term monitoring and evaluation program is needed to assess the impact on carotenoid levels, because the degree of compliance with eating additional fruits and vegetables is not known.

- strongly supports the inclusion of the advisory statement advising people to eat a low saturated fat diet.

19. Physicians and Scientists for Responsible Genetics New Zealand

- expresses concerns relating to phytosterols as substances from genetically engineered plants.
- policing consumption of phytosterol fortified foods by the target group would be impossible.
- consumption of large quantities of phytosterols has been shown to lower carotenoids and antioxidants, deficiencies of which are associated with increased risks of some cancers, especially in babies, children, pregnant or breast-feeding women.
- there should be mandatory warning statements so that there is no doubt what the products contain. However, children generally would not be able to read a warning, and a product carrying a nuclear symbol would not cover all possibilities.
- adding phytosterols to milk and milk products could endanger human health, particularly children, pregnant women and nursing mothers.

20. Fonterra Cooperative Group Ltd (New Zealand)

- supports approval of this Application for the addition of phytosterol esters to low-fat milk and low-fat yoghurt products.

21. Dairy Australia

- supports strong approval of this Application for the addition of phytosterol esters to low-fat milk and low-fat yoghurt products as dietary consumption of phytosterol esters represents an effective and safe method to lower cholesterol levels, and would provide increased consumer choice in products.
- low-fat milk and yoghurt have been shown in studies to be superior carriers of plant sterols and are consistent with a low-fat diet for reducing the risk of heart disease.
- several modifications to the risk management measures are suggested: (i) the number of serves across all phytosterol enriched foods to be clearly articulated at 2-3 serves, (ii) proposed permissions for milk and yoghurt should be less restrictive in terms of phytosterol content to allow for normal production variations – approximately 10%, and (iii) the permission for yoghurt should be extended to drinking yoghurt.

22. Australian Consumers' Association

- opposed to all three applications (A433, A434 and A508) because the organisation considers that some of the issues raised by submitters at Initial Assessment have not been adequately addressed, including: potential long term effects, safety of higher doses especially for vulnerable groups, the potential impact on non-target consumers, potential nutritional effects, the potential for over consumption if more permissions are granted, and the lack of up-to-date national consumption data on which to base an assessment.
- should the application be approved, the ACA supports the mandatory requirement for advisory statements, however warns FSANZ against relying on such statements as they place the onus of responsibility on the consumer.
- expresses concern that increasing permissions for foods containing phytosterols may lead to over consumption among both target and non-target consumer groups and may have a potential impact on beta carotene levels.
- believes there should be a more considered and systematic approach to the addition of phytosterols to foods.
- considers that post-market monitoring would be useful for phytosterol enriched products.
- the impact analyses in the Draft Assessment Reports of these Applications do not consider the full range of potential impacts for consumers.

Attachment 9

5-05
3 August 2005

FIRST REVIEW REPORT

APPLICATION A433

PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN BREAKFAST CEREALS

APPLICATION A434

PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN LOW-FAT MILK & YOGHURT

APPLICATION A508

PHYTOSTEROLS DERIVED FROM TALL OILS AS INGREDIENTS IN LOW-FAT MILK

CONTENTS

Decision

FSANZ re-affirms its approval of Applications A433, A434 and A508, subject to the specified amendments in this First Review, and supported by the risk management strategies proposed at Final Assessment because:

1. The assessment of Applications A433, A434 and A508 was consistent with existing policy guidance on novel foods, endorsed by the Ministerial Council in December 2003;

2. Policy guidance for substances other than vitamins and minerals is under development and is not a basis for delaying these Applications;

3. A health claim for phytosterols was not assessed as part of these Applications as, at this time, such claims are not permitted;

4. Two independent expert reviewers agree that FSANZ comprehensively evaluated the nutritional effects of phytosterols at Final Assessment, and lower serum beta-carotene levels are not a public health concern;

5. Expert medical opinion on the impact of phytosterols on individuals with the metabolic syndrome or diabetes raises no particular nutritional concerns;

6. FSANZ agrees that mandatory advisory statements should be more conspicuous on packaging and therefore an Editorial Note has been inserted in Standard 1.2.9 Legibility Requirements, to clarify the requirements of the Code, pending a full review of this Standard; and

7. FSANZ will prepare a fact sheet on plant sterols for wide distribution to medical and health care professionals and the general public. In conjunction with information from public health organisations and a wide range of industry-initiated activities including advertising, brochures, pamphlets and consumer advice lines, this will ensure that there is sufficient educational material available to allow informed consumer choice.

Summary Table

Matters addressed in the First Review of Applications A433, A434 and A508 seeking to broaden the use of phytosterol esters and tall-oil phytosterols

Ministerial Council issue	Measures taken at Final Assessment	Additional measures at First Review
1. Consistency with existing policy guidance on **(i) novel foods;** **(ii) health claims; and** **(iii) the addition to food of substances other than vitamins and minerals.**	• **FSANZ must comply with statutory obligations in relation to the assessment of applications.** • **Applications cannot be delayed to await new policy guidelines.** **Novel foods** • Phytosterol-esters and tall-oil phytosterols already approved in the Code as novel foods. • Current applications seek to broaden use to other foods. • Existing guidelines require a pre-market safety assessment. • Assessments consistent with existing policy guidelines for novel foods. **Health claims** • Currently not permitted. • No previous or current assessment of a health claim for phytosterols.	• **FSANZ has addressed the standards issues only. Policy issues are discussed briefly:** **Novel Foods** • Existing policy guidelines endorsed in December 2003. • Proposal P291 to review Standard 1.5.1 Novel Foods (at Draft Assesm'nt) will not change the existing policy. • No impact on the assessment of the current Applications. **Substances other than vitamins and minerals** • FRSC sub-committee developing policy guidance on a broad range of substances. • No delay of the current Applications is justified. **Health claims** • Proposal P293 is at Draft Assessment. A claim relating to phytosterols would need to be an application under the new standard.
2. Protection of public health and safety. **(i) Consumption of phytosterol-enriched foods can result in a decrease in serum β-carotene; and** **(ii) There is evidence that individuals with metabolic syndrome or diabetes already have lower β-carotene levels than the normal population.**	• **FSANZ linked permissions to**: High-fibre breakfast cereal • Restrictions on sugar content • No breakfast cereal bars Low-fat milk • Maximum 1 litre container • No flavourings Low-fat yoghurt • Maximum 200 g punnet size **Current mandatory statements**: • Diet should be low in saturated fats and high in fruit and vegetables; • Not recommended for infants, children, pregnant or lactating women; • Seek medical advice with cholesterol-lowering medications. **Additional mandatory statement:** • No additional benefits when consumed in excess of 3 serves/day. **Additional condition of use:** Foods to which phytosterols have been added may not be used as ingredients in other foods.	• **FSANZ sought external opinion on the nutritional issues, which confirmed that there are no outstanding health concerns.** • Professor John W. Erdman (USA) agrees with FSANZ that lower β-carotene levels are not a nutritional concern. • Professor Martijn Katan (The Netherlands) does not consider lower serum β-carotene levels as a safety concern. • Professor John McNeil (FSANZ Fellow) does not consider that phytosterols are of particular nutritional concern for individuals with metabolic syndrome or diabetes. • Dr Bob Boyd (FSANZ Chief Medical Advisor) does not consider that there is evidence for harmful effects from a reduction in β-carotene.
3. Provision of adequate information to enable informed choice.	• **Ingredient labelling** – either tall oil phytosterols or phytosterol esters. • Industry advertising, brochures, leaflets and consumer advice lines. • Consumer familiarity with existing products.	• **Insertion of an Editorial Note** to reinforce the legibility and presentation requirements of the Code for mandatory statements. • **Pledge to review Standard 1.2.9 – Legibility Requirements.**

1. Introduction

On 10 December 2004, the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) requested a First Review of Applications A433, A434 and A508, which seek to broaden the range of foods to which phytosterols (plant sterols) may be added. Applications A433 and A434 seek permission to add phytosterol esters derived from vegetable oils to breakfast cereals, low-fat milk and yoghurt; A508 seeks permission to add tall oil phytosterols (TOPs) to low-fat milk. Approval of all three applications involves variations to Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations, Standard 1.5.1 – Novel Foods, Standard 2.5.1 – Milk, and Standard 2.5.3 Fermented Milk Products of the *Australia New Zealand Food Standards Code* (the Code).

Following a request for a formal review, FSANZ normally has three months to prepare a response, however, due to the complexity of issues in this case, FSANZ sought an extension of time and is required to complete the review by 12 August 2005.

2. Objectives of review

The objective of this Review is to reconsider the draft variations recommended to the Ministerial Council by FSANZ in October 2004 in light of the Council's concerns as outlined in Section 3.

3. Grounds for the review

A First Review was requested on the grounds that approval of the Applications:

- is not consistent with existing policy guidelines set by the Ministerial Council;
- does not protect public health and safety; and
- does not provide adequate information to enable informed choice.

The Ministerial Council provided additional information (see **Attachment 2**) concerning the grounds on which the First Review is based, which have been summarised by FSANZ as follows:

- the draft variations to the standards are not consistent with existing policy guidelines on novel foods, health claims and fortification of food set by the Ministerial Council;

- the Applications do not adequately address Public Health Nutritionists' concerns about the observed reductions in serum beta-carotene of approximately 20% as a consequence of consuming foods with added phytosterol esters;

- mandatory advisory statements on currently approved phytosterol-enriched table spreads are inadequately presented on packages, raising questions about whether information is accessible to consumers;

- these foods represent a trend towards medicalisation of the food supply;

- based on overseas approvals for foods with added phytosterols, it is likely that there will be an increase in the number of applications seeking approval in Australia, which will lead to an increased level of health claims, either implied or stated;

- approvals will inevitably lead to potential problems with health claims, especially in regard to products that have low efficacy such as breads and cereals; and

- there is an apparent lack of supporting education and awareness programs for health professionals to advise patients on how such products should be used, especially in combination with cholesterol-lowering medicines.

In addition at Final Assessment, FSANZ reviewed six research papers (submitted by two jurisdictions) reporting on low serum beta-carotene levels associated with metabolic syndrome or diabetes (see below). After evaluating the papers, FSANZ concluded that the information was not directly relevant to the assessment of these applications because the studies did not fully assess confounding risk factors, which may reduce beta-carotene levels in the subjects. The Ministerial Council requested that FSANZ re-examine the information contained in these publications and identify which of the studies did not control for confounding factors.

The following studies were reviewed by FSANZ at Final Assessment:

- Ford, ES, Will, JC, Bowman, B. (1999). Diabetes mellitus and serum carotenoids: Findings from the 3rd NHANES. *Am J Epi* 149 (2): 168-176.
- Suzuki, K, Yoshinori, I, Nakamura, S. (2002). Relationship between serum carotenoids and hyperglycemia: a Population based cross sectional study. *J Epi* 12(5):357-366.
- Abahusain, MA, Wright, J, Dickerson J.W.T. (1999). Retinol, alpha-tocopherol and carotenoids in diabetes. *Eur J Clin Nutr* 53:630-635.
- Ylonen, K, Alfthan G, Groop, L (2003). Dietary intakes and plasma concentrations of carotenoids and tocopherols in relation to glucose metabolism in subjects at high risk of type 2 diabetes: the Botnia dietary study. *Am J Clin Nutr* 77:1434-41.
- Ford, ES, Mokdad, AH, Giles, W.H. (2003). The metabolic syndrome and antioxidant concentrations; Findings from the 3rd NHANES. *Diabetes* 52:2346-2352.
- Osganian, SK, Stampfer, MJ, Rimm, E. (2003). Dietary carotenoids and risk of coronary artery disease in women. *Am J Clin Nutr* 77:1390-9.

4. Background

Currently, phytosterol esters (derived from vegetable oils) and un-esterified phytosterols (derived from tall oils) are permitted for use in edible oil spreads under Standard 1.5.1 - Novel Foods. This standard requires a pre-market safety assessment. Novel foods or novel food ingredients that have been assessed under the Standard, when approved, are listed in the Table to clause 2 and may have specified conditions of use. In this case, phytosterols must be declared in the ingredient list, and three advisory statements must be presented on packaging to advise consumers on how to use the products appropriately[14].

[14] It should be noted that although the permission for tall oil phytosterols exists in the Code, there are no tall oil products on the market. The two currently available brands of phytosterol-enriched table spreads (Logicol® and ProActive®) both contain vegetable oil-derived phytosterol esters.

The Applicants for A433, A434 and A508 consider there is demand in Australia and New Zealand to expand the range of phytosterol-enriched products, in addition to the table spreads, to broaden consumer choice and support innovation in the food industry. The Applications seek permission to add 0.8 – 1.0 g plant sterols per serve to food categories such as high-fibre breakfast cereal, low-fat milk and low-fat yoghurt.

Consumption of phytosterols has been shown to reduce absorption of dietary cholesterol leading to lower serum LDL-cholesterol levels, and thus foods with added phytosterols are targeted primarily to consumers over the age of 40 with concerns about their cholesterol levels. Many studies have found that the optimal cholesterol-lowering effect is achieved when consumption is between 2-3 g plant sterols per day, irrespective of the type of sterols consumed. The FSANZ assessment focused on (i) the safety of phytosterol esters and tall oil phytosterols at proposed levels of use when used in breakfast cereal, low-fat milk and yoghurt, (ii) their efficacy in the relevant food matrices to ensure truth in labelling, and (iii) the suitability of the products to target consumers.

Considering the range of phytosterol-enriched foods already available in overseas markets, Applications A433, A434 and A508 represent a conservative request for expanding the choice of products available to consumers in Australia and New Zealand. Further constraints on products were imposed by FSANZ during the course of the assessments by (i) restricting the sugar content of the cereal product, (ii) restricting the maximum permitted unit size of milk and yoghurt products, and (iii) permitting only a very narrow range of additives in milk necessary for technical reasons to suspend vegetable fats in an aqueous environment. Flavourings, for example, are not permitted in phytosterol-enriched milk.

4.1 Efficacy of plant sterols

Most studies showing the cholesterol-lowering effect have used edible oil spreads or margarine-type products enriched with plant sterols. Before other categories of phytosterol-enriched foods could be approved, FSANZ required evidence of the cholesterol lowering effect in the relevant food matrices. The efficacy data were considered necessary to ensure that any statements used by manufacturers relating to the cholesterol-lowering effects were valid for foods such as cereals and dairy products. A health claim was not part of the assessment of these applications.

4.2 Overseas regulation

In Europe, plant *sterols* in their various forms are permitted in yellow fat spreads, milk based products, yoghurt products, salad dressings, spicy sauces, fermented milk type products, soya drinks and low-fat cheese type products. Plant *stanols* are permitted on the market in the EU, without being subject to review, because they were marketed in a member State before the Novel Foods Regulation came into force. Initially, the products were edible oil spreads (margarines), but this has broadened to other foods such as fresh cheese, snack bars, salad dressing and yoghurt. Given the similarities in composition of the plant sterols (sterols, stanols and their conjugated esters), and similar conclusions regarding safe levels of consumption, the EC has moved to common labelling requirements and specifications for all phytosterol products, irrespective of their plant source. In addition, the UK Advisory Committee on Novel Foods and Processes (ACNFP) has recently issued a positive opinion for an application proposing to add 0.4% of phytosterols to fruit juices including tomato juice and nectars (May, 2005).

In the USA, the Food and Drug Administration (FDA) have raised no objection to a number of food products that may contain plant sterol and stanol esters in amounts up to 20%, on the basis of the GRAS notification. Notifications include vegetable oil spreads, salad dressings, health drinks, cereal health bars, yoghurt type products, fruit juice (orange) and vegetable oils for baking and frying. The FDA has also allowed manufacturers of products containing added phytosterol and stanol esters to make a health claim (for reducing the risk of coronary heart disease). There are a number of specific restrictions with which the products must comply before such a health claim may be made. Foods that are allowed to use this interim health claim include sterol esters in spreads and salad dressings, and stanol esters in spreads, salad dressings and snack bars.

5. Conclusions from the Final Assessment Reports

Applications A433, A434 and A508 were progressed in parallel because of similarities in terms of safety, labelling issues and food categories under assessment. The Executive Summary and Statement of Reasons for each of these applications, which were approved at FSANZ13 in October 2004, are in this report at **Attachment 2**.

The Board agreed to the recommendations at Final Assessment in view of the stringent risk management measures developed by FSANZ for all phytosterol-enriched products, including the existing table spreads. In terms of labelling, an additional mandatory advisory statement to the effect that *foods containing added plant sterols do not provide additional benefits when consumed in excess of three serves per day* was proposed to ensure that target consumers would be fully informed on the appropriate use of the products, irrespective of whether the added sterols were from a vegetable-oil or tall-oil source. Conditions of use were also extended to the effect that *foods containing added plant sterols must not be used as ingredients in other foods.*

6. Issues addressed in First Review

6.1 Policy issues

The Ministerial Council considered that the proposed draft variations to the Code were not consistent with existing policy guidelines set by the Council in relation to (i) novel foods, (ii) health claims, and (iii) fortification.

6.1.1 Response

In addressing the review of these applications, FSANZ considers it necessary to separate the standards issues from the policy issues raised by the Ministerial Council.

In dealing with applications to amend the Code, FSANZ must comply with its statutory obligations under the FSANZ Act. There are no provisions in the Act for an assessment to be deferred or delayed on the grounds that the application intersects with issues currently under consideration by FRSC, which will lead to the development of policy guidelines.

In the case of the three current phytosterol applications, the information detailed below indicates that FSANZ has been consistent with existing policy guidelines.

6.1.1.1 Policy guidance on novel foods

FSANZ received policy guidance on novel foods from the Ministerial Council recommending that FSANZ review Standard 1.5.1 – Novel Foods, while giving consideration to the higher order and specific principles of that policy guidance and to a number of issues raised during consultation on policy development. The main issues identified were the ambiguity of the definitions for 'non-traditional food' and 'novel food', how determinations are made with respect to novelty (i.e. whether a food is deemed to be novel and subject to the pre-market requirements of the standard) and difficulties with enforcement of the standard.

In response to this policy guidance, FSANZ has raised a Proposal (Proposal P291) to review the regulations for novel foods and the mechanism for making determinations as to novelty. A Standard Development Advisory Committee (SDAC) has been established to assist during the review. It is not intended that existing novel food permissions be revisited during the review. Similarly, it was not anticipated that any novel food application being assessed during the review of the Novel Foods Standard would be delayed as a result of the review.

It has been acknowledged at the first SDAC meeting and through submissions to the Initial Assessment Report that the current standard effectively ensures public health and safety by requiring a pre-market safety assessment of novel foods. In this regard, progressing Applications A433, A434 and A508 while Standard 1.5.1 is being reviewed is appropriate and not inconsistent with current policy guidance.

6.1.1.2 Policy guidance on health claims

There was no consideration of a health claim in the assessment of the previous applications for use of phytosterols (in edible oil spreads) and health claims have not been considered in relation to the current applications. Any such consideration would need to be the subject of a future application contingent upon the establishment of a standard for health claims.

In December 2003, the Ministerial Council agreed to a Policy Guideline on Nutrition, Health and Related Claims, with the exception of biomarker maintenance claims. This latter issue was subsequently resolved in May 2004.

In response to the Ministerial Council Policy Guideline, FSANZ raised Proposal P293, in order to develop a new Standard for the regulation of nutrition, health and related claims. Proposal P293, is developing a regulatory framework for both high level and general level claims. High level claims, which reference a serious disease or condition, will be prohibited unless pre-approved by FSANZ. For example, serum cholesterol is proposed as a biomarker for cardiovascular disease. However, general level claims which do not reference a serious disease or condition will be generally permitted provided they can be substantiated and provided they comply with any criteria or conditions specified in the Standard.

The issues surrounding the development of the Standard are highly complex and FSANZ is currently undertaking a range of activities, including consumer research, to support the development of the Standard. Proposal P293 is currently at Draft Assessment.

Until the new Standard is finalised and agreed to by Ministers, manufacturers must comply with the current requirements in the Transitional Standard for Health Claims, Standard 1.1A.2 in the Code.

In addition to other matters, this Standard prohibits claims in food labels and advertising that contain the name of, or make reference to, any disease or physiological condition. Failing to comply with this requirement when making any voluntary statement about a food constitutes a breach of the Code. Any labelling statement about a food that is required under the Code is not a 'claim' and so is not subject to Standard 1.1A.2.

6.1.1.3 Policy guidance on the addition to food of substances other than vitamins and minerals

The Food Regulation Standing Committee (FRSC) sub-committee that developed policy on fortification for vitamins and minerals has commenced work on the addition to food of substances other than vitamins and minerals with a view to developing a policy guideline. The scope of what is being considered by the sub-committee is broad and includes substances such as non-culinary herbs, plant and animal extracts, amino acids and amino acid derivatives, probiotics and others, some of which may have some pharmacological or physiological properties. Excluded from the scope of the considerations are substances added to foods for a technological purpose, vitamins and minerals and whole foods. Phytosterols would be included in the initial scope of this work by the FRSC sub-committee, as would other substances that have already been considered by FSANZ as novel foods.

There are inter-relationships with this policy development process and health claims, novel foods and the foods-therapeutic goods interface. An issues paper was released for public comment on 22 February 2005 and the submissions received have been summarised. In addition, a stakeholder workshop was held on 1 March to clarify the intent and scope of the policy guideline. Both of these processes informed the development of a policy options consultation paper which has now been endorsed by FRSC and will be released for public comment. It is not yet clear what the resulting policy guideline will address. However, progression of Applications A433, A434 and A508 does not depend on the outcome of this process since there is currently a clear mechanism for dealing with novel food applications under Standard 1.5.1 – Novel Foods.

6.2 Nutritional issues – Reduction in β-carotene

The Ministerial Council considered that the proposed draft variations to the Code do not protect public health and safety. This concern primarily relates to the observed reduction in serum beta-carotene levels with consumption of phytosterol esters.

The Ministerial Council also requested a second appraisal of six published research papers submitted as references to FSANZ by two jurisdictions at Final Assessment. The papers report on observational studies showing low serum beta-carotene levels in association with the metabolic syndrome or chronic disease such as diabetes.

6.2.1 Response

It is well established that consumption of plant sterols reduces the absorption of cholesterol in the intestine, leading to lower LDL-cholesterol levels in the blood. At the same time, consumption of phytosterol-enriched foods (particularly those with added phytosterol esters) can result in a decrease in serum β-carotene levels of approximately 20-25%.

However, the levels of β-carotene in serum are known to fluctuate widely as a consequence of many dietary and environmental factors and a decrease of this magnitude falls within a broad natural variation. As β-carotene has the most potent pro-vitamin A activity of the carotenoids, it is important to note the evidence consistently showing no change in vitamin A levels in consumers of phytosterol-enriched products.

Assigning a level of significance to a reduction in β-carotene levels has therefore proved elusive due to evidence that:

1. Pro-vitamin A activity is the only universally accepted biological function of β-carotene[15];
2. serum retinol levels (vitamin A) are *not* reduced with consumption of phytosterol esters; and
3. as carrier LDL-cholesterol decreases by whatever means, a decrease in serum β-carotene is expected.

Moreover, published epidemiological studies and properly conducted trials on dietary antioxidants such as β-carotene have generated equivocal results with respect to potential health benefits of these compounds, and have even reported that high levels could be harmful. At Final Assessment, FSANZ therefore considered it reasonable to conclude that as reduced serum β-carotene levels arising from the consumption of phytosterol-enriched foods were clearly not associated with decreases in vitamin A, a public health and safety concern could not be demonstrated.

It should also be noted that there were no statistically significant reductions in β-carotene levels following consumption of TOPs, however reductions in α-carotene (23%) were observed at the highest levels of exposure (3.6g/day). FSANZ concluded at Final Assessment that this reduction in α-carotene does not suggest a public health and safety concern particularly as reductions in vitamin A following consumption of TOPs were not observed.

6.2.2 External review of nutrition assessment

To address this issue as part of the review, FSANZ sought the opinion of two independent experts who were specifically asked to comment on the significance of the decrease in β-carotene in terms of nutritional health, and the overall validity of the conclusions of the nutrition assessment report prepared by FSANZ at Draft Assessment. The reviewers were:

(i) Dr John W. Erdman, Professor, and Nutrition Research Chair, Department of Food Science and Human Nutrition of the University of Illinois at Urbana - Champaign in the United States; and
(ii) Professor Martijn Katan, Wageningen Centre for Food Science, in the Netherlands.

These reviewers were chosen for their knowledge and expertise in carotenoid nutrition or their familiarity with safety issues associated with the use of plant sterols in foods. Professor Erdman's report is at **Attachment 3** to this Report.

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[15] Carotenoids: Linking Chemistry, Absorption, and Metabolism to Potential Roles in Human Health and Disease, Deming, D.M. *et al.*, Ch. 10, Handbook of Antioxidants, 2nd Edition, 2002, ISBN: 0-8247-0547-5

The European reviewer, Professor Katan, was the principal author of a comprehensive Review entitled *Efficacy and Safety of Plant Stanols and Sterols in the Management of Blood Cholesterol Levels,* published in 2003 in the Mayo Clinic Proceedings. This paper reviewed the results of 18 trials testing the effects of plant sterols on plasma concentrations of fat-soluble vitamins, showing that reductions in the plasma concentrations of the carotenes were observed. Concerning these reductions, the Review states: *part of this reduction probably is due to reduced absorption of carotenes and the rest to reduced concentrations of the lipoprotein carrier, LDL*. Once the results were corrected for lower cholesterol levels, only a statistically significant reduction in β-carotene remained. The authors later refer to further research showing that *the decrease in beta carotene could be prevented by adding sufficient fruits and vegetables to the diet*. When approached by FSANZ, Professor Katan did not provide a formal report on the nutrition assessment but provided the following comments:

Personally I would not be concerned about beta-carotene, as there is no evidence for a beneficial effect of beta-carotene apart from a weak vitamin A activity, and there is even definite evidence for harm of high intakes.

In general, both external reviewers expressed no concerns about the reduction in β-carotene levels arising from the consumption of phytosterol-enriched foods. Apart from minor corrections, Professor Erdman considered the FSANZ analysis of nutritional issues to be thorough and balanced, and endorsed the conclusions reached in the FSANZ nutrition report.

While fortification with β-carotene is not a consideration for phytosterol-enriched products, a mandatory advisory statement encouraging the consumption of additional fruits and vegetables in conjunction with phytosterol-enriched foods is required on product labels. This approach is now supported by additional recently published evidence showing that there are compensatory increases in the serum levels of carotenoids (α- and β-carotene, lycopene) with consumption of fruits and vegetables, especially varieties rich in these nutrients. The mandatory advisory statement thus aims to ensure that consumers will be provided with sufficient information to enable them to use phytosterol-enriched products safely.

6.2.3 Review of the dossier of references by FSANZ

FSANZ considers the information provided in the six references (listed in Section 3) was not directly relevant to the assessment of phytosterol-enriched foods because the studies focused on examining the relationship between nutritional parameters (carotenoids, dietary antioxidants) in population groups with metabolic syndrome and therefore at high risk of developing diabetes, or who were already in a diabetic state. Given the range of significant metabolic changes that are known to occur with this condition, and the concomitance of other known associated risk factors (high blood pressure, obesity, low HDL-cholesterol, elevated triglycerides and blood sugar), a lower β-carotene level could well be an indicator for a number of adverse physiological changes that have occurred in association with the condition or the onset of disease.

Therefore, it could reasonably be argued that the results of these studies report on subjects who already have impaired health status and have progressed towards a diabetic state, and are therefore not typical consumers in the target age group. Furthermore, it is likely that individuals displaying the signs and symptoms of metabolic syndrome would be seeking medical or other health professional advice, particularly in relation to their dietary requirements and food choices.

With sufficient educational material available to health and medical professionals, FSANZ considers that individuals in this distinct population group with metabolic syndrome would be under supervision and would therefore have access to informed dietary advice concerning foods appropriate for their health needs.

In an otherwise healthy population of consumers, no such conclusions can be drawn concerning the significance of a lower β-carotene level as a consequence of consuming phytosterol-enriched foods. Whereas the link between elevated LDL-cholesterol levels and a risk of developing chronic diseases such as atherosclerosis and coronary heart disease is well established, the effects of a reduced level of β-carotene on general nutrition are not known, particularly where vitamin A levels are maintained.

The Mayo Clinic Review concluded: ***Adverse health outcomes due to observed decreases in beta-carotene levels in plasma are speculative and are of no major concern***.

6.2.4 Expert medical review of the dossier of references

To address this issue as part of the First Review, the dossier of references on metabolic syndrome and diabetes was provided to the Chief Medical Advisor for FSANZ, Dr Bob Boyd, and to an external reviewer - Professor John McNeil, Department of Epidemiology & Preventive Medicine, Monash University, for independent evaluation. A full report of these evaluations is provided at **Attachment 4**.

The Chief Medical Advisor provided the following comments:

Taken together, there is no evidence in these papers that reduced carotenoid intake increases the risk of diabetes or cardiovascular disease. There is evidence of an inverse relationship between serum carotenoid levels and glucose intolerance, but not even possible evidence of what is the cause / effect. Nothing in these papers studies the difference in diabetes rates or glucose intolerance between populations who have different diets or seasonal changes in their diet, which might equate to the changes in dietary intake of fat-soluble anti-oxidants caused by intake of phytosterols.

In summarising the study reports, Professor McNeil provided the following comments:

Persons in the early stages of glucose intolerance were shown to have lower circulating levels of carotenoids in several studies reviewed above. These results appear to be relatively consistent across different populations and study types.

There are several possible explanations for this finding, ranging from impaired absorption to suppression of levels as a result of increased oxidant activity. The possibility also exists that high levels of carotenoids are protective against the development of diabetes, but at present it is not possible to be sure which of these possibilities is most likely. It is possible/likely also that increased beta-carotene levels reflect a generally healthier diet (possibly accompanied by other aspects of a healthy lifestyle).

Present data does not warrant use of beta-carotene supplementation for prevention of diabetes since present evidence falls well short of proving a causal relationship. This is also supported by other data including:

1. *Large scale trials of beta-carotene have failed to identify a health benefit (these provide more reliable data than do observational studies), and may cause harm. These studies are briefly reviewed in Osganian et al (2003);*

2. *Positive data presented largely concerns surrogate health measures (eg fasting, glucose levels, HbA1c) rather than clinically significant endpoints; and*

3. *An analogy may exist with other anti-oxidants, eg. vitamin E, which have shown positive associations in observational studies, but negative results in trials.*

Concerns about small decreases in beta-carotene levels of the order likely to occur with phytosterols consumption (20%) are not supported by presently available evidence.

In summary, the data presented raise matters worthy of additional study, but fall well short of proving any causal relationship between beta-carotene intake and the development or worsening of diabetes.

Despite the lack of evidence for adverse nutritional outcomes, FSANZ has adopted a cautious approach to the regulation of phytosterol-enriched foods, and the current standard requires manufacturers to advise consumers that these products should be consumed as part of a diet low in saturated fats and high in fruits and vegetables. This advice is also consistent with current public health messages on the nature of a healthy diet.

6.3 Labelling issues

In requesting a First Review of Applications A433, A434 and A508, the Ministerial Council expressed the concern that should phytosterol-enriched breakfast cereal, low-fat milk and low-fat yoghurt be available on the market, there are no requirements to compel manufacturers to present the mandatory advisory statements (MAS) more conspicuously on packaging. Therefore, the Ministerial Council argues that the availability of a broader range of phytosterol-enriched products could be more likely to lead to inappropriate use of the products by consumers.

6.3.1 Response

The issue of specific legibility criteria for mandatory advisory statements[16] was examined and discussed with the jurisdictions during the review of the *Australian Food Standards Code* and the New Zealand Food Regulations, culminating in the development of Standard 1.2.9 Legibility Requirements of the Code. At that time it was agreed that as advisory statements were of lesser importance in relation to protection of public health and safety (compared to mandatory warning statements), it was not necessary to prescribe additional specific legibility criteria or a minimum print size.

General provisions regarding legibility and prominence are supported by a ‘User Guide to Standard 1.2.9’ to assist manufacturers with adherence to the principles on which the standard operates. Whether the presentation of MAS on the current packaging of phytosterol-enriched table spreads can be considered adequate and in compliance with these general principles is an enforcement matter.

[16] Under Proposal P 142-Print Size and Quality of Prescribed Information Appearing on a Food Label

However, changes to the labelling standards and general legibility requirements in the Code would have a major impact on industry. In addition, changes made on the basis of specific permissions for novel foods must be considered as setting a precedent and could potentially lead to broader trade implications by creating inconsistencies with Codex and/or European Union requirements.

In the context of the current applications, FSANZ therefore considered a number of options for strengthening the presentation of MAS on packaging of phytosterol-enriched foods without causing conflict with the existing framework of the Code. The background to this issue, and four possible regulatory options are discussed more fully in **Attachment 5**.

Following comprehensive evaluation of the options, the preferred course of action is to clarify the legibility requirements in Standard 1.2.9 by the addition of an editorial note. An editorial note is preferred at this stage because:

- it is the least prescriptive option and therefore is most consistent with the principles upon which Standard 1.2.9 and the Code are based;
- it would apply more generally to all labelling requirements rather than just to advisory statements on phytosterol products;
- it goes some way to addressing jurisdictional concerns; and
- it is more consistent with Codex and the EU requirements.

In addition, within a defined time period after completion of this First Review of Applications A433, A434 and A508, FSANZ proposes to undertake a broader review of Standard 1.2.9 in relation to the legibility of all mandatory warning statements, advisory statements and declarations. The benefits of this approach are:

- FSANZ would be able to assess Standard 1.2.9 within the context of the whole Code and the principles on which it was developed, rather than within the confined context of the three current phytosterol Applications;
- the effectiveness of Standard 1.2.9 could be re-evaluated in terms of public health and safety considerations;
- the concerns of the jurisdictions would be addressed in a more systematic way; and
- any amendment resulting from such a review would be based on evidence and would be less likely to have a negative impact on the operation of the other labelling standards.

The insertion of an editorial note to Standard 1.2.9 is a minor amendment that is considered to address the labelling concerns expressed by the Ministerial Council without compromising the integrity of the existing labelling provisions and without imposing undue regulatory burden on the food industry. The Editorial Note proposed for Standard 1.2.9 is included in the draft variations to the Code at **Attachment 1**.

It should be emphasised that manufacturers of phytosterol-enriched foods will undoubtedly ensure that consumers recognise these products through the use of product-specific promotional material, advertising and conspicuous labelling. The higher pricing regimens will further discriminate phytosterol-enriched foods from their conventional forms. With additional information on phytosterols available through consumer information lines, brochures, advertising, FSANZ fact sheets, public health organisations (such as the National Heart Foundation), health departments and health professionals, the MASs should be regarded as merely one means of communicating information to target consumers to ensure that they receive adequate guidance on the appropriate use of the products.

6.4 Education for health professionals

The Ministerial Council considers that health professionals have insufficient knowledge to enable them to provide advice or instruct consumers on the appropriate use of phytosterol-enriched products, especially for individuals who may be under medical supervision and also using cholesterol-lowering medication on prescription.

6.4.1 Response

As submissions were received from organisations such as the Australian Heart Foundation, the Dietitians Association of Australia and the New Zealand Dietetic Association, as well as from a number of individual dietitians and nutritionists, FSANZ concluded that there was a high level of awareness amongst health professionals and the community in general concerning the availability of phytosterol-enriched foods in the market place. Edible oil spreads containing phytosterol esters have been permitted in Australia and New Zealand since 1999 and consumers have therefore been exposed to these products for at least 5 years. Based on this period of use, it would be reasonable to conclude that there is already a background level of knowledge in the community concerning plant sterols, especially with those consumers who currently use the phytosterol ester-enriched table spreads.

Nevertheless, in view of the concerns expressed by the Council, if the current Applications are approved, FSANZ will prepare a fact sheet on phytosterols that could be used by health professionals in their capacity as advisors on dietary interventions for individuals with concerns about a high LDL-cholesterol level. The fact sheet would include information on:

(i) the safe and appropriate use of phytosterol-enriched products;
(ii) the optimal amounts of phytosterols (2-3 g per day) that have been shown to result in a cholesterol lowering effect;
(iii) the benefits of eating at least 5 serves per day of fruits and vegetables when using phytosterol-enriched products;
(iv) the need to continue to use any medication prescribed by a doctor for control of cholesterol levels; and
(v) the unsuitability of these products for infants, children and pregnant or lactating women who do not, in general, need to lower cholesterol levels.

These messages reinforce the mandatory advisory statements that manufacturers are required to portray on the packaging of their products, and are consistent with other publicly available information on plant sterols from organisations such as the National Heart Foundation.

6.4.1.1 <u>Adequate information to enable informed choice</u>

Consumers of approved phytosterol-enriched products currently have access to a range of information sources. These include a consumer information line to assist with advice on purchasing and consumption of phytosterol-containing table spreads, and leaflets attached to the packaging. Additional strategies proposed by the Applicants include (i) advertising specific for the target audience, and (ii) educational material distributed to medical and other health professionals.

7. Additional issues

7.1 Food technology requirements

Since completion of the Final Assessment Report, the applicants seeking permission to use phytosterol-esters and tall-oil phytosterols in low-fat milk (Dairy Farmers and Parmalat respectively) have advised FSANZ that the draft variations to the Code do not allow the product formulations necessary to suspend vegetable-oil components (plant sterols) in the aqueous environment of milk. Emulsifiers are required for technical reasons in order to solubilise the sterol components and distribute them evenly through the product.

FSANZ purposefully linked the proposed permissions for phytosterol-enriched low-fat milk in the Code to Standard 2.5.1 Milk in order to ensure that the products would not be open to the full suite of additives listed in Standard 1.3.1 Food Additives, particularly the flavourings, and would be consistent with the current permissions for phytosterols, which are linked to Standard 2.4.2 Edible Oil Spreads.

Minor drafting changes have therefore been necessary to ensure that manufacturers are able to produce a phytosterol-enriched milk using the necessary additives required by their specific product formulations. The drafting changes include permissions to use emulsifiers and thickeners such as sodium alginate, carrageenan and guar gum with phytosterol-esters, and microcrystalline cellulose with tall-oil phytosterols. These additive inclusions are considered minor and have been inserted into the revised draft variations to the Code, at **Attachment 1** to this report.

7.2 Use of generic term 'plant sterols'

The New Zealand Food Safety Authority (NZFSA) raised the issue that the proposed mandatory advisory statement referred to 'phytosterol-esters' for Applications A433 and A434, but to 'plant sterols' for Application A508. The NZFSA suggested that the use of the same generic term 'plant sterols' would be preferable for all Applications, to reinforce the message to consumers that 2-3 serves per day of phytosterols from any source, either vegetable-oil or tall-oil, would be equivalent in terms of their daily consumption.

FSANZ acknowledges that this small change standardises the mandatory advisory statement for all products enriched with phytosterols and ensures that consumers will regard both TOPS and phytosterol-esters as one group of compounds with similar properties, and therefore will assist in their use of the products. Accordingly, the Ministerial Council is asked to note the minor change in the draft variation to Standard 1.2.3 (statement 4) for Applications A433 (and A434) to bring the wording in line with the draft variations proposed for Application A508, at **Attachment 1**. The statement thus reads for all three Applications:

Foods containing added plant sterols do not provide additional benefits when consumed in excess of three serves per day.

8. Review Options

Three options were considered in this Review:

1. re-affirm approval of the previous draft variations to Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations, Standard 1.5.1 – Novel Foods, Standard 2.5.1-Milk, or Standard 2.5.3 – Fermented Milk Products of the Code; or

2. re-affirm approval of the previous draft variations to the Code as listed above, subject to specified amendments as a result of the Review; or

3. withdraw approval of the previous draft variations to the Code as listed above.

In view of the insertion of an Editorial Note to address the labelling concerns of the Ministerial Council and the insertion of specific additive permissions to address the food technology requirements of the Applicants, Option 2 is the preferred option. The revised draft variations to the Code are at **Attachment 1**.

9. Decision summary

FSANZ has considered the policy issues, public health and safety concerns and labelling issues raised by the Ministerial Council in relation to the applications to approve the use of phytosterol esters in breakfast cereal, low-fat milk and low-fat yoghurt and tall-oil phytosterols in low-fat milk. These applications were assessed in the context of the existing regulatory framework for novel foods, and represent an extension of use of currently permitted novel foods. The safety and nutritional aspects of phytosterol-enriched foods have been adequately assessed and no outstanding issues remain. The insertion of an Editorial Note should clarify and reinforce the requirements of the Code with respect to the legibility and presentation of mandatory advisory statements.

The issues raised by the Ministerial Council in this First Review, have been addressed by the measures adopted at Final Assessment and by the additional measures carried out during this First Review period. These are presented in the **Summary Table** at the front of this report.

10. Conclusion

On completion of this First Review, FSANZ reaffirms its approval of the draft variation to Standards 1.2.3, 1.5.1, 2.5.1 and 2.5.3 of the Code permitting the extended use of phytosterol esters and tall oil phytosterols, subject to the amendments specified in this report, and supported by the extensive risk management measures proposed at Final Assessment.

ATTACHMENTS

1. Draft variations to the *Australia New Zealand Food Standards Code.*
2. Applications A433, A434 and A508 – Executive Summary and Statement of Reasons from Final Assessment Reports
3. External reviewer's report on FSANZ Nutrition Report
4. Evaluation of published references
5. Options for labelling of phytosterol-enriched foods

ATTACHMENT 1

Draft Variations to the *Australia New Zealand Food Standards Code*

APPLICATION A433

To commence: On gazettal

[1] ***Standard 1.2.3*** *of the Australia New Zealand Food Standards Code is varied by omitting from the* Table to clause 2 –

Food regulated in Standard 2.4.2 containing phytosterol esters	Statements to the effect that - 1. the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables; 2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and 3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication.

substituting –

Foods containing added phytosterol esters	Statements to the effect that - 1. the product should be consumed as part of a diet low in saturated fats and high in fruit and vegetables; 2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; 3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication; and 4. foods containing added plant sterols do not provide additional benefits when consumed in excess of three serves per day.

[2] ***Standard 1.2.9*** *of the Australia New Zealand Food Standards Code is varied by inserting after subclause 2(1) –*

Editorial note:
The requirements of this Standard will not be met where prescribed information is placed other than on the outside of a package where it is readily accessible by a consumer prior to purchase and not obscured by an outer covering. The requirements of this Standard will also not be met where prescribed information is printed in a small font so the statement cannot be read easily.

Within 24 months of the gazettal of this editorial note, Standard 1.2.9 Legibility Requirements will be reviewed.

[3] **Standard 1.5.1** *of the Australia New Zealand Food Standards Code is varied by –*

[3.1] *omitting from the* Table to clause 2 –

Phytosterol esters	The requirements in clause 2 of Standard 1.2.3. The name 'phytosterol esters' or 'plant sterol esters' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to food – (1) according to Standards 1.3.4 and 2.4.2; and (2) where the total saturated and trans fatty acids present in the food is no more than 28% of the total fatty acid content of the food.

substituting –

Phytosterol esters	The requirements in clause 2 of Standard 1.2.3. The name 'phytosterol esters' or 'plant sterol esters' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to edible oil spreads – (1) according to Standard 2.4.2; and (2) where the total saturated and trans fatty acids present in the food are no more than 28% of the total fatty acid content of the food. May only be added to breakfast cereals, not including breakfast cereal bars, if – (1) the total fibre content of the breakfast cereal is no less than 3 g/50 g serve; (2) the breakfast cereal contains no more than 30g/100g of total sugars; and (3) the total phytosterol ester added is no more than 26g/kg. Foods to which phytosterol esters have been added may not be used as ingredients in other foods.

[3.2] *inserting after the* Table to clause 2 –

Editorial note:
Novel Foods must meet the requirements of Standard 1.3.4 - Identity and Purity.

APPLICATION A434

To commence: On gazettal

[1] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in* Schedule 1*, after* item 1.1.2 –

1.1.3 Liquid milk to which phytosterol esters have been added

401	Sodium alginate	2	g/kg
407	Carrageenan	2	g/kg
412	Guar gum	2	g/kg
471	Mono- and diglycerides of fatty acids	2	g/kg

[2] ***Standard 1.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in* column 2 *of the* Table to clause 2 *corresponding to the entry for* Phytosterol esters –

May only be added to milk in accordance with Standard 2.5.1. May only be added to yoghurt in accordance with Standard 2.5.3.

[3] ***Standard 2.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting after the* Editorial note *to clause 4 –*

5 Phytosterol Esters

Phytosterol esters may only be added to milk –

(a) such that the milk contains no more than 1.5 g total fat per 100 g; and
(b) that is supplied in a package, the labelled volume of which is no more than 1 litre; and
(c) where the total phytosterol ester added is no more than 5.2 g/litre of milk.

[4] ***Standard 2.5.3*** *of the Australia New Zealand Food Standards Code is varied by inserting after the* Editorial note *to clause 3 –*

4 Phytosterol Esters

Phytosterol esters may only be added to yoghurt –

(a) that contains no more than 1.5 g total fat per 100 g; and

(b) that is supplied in a package, the capacity of which is no more than 200 g; and

(c) where the total phytosterol ester added is no more than 1.3 g.

APPLICATION A508

To commence: On gazettal

[1] ***Standard 1.2.3*** *of the Australia New Zealand Food Standards Code is varied by omitting from the* Table to clause 2 –

Food regulated in Standard 2.4.2 containing tall oil phytosterols	Statements to the effect that – 1. the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables; 2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and 3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication.

substituting –

Foods containing added tall oil phytosterols	Statements to the effect that - 1. the product should be consumed as part of a diet low in saturated fats and high in fruit and vegetables; 2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; 3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication; and 4. foods containing added plant sterols do not provide additional benefits when consumed in excess of three serves per day.

[2] **Standard 1.3.1** *of the Australia New Zealand Food Standards Code is varied by inserting in Schedule 1 after* item 1.1.2

1.1.3 Liquid milk to which tall oil phytosterols have been added

460	Microcrystalline cellulose	5	g/kg

[3] ***Standard 1.5.1*** *of the Australia New Zealand Food Standards Code is varied by omitting from the* Table to clause 2 –

Tall oil phytosterols	The requirements in clause 2 of Standard 1.2.3. The name 'tall oil phytosterols' or 'plant sterols' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to food - (1) according to Standards 1.3.4 and 2.4.2; and (2) where the total saturated and trans fatty acids present in the food is no more than 28% of the total fatty acid content of the food.

substituting –

Tall oil phytosterols	The requirements in clause 2 of Standard 1.2.3. The name 'tall oil phytosterols' or 'plant sterols' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to edible oil spreads – (1) according to Standard 2.4.2; and (2) where the total saturated and trans fatty acids present in the food is no more than 28% of the total fatty acid content of the food. May only be added to milk in accordance with Standard 2.5.1. Foods to which tall oil phytosterols have been added may not be used as ingredients in other foods.

[4] ***Standard 2.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting after the Editorial note to clause 4 –*

5 Tall oil phytosterols

Tall oil phytosterols may only be added to milk –

(a) such that the milk contains no more than 1.5 g total fat per 100 g; and
(b) that is supplied in a package, the labelled volume of which is no more than 1 litre; and
(c) where the total phytosterol (from a tall oil source) added is no more than 3.6 g/litre of milk.

ATTACHMENT 2

Executive Summary and Statement of Reasons from Final Assessment Reports

Application A433 – Final Assessment Report

Statement of Reasons

FSANZ agrees to approve the use of phytosterol esters derived from vegetable oils in breakfast cereals, subject to specified conditions of use, for the following reasons:

- there are no anticipated public health and safety concerns associated with the use of phytosterol esters derived from vegetable oils in high fibre, low sugar breakfast cereal when used in conjunction with the risk management measures proposed;

- there is evidence that phytosterol esters derived from vegetable oils can, following consumption, reduce levels of LDL cholesterol in humans when incorporated into breakfast cereals;

- the nutrition assessment indicates that phytosterol esters derived from vegetable oils have no significant adverse nutritional effects at the proposed levels of use. The reduction in the absorption of β-carotene is within the normal variation which results from physiological and environmental factors;

- conditions of use, including an additional labelling statement, are proposed as part of a comprehensive risk management strategy to ensure appropriate use of phytosterol-containing foods by target consumers, and to discourage use by non-target consumers;

- the proposed changes to the Code are consistent with the section 10 objectives of the FSANZ Act; and

- the Regulatory Impact Statement indicates that, for the preferred option, namely, to approve the use of phytosterol esters derived from vegetable oils as novel food ingredients in breakfast cereals, the benefits of the proposed amendment outweigh the costs.

Executive Summary

Goodman Fielder has submitted an application to FSANZ seeking approval for the use of phytosterol esters derived from vegetable oils as a novel food ingredient in breakfast cereals under Standard 1.5.1 – Novel Foods, in the *Australia New Zealand Food Standards Code* (the Code). Originally, the applicant sought approval for breakfast cereal bars, fibre-increased bread and low-fat salad dressing. The latter two foods were withdrawn by the applicant. Since breakfast cereal bars are compositionally similar to breakfast cereals, the scope of the assessment was broadened to breakfast cereals.

Standard 1.5.1 prohibits the sale of novel foods or novel food ingredients unless they are listed in the Table to clause 2 of the Standard, and comply with any special conditions of use stipulated in the Table. Approval for use requires a safety assessment to be undertaken. Current permissions to use phytosterol-esters as novel food ingredients are limited to edible oil spreads and margarines. There is currently no permission to add phytosterol esters to a broader range of foods.

Purpose and scope of the Application

Free phytosterols are chemically and structurally related to animal-derived cholesterol. These properties confer the ability to interfere with the mechanism of cholesterol absorption in the human intestine. When ingested in various food matrices, phytosterol esters can potentially decrease low density lipoprotein (LDL) cholesterol levels in the blood. Products with added phytosterol esters are primarily targeted to adult consumers, particularly those over 40 years of age. The purpose of the Application is to increase the range of phytosterol enriched foods available to these consumers.

Approval of a health claim is not a consideration in this assessment. Clinical data establishing that phytosterol esters can lower LDL cholesterol levels when added to breakfast cereal have been evaluated to ensure the validity of labelling statements associating plant sterols with a reduction in the absorption of cholesterol.

Risk assessment

Two new clinical studies were submitted in support of the Application. As well as testing efficacy in different food matrices (breakfast cereal, fibre-increased bread, low-fat milk and low-fat yoghurt), a range of physiological/biochemical parameters were also measured to detect potential adverse health effects. When incorporated into breakfast cereal, phytosterol esters have a modest cholesterol lowering effect. Daily consumption rates between 2.6 g and 10.7 g phytosterol esters are well tolerated, and no adverse physical or physiological effects were detected. The results from the clinical studies are consistent with other published studies, some investigating consumption of phytosterols for periods up to 12 months.

The investigations into the nutritional effects of phytosterols on absorption of carotenoids and some fat-soluble vitamins found that serum β-carotene levels were most affected, showing a reduction of approximately 25%, which to some extent was dependent on the nature of the food matrix and on cholesterol-lowering effects. However, the reduction in β-carotene levels is not associated with a reduction in retinol or vitamin A levels and is within a broad natural variation for this provitamin.

The results from the dietary exposure assessment which considered phytosterol-containing spreads and/or breakfast cereal indicate that mean exposure to free phytosterols did not exceed 1.7 g/day for any population group assessed in this scenario. At the highest level of consumption, estimated exposure to free phytosterols is between 4.0 g/day and 4.4 g/day for all population groups assessed. Estimated mean and maximum dietary exposures are expected to be highest for consumers aged 40-64 years (a major fraction of the target group) in both New Zealand and Australia.

When all proposed foods in Applications A433 and A434[17] (high-fibre, moderate-sugar breakfast cereal plus low fat milk and yoghurt) are considered, the results of the dietary exposure assessment indicate that estimated mean dietary exposure from all foods did not exceed 1.9 g/day in any population group, and highest mean consumption levels were in the target population groups (over 40 years of age) in both Australia and New Zealand. At the 95th percentile of exposure, no population group exceeded 4.7 g free phytosterols per day, equivalent to 7.6 g phytosterol esters. The highest consumers of phytosterol esters are therefore likely to be well under the upper level of consumption of 10.7 g/day used in the clinical studies which produced no evidence of adverse health effects. The results also suggest that the major source of dietary exposure to added phytosterols is from edible oil spreads for all population groups assessed.

The overall conclusion of the risk assessment is that phytosterol ester enriched breakfast cereal is not associated with adverse health effects at the levels proposed by the Applicant, and can result in a cholesterol lowering effect. Adult consumers in the target population group are major consumers of the foods in question, and by maintaining their established dietary habits are likely to use the foods in amounts considered safe and appropriate.

Risk management

Phytosterol ester enriched foods can be consumed safely by the target population group and may assist in reducing LDL cholesterol levels. However, in general, children and pregnant or lactating women do not need to reduce cholesterol absorption, and products containing added phytosterols are therefore less appropriate for these groups.

Comprehensive risk management options have been considered, to encourage appropriate use by the target population group and discourage consumption by non-target groups. The recommended measures include (i) allowing high-fibre, moderate-sugar breakfast cereal to contain phytosterol esters (this excludes breakfast cereal bars); (ii) prescribing the maximum amount of phytosterol esters that may be added to breakfast cereal; (iii) retaining the three mandatory advisory statements currently required under Standard 1.2.3 (for edible oil spreads and margarines), and adding one additional mandatory advisory statement to the effect that phytosterol-enriched foods do not provide additional benefits when consumed in excess of three serves per day; and (iv) imposing an additional condition of use prohibiting phytosterol enriched foods from being used as ingredients in other foods.

It is proposed that the new labelling requirements apply to all foods with added plant sterols, including the edible oil spreads and margarines.

Public consultation

Fifteen submissions were received in the first round of public consultation and twenty-five submissions were received during the second public consultation period. Approximately half of the submissions were in favour of the application. These submissions supported a more varied range of products than the current permission allows to expand consumer choice and improve opportunities for product innovation.

[17] Application A434 seeks permission to add phytosterol esters derived from vegetable oils in low-fat milk and low-fat yoghurt.

The major issues of concern raised by those opposed were the potential nutritional effects, the potential for adverse effects in non-target consumers, and the choice of food products, namely breakfast cereal, milk and yoghurt which are widely consumed in Australia and New Zealand. The issues raised in public submissions have been addressed in the report and, where appropriate, through the risk management strategies outlined.

Application A434 – Final Assessment Report

Statement of Reasons

FSANZ agrees to approve the use of phytosterol esters derived from vegetable oils in low-fat milk and low-fat yoghurt, subject to specified conditions of use, for the following reasons:

- there are no anticipated public health and safety concerns associated with the use of phytosterol esters derived from vegetable oils in low-fat milk and low-fat yoghurt when used in conjunction with the risk management measures proposed;

- there is evidence that phytosterol esters derived from vegetable oils can, following consumption, reduce levels of cholesterol in humans when incorporated into low-fat milk and low-fat yoghurt products;

- the nutrition assessment indicates that phytosterol esters derived from vegetable oils have no significant adverse nutritional effects at the proposed levels of use. The reductions in the absorption of β-carotene are within the normal variation which results from physiological and environmental factors;

- conditions of use, including an additional labelling statement, are proposed as part of a comprehensive risk management strategy to ensure appropriate use of phytosterol-containing foods by the target consumers, and to discourage use by non-target consumers;

- the proposed changes to the Code are consistent with the section 10 objectives of the FSANZ Act; and

- the Regulatory Impact Statement indicates that, for the preferred option, namely, to approve the use of phytosterol esters derived from vegetable oils as novel food ingredients in low-fat milk and low-fat yoghurt, the benefits of the proposed amendment outweigh the costs.

Executive Summary

Dairy Farmers submitted an application to FSANZ seeking approval for the use of phytosterol esters derived from vegetable oils as a novel food ingredient in low-fat milk and low-fat yoghurt under Standard 1.5.1 – Novel Foods, in the *Australia New Zealand Food Standards Code* (the Code).

Standard 1.5.1 prohibits the sale of novel foods or novel food ingredients unless they are listed in the Table to clause 2 of the Standard, and comply with any special conditions of use stipulated in the Table.

Approval for use requires a safety assessment to be undertaken. Current permissions to use phytosterol esters as novel food ingredients are limited to edible oil spreads and margarines. There is currently no permission to add phytosterol esters to a broader range of foods.

Purpose and scope of the Application

Free phytosterols are chemically and structurally related to animal-derived cholesterol. These properties confer the ability to interfere with the mechanism of cholesterol absorption in the human intestine. When ingested in various food matrices, phytosterol esters can potentially decrease low density lipoprotein (LDL) cholesterol levels in the blood. Products with added phytosterol esters are primarily targeted to adult consumers, particularly those over 40 years of age, interested in achieving a lower cholesterol level without major changes to their diet. The purpose of the application is to increase the range of phytosterol-enriched foods available to these consumers.

Approval of a health claim is not a consideration in this assessment. Clinical data establishing that phytosterol esters can lower LDL cholesterol levels when added to low-fat milk and low-fat yoghurt have been evaluated to ensure the validity of labelling statements associating plant sterols with a reduction in the absorption of cholesterol.

Risk assessment

Two new clinical studies were submitted in support of the Application. As well as testing efficacy in different food matrices (breakfast cereal, fibre-increased bread, low-fat milk and low-fat yoghurt), a range of physiological/biochemical parameters were also measured to detect potential adverse health effects. When incorporated into low-fat milk and low-fat yoghurt, phytosterol esters had a modest cholesterol lowering effect. Daily consumption rates between 2.6 g and 10.7 g phytosterol esters were well tolerated, and no adverse physical or physiological effects were detected. The results from the clinical studies are consistent with other published studies, some investigating consumption of phytosterols for periods up to 12 months.

The investigations into the nutritional effects of phytosterols on absorption of carotenoids and some fat-soluble vitamins found that serum β-carotene levels were most affected, showing a reduction of approximately 25%, which to some extent was dependent on the nature of the food matrix and on cholesterol-lowering effects.

However, the reduction in β-carotene levels was not associated with a reduction in retinol (Vitamin A) levels and was within a broad natural variation for this provitamin.

The results from the dietary exposure assessment which considered phytosterol-containing spreads, low-fat milk and low-fat yoghurt indicate that mean exposure to free phytosterols would be 1.6 g/day for the Australian population and 1.9 g/day for the New Zealand population. For both countries, estimated mean dietary exposure is expected to be highest for consumers aged 40-64 years, which is a major fraction of the target group. At the highest level of consumption (95th percentile), estimated exposure to phytosterols is expected to be between 4.2 g/day and 4.7 g/day for all population groups assessed.

When all proposed foods in Applications A433[18] and A434 (high fibre/moderate sugar breakfast cereal, plus low fat milk and yoghurt) are considered, the results of the dietary exposure assessment indicate that estimated mean dietary exposure from all foods did not exceed 1.9 g/day in any population group, and highest mean consumption levels were in the target population groups (over 40 years of age) in both Australia and New Zealand. At the 95th percentile of exposure, no population group exceeded 4.7 g free phytosterols per day, equivalent to 7.6 g phytosterol esters. The highest consumers of phytosterol esters are therefore likely to be well under the upper level of consumption of 10.7 g/day used in the clinical studies which produced no evidence of adverse health effects. The results also suggest that the major source of dietary exposure to added phytosterols is from edible oil spreads for all population groups assessed.

The overall conclusion of the risk assessment is that phytosterol ester-enriched low-fat milk and low-fat yoghurt are not associated with adverse health effects at the levels proposed by the Applicant, and can result in a cholesterol lowering effect. Adult consumers in the target population group are major consumers of the foods in question, and by maintaining their established dietary habits are likely to use the foods in amounts considered safe and appropriate.

Risk management

Phytosterol ester enriched foods can be consumed safely by the target population group and may assist in reducing LDL cholesterol levels. However, in general, children and pregnant or lactating women do not need to reduce cholesterol absorption, and products containing added phytosterols are therefore less appropriate for these groups.

Comprehensive risk management options have been considered, to encourage appropriate use by the target population group and discourage consumption by non-target groups. The recommended measures include (i) prescribing the maximum amount of phytosterol esters that may be added to low-fat milk and low-fat yoghurt; (ii) retaining the three mandatory advisory statements currently required under Standard 1.2.3 (for edible oil spreads and margarines), and adding one additional mandatory advisory statement to the effect that phytosterol-enriched foods do not provide additional benefits when consumed in excess of three serves per day; (iii) imposing a restriction on the maximum container size to 1 litre for milk, and 200g for yoghurt; and (iv) imposing an additional condition of use prohibiting phytosterol enriched foods to be used as ingredients in other foods.

It is proposed that the new labelling requirements apply to all foods with added plant sterols, including the edible oil spreads and margarines.

Public consultation

Sixteen submissions were received in the first public consultation period and twenty-two submissions were received during the second consultation period. A small majority of submissions were in favour of the Application. Of those in favour, all supported increased consumer choice and improved opportunities for product innovation.

[18] Application A433 from Goodman Fielder seeks permission to add phytosterol esters to breakfast cereal.

The major issues of concern raised by those opposed were the potential nutritional effects, the potential for adverse effects in non-target consumers, and the choice of food products, namely milk and yoghurt which are widely consumed in Australia and New Zealand. The issues raised in public submissions have been addressed in the report and, where appropriate, through the risk management strategies outlined.

Application A508 – Final Assessment Report

Statement of Reasons

FSANZ agrees to approve the use of TOPs in low-fat milk subject to specified conditions of use, for the following reasons:

- there are no anticipated public health and safety concerns associated with the use of TOPs in low-fat milk when used in conjunction with the risk management measures proposed;

- there is evidence that TOPs when incorporated into low-fat milk can, following consumption, reduce cholesterol absorption in humans;

- the nutrition assessment indicates that TOPs have no significant adverse nutritional effects at the proposed levels of use;

- conditions of use, including an additional labelling statement, are proposed as part of a comprehensive risk management strategy to ensure appropriate use of TOP-enriched low-fat milk by the target consumers, and to discourage use by non-target consumers;

- the proposed changes to the Code are consistent with the section 10 objectives of the FSANZ Act; and

- the Regulatory Impact Statement indicates that, for the preferred option, namely, to approve the use of TOPs as a novel food ingredient in low-fat milks; the benefits of the proposed amendment outweigh the costs.

Executive Summary

Purpose and scope of the Application

Parmalat Australia Ltd has submitted an Application to FSANZ seeking approval for the use of tall oil phytosterols[19] (TOPs) as a novel food ingredient in low-fat milk under Standard 1.5.1 – Novel Foods, in the *Australia New Zealand Food Standards Code* (the Code). Parmalat is specifically seeking to extend the current permissions to allow use of TOPs in low-fat milk.

Standard 1.5.1 requires that novel foods undergo a safety assessment before being permitted in the food supply. If approved, the novel food is listed in the Table to the Standard and must comply with any special conditions of use also listed in the Table.

[19] i.e. phytosterols derived from tall oils

Efficacy of TOPs

TOPs are added to foods with the intended purpose of lowering cholesterol absorption. The Applicant has submitted efficacy studies including the data and results from clinical studies involving mildly hypercholesterolaemic individuals in a variety of food matrixes, including milk. The available human studies do provide information in relation to the effectiveness of TOPs incorporated into food products to reduce cholesterol absorption. However, there is no specific evaluation of any health claim being considered as part of this Application. Irrespective of whether any statement is considered a health claim, all statements on the label should be true and not mislead consumers.

Technical properties of TOPs

Tall oil phytosterols as well as phytosterols derived from edible vegetable products are comprised of varying ratios of the same four primary phytosterol substances sitosterol, sitostanol, campesterol and campestanol, with varying amounts of minor components such as stigmasterol and brassicasterol. The physiological activity of phytosterol products is due to the presence of these compounds. However, TOPs do not necessarily need to be esterified to improve their solubility as the Applicant has indicated that they can be incorporated into low-fat milks.

Risk assessment

The data support the safety of TOPs in both the target and non-target population at the level of dietary exposure that would be achieved by addition of TOPs to low-fat milk at the levels proposed to be used by the Applicant (0.9g/250 mL serve). The estimated mean dietary exposure to TOPs did not exceed 1.9 g/day in any population group assessed. The 95th percentile dietary exposure for the target population was 4.8 g/day, the majority of which is derived from edible oil spreads. While this level of exposure is higher than that used in the human studies, FSANZ is proposing additional risk management measures to reduce over-consumption of TOP containing low-fat milks. The overall conclusion of the risk assessment is that low-fat milk enriched with TOPs is not associated with any adverse effects.

Risk management

In order to ensure appropriate use of TOP-enriched low-fat milk by the target group and to discourage use by the non-target groups, the following risk management measures are proposed:

1. retain the current mandatory advisory statements in Standard 1.5.1;

2. prescribe an additional labelling statement that indicates that there is no additional benefit from consuming greater than 2-3 serves/day; and

3. prescribe additional conditions of use, namely: (i) that low-fat milk must not contain more than 3.6g/litre of free phytosterols (from a tall oil source); (ii) the fat content must not contain more than 1.5g total fat/100g liquid, and (iii) maximum container size is to be specified at 1 litre (i.e. the labelled volume must be no more than 1 litre); and (iv) that foods containing added plant sterols must not be used as ingredients in other foods,

Additional risk management strategies have been proposed by the Applicant. Ongoing monitoring (possibly via a survey) of the use of phytosterols in foods would provide additional reassurance of the effectiveness of the proposed risk management measures.

Other issues raised in public submissions

Other issues raised in the public submissions consisted of comments on the specific requirements and intent of the novel foods standard, specifications and labelling for phytosterols in general, the possibility of inequity for consumers of lower socio-economic groups and the issue of medicalisation of the food supply if TOP-containing products are approved.

Impact analysis of regulatory options

The options identified were to permit or not permit the use of TOPs in low-fat milk, or to permit the use of TOPs generally. The impact analysis shows that the second option (to permit TOPs in low fat milk) satisfies the objectives based on the outcome of the scientific risk assessment and the Regulatory Impact Statement (RIS), taking into account matters raised following the public consultation period.

These matters included the following:

- an assurance of the safety of TOPs;
- the provision of adequate labelling so as to give consumers informed choices for purchases of products containing TOPs;
- advisory statements and conditions of use to manage inappropriate use and over-consumption of products; and
- the provision of benefits to industry and governments, in terms of enhanced market opportunities and trade.

ATTACHMENT 3

Evaluation of the Nutrition Assessment Report

Fortification of phytosterol esters in breakfast cereals and yoghurt

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Department of Food Science and Human Nutrition
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Overall, this is an excellent report that provides an accurate and complete assessment of the published scientific evidence of the impact of consumption of phytosterol/stanols and their esters upon carotenoid bioavailability. In the "Summary of nutritional effects of phytosterol esters" (Section 3.4), the conclusion that consumption of phytosterol-enriched foods generally results in a reduction in B-carotene levels of approximately 20-25% is supported both by literature cited and by the European and Mayo Clinic assessments (Sections 4.1 and 4.2, respectively). There appears to be no safety issues with consumption of foods containing these phytosterols other than the small effect on carotenoids and the concern that children and pregnant and lactating women should not consume these products.

Clearly, the question is whether the small reduction of serum B-carotene is an acceptable risk considering the positive cholesterol reduction resulting from these products. To date, the answer has been yes, that the small reduction of B-carotene does not present a public health concern. There has not been any evidence that vitamin A status is altered. While it has been suggested that carotenoids may play other roles in health, none has been demonstrated in vivo for B-carotene. Carotenoids are excellent in vitro singlet oxygen quenchers but the significance of this antioxidant function in vivo is unclear. Lutein and zeaxanthin appear to be important for proper macular pigment function and consumption of lycopene from tomato products may reduce the risk of prostate cancer. However, B-carotene appears only to function as a source of Vitamin A. Until there is in vivo evidence to contrary, this is only this function that should be considered in regards to this report.

This reviewer concurs with the conclusions of the report. While a decrease of 20% in serum B-carotene is not ideal, it could be attenuated with dietary adjustment. There is a mandatory advisory statement on the label of foods in Australia that reads, "the product should be consumed in moderation as part of a diet low in saturated fats and high in fruits and vegetables". This label should inform the consumer to enhance intake of foods high in carotenoids. Further, urging consumers to meet the 5-A-Day recommendations for fruits and vegetables would also be advisable. Food Standards Australia New Zealand could also consider suggesting an enrichment of products with a small amount of B-carotene, although this reviewer would not deem this necessary.

There are a few minor comments on the document:

1. Section 2.2, first sentence. Vitamin A is not an antioxidant. Only the carotenoids are antioxidants.

2. Section 2.3.4 and paragraph 2 under section 3.3.7. Is it known what percentage of adults in Australia or New Zealand have very low total vitamin A intake? For example, if a small percentage is below the EAR for Vitamin A, then there is less concern about the impact of phytosterols. Evaluation of mean intakes of RAE is important but more important is the percentage of person with very low intake. Often there is a biphasic, not a bell shaped intake curve for this vitamin.

3. Section 2.4. In the USA, the DRI report concluded that only 2R forms of alpha tocopherol are considered as having Vitamin E activity.

ATTACHMENT 4

Evaluation of Published References

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The question is whether carotenoids such as beta-carotene:

1. Protect against the development of diabetes
2. Protect against the adverse vascular and other effects associated with diabetes

Carotenoids:
- Diverse group of compounds found in plants
- Include the compounds that give flowers their colour
- Possess antioxidant activity
- Protect cells from oxidative stress by quenching free radicals
- Together with tocopherols, carotenoids are thought to be an important defence against oxidative stress

Glucose intolerant states:
- Characterised by chronic hyperglycaemia due to relative deficiency of insulin
  - Chronic hyperglycaemia leads to auto-oxidation of glucose and causes nonenzymatic glycation of proteins, associated with increased oxidative stress
  - increased lipid peroxidation
  - increased free radical activity
- Free radicals shown to impair insulin action
  - Some dietary studies of diabetes incidence have suggested that increased consumption of vegetables may reduce risk of developing diabetes

The papers provided are summarised viz:

1. Ford, E.S. *et al* Diabetes mellitus and serum carotenoids: findings from the third National Health and Nutrition Examination Survey
1.1.1.1.1 Am J Epidemiology 1999;149: 168-76

Methods:

- cross- sectional study conducted in US between 1988 and 1991
- multistage probability design making results generalisable to US population
- 1665 participants had glucose tolerance test, analysed according to old WHO criteria
- concurrent collection of socio-demographic variables, health status, lifestyle variables, 24 hr diet recall & physiological variables

Results:

277 impaired glucose tolerance, 148 newly diagnosed diabetics, 230 known diabetics;

- diabetics & IGT group differed from non-diabetics in age, race, education, health status, smoking status, physical activity, prevalence of overweight, alcohol consumption, blood pressure, serum cotinine and diet
- after adjusting for these potential confounders, variation in serum carotenoid concentrations remained with higher levels in non-diabetics
- beta-carotene showed the strongest relationship with levels 13% lower in ITTs and 20% lower in newly diagnosed diabetics cf normals
- lycopene levels also inversely related with levels 6% and 17% lower than in normal

Author's conclusions:

- cross-sectional nature of data limits inferences on temporality and causation
- data emanate from a cross-sectional study and therefore directionality of any relationship is always an issue
- several possibilities to explain results including residual confounding, unadjusted confounding, diabetes causing poor absorption, or carotenoids protecting against development of diabetes.

2. Abahusain, M.A. *et al* Retinol, alpha-tocopherol and carotenoids in diabetes Eur J Clin Nutr 1999; 53: 630-35

Methods:

- clinic-based case-control study undertaken in Saudi Arabia
- 107 type 2 diabetic patients recruited from diabetic clinic of a hospital (aged 28-74 years)
- 43 healthy controls selected from university faculty staff & employees
- fasting blood sample and 10h urine collection from all subjects
- retinol binding protein (RBP), alpha & beta-carotene and alpha tocopherol measured by HPLC
- dietary questionnaires

Results:

- serum beta-carotene and serum & urine RBP were significantly lower in diabetics than in controls ($p=0.002$ for beta-carotene)
- negative correlation between beta-carotene levels and fasting blood glucose levels ($r = -0.18$, $p<0.008$)

Author's conclusions:

- multiple factors may be responsible for lower beta-carotene levels including malabsorption, infections, low dietary intake or low fat in diet
- increased oxidation in diabetics may result in reduced antioxidant levels

- "whether beta-carotene should be considered as a therapeutic agent in diabetes requires further studies".

3. Suzuki *et al* Relation between serum carotenoids and hyperglycaemia: a population based cross-sectional study
Journal of Epidemiology 2002;12:357-366

Methods:

- case-control comparison conducted amongst rural Japanese
- cases selected from population based survey undertaken annually
- of 1691 subjects studied , 151 had HbA1c values of 5.6% or greater and another 133 were known diabetics
- two controls randomly selected for each subject in the 'elevated HbA1c group and for each known diabetic
- fasting serum levels analysed for alpha and beta carotene, beta-cryptoxanthin, zeaxanthin & lutein, canthaxanthin, retinol & alpha-tocopherol. TBARS levels also measured as an indictor of oxidative stress
- health questionnaire including dietary intakes of major foods also sought

Results:

- serum levels of carotenoids excluding canthaxanthin were about 30% lower in the high HbA1c group than in healthy controls or than in the diabetics (this was a statistically significant difference)
- high HbA1c group also reported higher intake frequency of carrot and pumpkin but not with other fruits and vegetables

Authors' conclusions:

- we suggest that individuals with high HbA1c values display lower serum carotenoids due to both low intake frequencies of fruit and vegetables and increased production of reactive oxygen species by chronic hyperglycaemia
- results from this study suggest that intake of fruit and vegetables rich in carotenoids might be a protective factor against hyperglycaemia

4. Ylonen *et al* Dietary intake and plasma concentrations of carotenoids and tocopherols in relation to glucose metabolism in subjects at high risk of type 2 diabetes: the Botnia Dietary Study
Am J Clin Nutr 2003; 77: 1434-41

Methods:

- cross sectional study involving 81 male and 101 female first and second degree non-diabetic relatives of patients with type 2 diabetes
- fasting and 2-hr blood glucose levels, plus insulin & non-esterified fatty acid levels, measured during glucose tolerance test
- plasma antioxidant concentrations measured by HPLC
- antioxidant intake data based on three day dietary records

- linear regression used to relate study relationship between glucose & fatty acid levels and plasma levels of alpha and beta carotenoid, lycopene, alpha and gamma-tocopherol.

Results:

- in males dietary carotenoids were lower in those with higher fasting plasma glucose concentrations ($p<0.05$)
- in males plasma beta-carotene levels were inversely associated with markers of insulin resistance ($p=0.003$)
- in females plasma beta-carotene concentrations were directly associated with fasting plasma glucose
- no association seen with levels of lutein/zeaxanthin, lycopene or beta-cryptoxanthin

Authors' conclusions:

- our finding of an inverse association between plasma beta-carotene concentrations in men is consistent with previous studies but our finding in women contrasts with these findings
- taken together the available data do not show a consistent effect of carotenoids and tocopherols on glucose metabolism
- the observed inverse relationship between dietary carotenoids and fasting plasma glucose concentrations warrants further studies to define whether a diet high in carotenoid rich fruit and vegetables has a role in the prevention of diabetes in a high risk population.

5. Osganian SK *et al* Dietary carotenoids and risk of coronary artery disease in women
Am J Clin Nutr 2003; 77: 1390-9

Methods:

- cohort study of 73,286 female nurses who completed a semi-quantitative food-frequency questionnaire in 1984
- questionnaire assessed consumption of carotenoids and other nutrients
- cohort followed for 12 years for development of incident coronary artery disease

Results:

- 998 incident cases of CAD identified during follow-up of cohort
- modest but statistically significant relationship between intake of alpha and beta carotene and CAD risk
- for women in highest versus lowest quintiles of alpha & beta-carotene intake the relative risk of developing CAD was 0.74 and 0.80 respectively ($p<0.05$)

Authors' conclusions:

- higher intakes of foods rich in alpha or beta-carotene are associated with a reduced risk of CAD

- at this time greater consumption of fruit and vegetables remains the most appropriate public health recommendation

6. Ford, E.S. *et al* The metabolic syndrome and antioxidant concentrations: findings from the third National Health & Nutrition Examination Survey Diabetes 2003; 52: 2346-52

Methods:

- cross-sectional analysis of data from third NHANES study in US (1988-94)
- examined data on circulating concentrations of vitamins A, C & E, retinyl esters, five carotenoids and selenium in 8808 US adults with and without metabolic syndrome
- adjusted for age, sex, race, ethnicity, education, smoking status, cotinine concentrations, physical activity, fruit and vegetable intake, and vitamin and mineral use

Results:

- individuals with metabolic syndrome had significantly lower concentrations of retinyl esters, vitamin C, and carotenoids (except lycopene)
- amongst 2254 persons with metabolic syndrome mean beta-carotene was 0.30 umol/l +/- 0.01 compared with 0.41 +/- 0.01 in remainder
- consumption of fruit and vegetables also lower amongst those with metabolic syndrome

Authors conclusions:

- because persons with metabolic syndrome have low concentrations of several antioxidants they may be an interesting group in whom to study effects of antioxidant supplementation or dietary modification to enhance antioxidant intake

ANALYSIS

Persons in the early stages of glucose intolerance shown to have lower circulating levels of carotenoids in several studies reviewed above. These results appear to be relatively consistent across different populations and study types.

There are several possible explanations for this finding, ranging from impaired absorption to suppression of levels as a result of increased oxidant activity. The possibility also exists that high levels of carotenoids are protective against the development of diabetes, but at present it is not possible to be sure which of these possibilities is most likely. It is possible/likely also that increased beta-carotene levels reflect a generally healthier diet (possibly accompanied by other aspects of a healthy lifestyle).

Present data does not warrant use of beta-carotene supplementation for prevention of diabetes since present evidence falls well short of proving a causal relationship. This is also supported by other data including:

1. Large scale trials of beta-carotene have failed to identify a health benefit (these provide more reliable data than do observational studies), and may cause harm. These studies are briefly reviewed in Osganian *et al* (2003);

2. Positive data presented largely concerns surrogate health measures (eg fasting, glucose levels, HbA1c) rather than clinically significant endpoints; and

3. An analogy may exist with other anti-oxidants, eg. vitamin E, which have shown positive associations in observational studies but negative results in trials.

Concerns about small decreases in beta-carotene levels of the order likely to occur with phytosterols consumption (20%) are not supported by presently available evidence.

In summary, the data presented raise matters worthy of additional study, but fall well short of proving any causal relationship between beta-carotene intake and the development or worsening of diabetes.

PHYTOSTEROLS AND CHRONIC DISEASES

Comments from Chief Medical Advisor for use in preparing the First Review of Applications A433, A434 and A508

12 June 2005

I have been provided with copies of six published papers submitted to Food Standards Australia New Zealand (FSANZ), all of which relate to relationships between dietary intake of carotenoids and chronic diseases. Five papers relate to the metabolic syndrome, hyperglycaemia and type II diabetes mellitus. One relates to risk of coronary heart disease in women.

Coronary heart disease

Summary

The 2003 paper by Osganian et al in the American Journal of Clinical Nutrition set out to study the relationship between the dietary intake of specific carotenoids and risk of coronary artery disease amongst women enrolled in the Nurses Health Study in the United States between 1984 and 1996. Phytosterol fortification of foods was not a factor in the American diet at the time the study was undertaken.
Numerous studies prior to this one had shown that a higher intake of fruits and vegetables was associated with a lower risk of coronary artery disease. One of the health claims being reviewed to see whether it can be accepted as a pre-approved high-level health claim upon the coming into force of Application 293-Nutrition, Health and Related Claims concerns just this relationship.

The result was a modest, but significant inverse relationship between higher intakes of β-carotene and α-carotene and the incidence of fatal and non-fatal myocardial infarction. (26% and 20% respectively between the highest and lowest quintiles of intake). There was no significant risk reduction shown with any of the other carotenoids. Several intervention studies have shown no effect from β-carotene supplementation of the diet and the authors admit that they have probably not ruled out confounding from issues such as heavier fruit and vegetable eaters having a generally more healthy lifestyle, or some other components of fruit and vegetables affecting cardiovascular health.

Conclusion

The general issues traversed in this paper were available to the experts involved in the Mayo Clinic Review of Phytosterols in 2003, and the European Union expert group. While supporting fruit and vegetable consumption, the paper does not draw any conclusion about the adverse effects of reducing the absorption of fat soluble vitamins and antioxidants.

This paper provides no convincing evidence that :

(a) anti-oxidants reduce the risk of cardiovascular disease
(b) reducing the absorption of carotenoids related to reduced abdominal absorption of dietary lipids is a risk factor for cardiovascular disease.

Metabolic Syndrome, Hyperglycaemia and Type II Diabetes

In a 2003 paper by Ford et al in *Diabetes* the Metabolic Syndrome is characterised by a person having at least 3 of the following criteria; abdominal obesity, hypertriglyceridaemia, low levels of LDL cholesterol, high blood pressure, and high fasting glucose. It is known that this group is more likely to develop Type II diabetes.

Between 1988 and 1996 some 23% of US adults from a random sample of 8,800 met the criteria for metabolic syndrome. They were older, more likely to be white, had fewer years of education, were less likely to be involved in regular physical exercise, had higher lipid concentrations, higher serum insulin levels and consumed fewer fruits and vegetables than the others in the sample. On serum analysis the metabolic syndrome group were reported as having sub-optimal levels of several antioxidants, including, inter alia, the carotenoids. The authors suggest that the relationship between antioxidant blood levels and the development of diabetes is a field for further study. There is no comment on the possible effect of altering abdominal absorption of lipids on diabetes.

The same principal author had used participants in the same Third National Health and Nutrition Examination Survey to compare the serum concentration of some five carotenoids in people with normal glucose tolerance, impaired glucose tolerance, newly diagnosed diabetes and long-standing diabetes. After adjustment for possible confounding, serum levels of β-carotene, α-carotene and lycopene were inversely related to the degree of abnormality of the glucose tolerance test. The evidence of an association and is backed up by other studies. However, the authors admit that little is known about the absorption of carotenoids and raise the question whether their findings could have been caused by the impaired glucose tolerance interfering with the absorption of lycopene and α and β-carotenes, rather than a “sub-optimal” carotene level failing to prevent developing diabetes.

There is no convincing evidence that reduced intake of dietary carotenes are related to diabetes in this paper.

A study from Finland, published in the American Journal of Clinical Nutrition in 2003 concluded that, in a population of men at high risk of diabetes, there was an inverse relationship between their intake and plasma concentration of carotenoids and plasma glucose levels, raising the question whether diets rich in fruit and vegetables may assist in the prevention of diabetes. This study cannot be considered as evidence of harm from lowering abdominal lipid absorption.

A Japanese study in 2002 by Suzuki et al, published in the Journal of Epidemiology found an inverse relationship between blood glucose levels and the consumption of pumpkin and carrots (but no other fruits and vegetables), and the same inverse relationship between the serum levels of six carotenoids and plasma glucose.
The evidence of a relationship is “probable” because of some confounders that may not have been fully corrected for. However, there is no convincing evidence about cause and effect and nothing to link these findings to dietary lipid consumption.

A Saudi Arabian paper in 1999 set out to study the effect of diabetes on serum levels of vitamin A and some carotenoids. It found serum β-carotene levels lower in diabetics than control subjects, but no other significant relationships. The discussion in the paper is solely around how diabetes (or the prescribed dietary regimens for people with diabetes) may affect the β-carotene levels.
Therefore there is no evidence provided to relate reduced carotenoid intake with the risk of developing diabetes.

Summary

Taken together, there is no evidence in these papers that reduced carotenoid intake increases the risk of diabetes or cardiovascular disease. There is evidence of an inverse relationship between serum carotenoid levels and glucose intolerance, but not even possible evidence of what is the cause / effect. Nothing in these papers studies the difference in diabetes rates or glucose intolerance between populations who have different diets or seasonal changes in their diet, which might equate to the changes in dietary intake of fat-soluble antioxidants caused by intake of phytosterols.

G R Boyd
Chief Medical Advisor
Food Standards Australia New Zealand

ATTACHMENT 5

OPTIONS FOR LABELLING OF PHYTOSTEROL-ENRICHED FOODS

1. Background

Under current permissions, there is a requirement for three mandatory advisory statements (MAS) to appear on labels of phytosterol-enriched edible oil spreads and margarines. As there are no legal requirements on the presentation of the statements, manufacturers are at liberty to present them according to their own requirements. The Ministerial Council expressed the view that depiction of these MAS on current packaging of phytosterol-enriched products is inadequate to ensure that consumers are informed about the appropriate use of the products.

In requesting a First Review of Applications A433, A434 and A508, the Ministerial Council expressed the concern that should phytosterol-enriched breakfast cereal, low-fat milk and low-fat yoghurt be available on the market, there are no requirements to compel manufacturers to present the MAS more prominently on packaging. Therefore, the Ministerial Council argues that the availability of a broader range of phytosterol-enriched products could be more likely to lead to inappropriate use of the products by consumers.

The issue of specific legibility criteria for mandatory advisory statements[20] was examined and discussed with the jurisdictions during the review of the *Australian Food Standards Code* and the New Zealand Food Regulations, culminating in the development of Standard 1.2.9 Legibility Requirements of the Code. A background to those discussions is in **Addendum 1**. At that time it was agreed that as advisory statements were of lesser importance in relation to protection of public health and safety (compared to mandatory warning statements), it was not necessary to prescribe additional specific legibility criteria or a minimum print size.

2. Review objectives

Specific objectives of the labelling review are to:

- consider the issues raised by the jurisdictions in relation to the adequacy of the presentation of mandatory advisory statements (MAS) on packaging of current phytosterol-enriched foods; and

- consider the impacts of a range of revised labelling options that aim to address these concerns.

2.1 Current labelling requirements

Three MAS are currently required on food regulated in Standard 2.4.2 (Edible Oil Spreads) containing phytosterol-esters and tall oil phytosterols. These requirements are listed in the Table to clause 2, Standard 1.2.3 and are statements to the effect that -

1. the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables;

[20] Under Proposal P 142-Print Size and Quality of Prescribed Information Appearing on a Food Label

2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and

3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication.

Other than the general legibility requirements in Standard 1.2.9, there are no specific legibility requirements in the Code for MAS.

As part of the risk management strategy for Applications A433, A434 and A508 an additional MAS was proposed as follows:

Consuming greater than 3 serves per day of products containing plant sterols provides no additional benefit.

At Final Assessment, FSANZ considered that this statement would encourage appropriate use of all phytosterol-enriched foods by consumers, and be consistent with the data that demonstrated the safety of plant sterols (both phytosterol-esters and tall oil phytosterols) for high level consumers within the target group.

3. Specific labelling issues raised in the Review

Jurisdictions have raised concerns that even on current phytosterol-enriched products, the presentation of the MAS is inadequate, sometimes found on the bottom of containers or inside the outer packaging, raising questions about whether consumer access to information and legibility is being adequately protected. For example, one product brand presents the MAS on a removable cardboard sleeve that is likely to be removed after purchase. Therefore the MAS may not be accessible by other members of a household.

In the context of Application A434, small punnets of yoghurt are normally sold in packs of two or four surrounded by a removable outer cardboard sleeve. The jurisdictions contend that for these products it is likely the MAS will again only be accessible to a purchaser of the product but not necessarily to all consumers in a household.

An additional issue raised by the Ministerial Council is that the statements are almost illegible because of the small font size used. These labelling concerns are therefore likely to apply to the broader range of phytosterol-enriched foods if the current applications are approved.

4. Revised labelling options

Four options were considered to address the issues raised by the jurisdictions:

4.1 Option 1 - Status quo

Under the status quo, the existing MAS for foods containing phytosterol esters and tall oil phytosterols would remain in Standard 1.2.3. Legibility and prominence issues would be covered by the general provisions in Standard 1.2.9, supported by the User Guide to Standard 1.2.9.

4.2 Option 2 - Use of an editorial note to clarify the legibility requirements in Standard 1.2.9

Under Option 2, the general legibility requirements in Standard 1.2.9 would be clarified. This could be done by including an editorial note after the general requirements in clause 2 to clarify the intent of the words 'written or set out legibly and prominently such as to afford a distinct contrast to the background…' . For example, the editorial note could state that words or statements provided on the inside or underside of a label would not be considered as 'legible' or 'prominent'.

4.3 Option 3 - Additional clause in Standard 1.2.9 to strengthen the legibility requirements for advisory statements

Under Option 3, an additional clause could be included in Standard 1.2.9 setting out specific legibility requirements for advisory statements. For example, the clause could specify that advisory statements should not be placed on a removable sleeve, must not be placed on the underside or inside of a label and must be in a minimum font size of X mm.

A similar provision would also be required in the Standard for warning statements, given that warning statements apply where there is a higher public health and safety risk.

4.4 Option 4 - Additional provisions in Standard 1.5.1

Under Option 4, the existing MAS for foods containing phytosterol-esters and tall oil phytosterols would be transferred from Standard 1.2.3 and transferred to Standard 1.5.1 - Novel Foods. These statements would be listed in Column 2 of the Table to clause 2 as Conditions of Use. Other specific requirements – for example, that advisory statements should not be placed on a removable sleeve, must not be placed on the underside or inside of a label and must be in a minimum font size of X mm, would also be included in Column 2.

5. Impact of regulatory options

OPTION 1	
Advantages	**Disadvantages**
• Less cost to manufacturers of phytosterol products that are currently complying with the Code, as relabelling or repackaging would not be required.	• Does not specifically address jurisdictional concerns in relation to labelling of phytosterol products although it could be argued that these issues could be dealt with by enforcement action.
• Consistent with the principles underpinning Standard 1.2.9 and the principle of minimum effective regulation on which the Code is based.	
• Consistent with EU requirements for phytosterol-containing foods and general labelling requirements by Codex, which are not prescriptive in terms of legibility/prominence of advisory statements.	

OPTION 2	
• By clarifying the general legibility requirements, it may better address jurisdictional concerns than Option 1.	• Editorial note is not legally enforceable therefore jurisdictional concerns may not be fully addressed.
• Clarification of legibility requirements would apply generally, rather than just to the advisory statements on phytosterol products.	• Could still be considered unnecessarily prescriptive and not consistent with principles underpinning Standard 1.2.9.
• Consistent with the principles underpinning Standard 1.2.9 and the principle of minimum effective regulation on which the Code is based.	
OPTION 3	
• More effective in addressing jurisdictional concerns than Options 1 and 2.	• Unnecessarily prescriptive and not consistent with principles underpinning Standard 1.2.9 or the Code generally.
• Would apply to all advisory statements not just advisory statements on phytosterol products.	• Potentially more prescriptive than warning statements which have a higher public health and safety risk, unless a similar provision is included for warning statements.
	• Inconsistent with EU requirements for phytosterol-containing foods and general labelling requirements by Codex, which are not prescriptive in terms of legibility/prominence of advisory statements. Possible implications for international trade.
	• Additional costs to manufacturers of phytosterol products associated with repackaging/relabelling.
OPTION 4	
• Addresses jurisdictional concerns in relation to labelling of phytosterol products.	• Inconsistent with FSANZ objectives of reduced prescriptiveness and minimum effective regulation and general labelling provisions in the Code.
• 'Disguises' mandatory advisory statements as 'conditions of use', thereby drawing attention away from what could be considered as a conflict with other advisory statements and labelling requirements in the Code.	• No evidence provided to indicate why advisory statements on phytosterol containing products should be more prescriptive than other labelling requirements (e.g. allergen labelling or warning statements).
	• Possible flow on effects to other advisory statements and other labelling provisions.
	• Effectively creating another class of statements without any clear rationale for this.
	• Additional costs for manufacturers of phytosterol products associated with repackaging/relabelling.

	• Inconsistent with EU requirements for phytosterol-containing foods and general labelling requirements by Codex which are not prescriptive in terms of legibility/prominence of advisory statements. Possible implications for international trade.

1.1.1.1.2 Evaluation of options

Option 1, may not be a viable option considering that jurisdictions have already indicated that they require strengthening of the current mandatory labelling statements. If this option is followed the Applications may not be approved by ANZFRMC.

Options 3 and 4 are not preferred for the following reasons:

- the labelling standards would be amended in the absence of any evidence that the specific issues outlined by the jurisdictions are a problem, either for consumers or enforcement agencies;
- the amendments jeopardise the principles, previously agreed to by the Ministerial Council, upon which the Code has been developed;
- the amendments compromise the integrity of the Code; and
- the amendments are matters of policy, which should more appropriately be referred to FRSC for policy guidance.

6. Preferred option

The preferred option is Option 2 – clarifying the legibility requirements in Standard 1.2.9 by use of an editorial note for the following reasons:

- other than Option 1, it is the least prescriptive option and therefore is most consistent with the principles upon which Standard 1.2.9 and the Code are based;
- it would apply more generally to all labelling requirements rather than just to advisory statements on phytosterol products;
- it goes some way to addressing jurisdictional concerns relating to phytosterol-enriched foods; and
- it is more consistent with the current general labelling requirements for MAS by Codex and the specific EU requirements for phytosterol-enriched foods.

Additional Recommendation

FSANZ also proposes a broader review of Standard 1.2.9 in relation to all mandatory warning statements, advisory statements and declarations via a specific Proposal that aims to address the issue of effectiveness of current labelling provisions in the longer term. However, approval of the current Applications (A433, A434 and A508) would not be conditional on completion of the review of Standard 1.2.9.

The benefit of this approach is that:

- FSANZ could assess the application of Standard 1.2.9 within the context of the whole Code and the principles on which it was developed rather than within the context of the three current phytosterol applications;
- the current effectiveness of Standard 1.2.9 would be evaluated;
- it allows consideration of any public health and safety considerations that have emerged since the first review of Standard 1.2.9;
- the concerns of the jurisdictions would be considered in a more systematic way; and
- any amendment resulting from such a review would be based on evidence and would be less likely to have a negative impact on the operation of the other labelling standards.

Addendum

1. Background to Standard 1.2.9: Proposal P142 – Print Size and Quality of Prescribed Information Appearing on a Food Label

Addendum 1

Background to Standard 1.2.9: Proposal P142 – Print Size and Quality of Prescribed Information Appearing on a Food Label

During the review of the Code considered issues relating to print size and quality of information appearing on labels in Proposal P142.

FSANZ considered that prescribed information should be regulated using basic legibility criteria only, and the requirement that all prescribed information be prominent, legible and in English ensures information is easily legible to the prospective purchaser while allowing manufacturers greater flexibility in label design. Including more words than this was considered to unnecessarily duplicate the intention of the requirement.

FSANZ considered that warning statements should be treated in a more prescriptive manner in relation to print size and quality than other prescribed information due to their direct role in the protection of public health and safety. Warning statements are subject to basic legibility criteria and a minimum print size of 3 mm (or 1.5 mm in the case of small packages) even though this is more stringent than Codex requirements. As advisory statements are of lesser importance in relation to protection of public health and safety FSANZ considered it was not necessary to prescribe additional specific legibility criteria or a minimum print size.

Requiring that warning statements be more noticeable, or regulating the positioning of the statement was also considered as part of P142. The majority of warning and other statements are placed at the manufacturers discretion and as there appeared to be no disadvantages to the consumer it was not considered necessary to prescribe the position of these statements.

Attachment 10

7-06
4 October 2006

SECOND REVIEW REPORT

APPLICATION A433
PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN BREAKFAST CEREALS

APPLICATION A434
PHYTOSTEROL ESTERS DERIVED FROM VEGETABLE OILS IN LOW-FAT MILK & YOGHURT

APPLICATION A508
PHYTOSTEROLS DERIVED FROM TALL OILS AS INGREDIENTS IN LOW-FAT MILK

For Information on matters relating to this Report or the assessment process generally, please refer to http://www.foodstandards.gov.au/standardsdevelopment/

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Decision

FSANZ <u>re-affirms</u> its approval of Applications A433, A434 and A508, subject to drafting amendments specified in this Second Review, and supported by appropriate risk management measures because:

8. The recently established Phytosterols Expert Advisory Group evaluated safety concerns raised by jurisdictions in relation to nutritional effects, possible interactions with cholesterol-lowering medications and long-term usage of phytosterol-enriched foods and concluded that there was no basis for health concerns;

9. A change to permit a minimum and maximum amount of plant sterols in a product will assist consumers to:

(i) more easily monitor a daily intake of plant sterols;
(ii) consume an efficacious amount; and
(iii) use the products cost effectively;

10. Revised mandatory advisory statements will provide information to consumers at the time of purchase that is consistent with the safety evidence for different population groups;

11. A survey of New Zealand and Australian consumers found that users of phytosterol-enriched margarines are in the target group, use the products in moderation and for the appropriate health reasons. Recent post-market monitoring in Europe, where a broader range of phytosterol-enriched foods has been available for some time, shows that consumers welcome choice of products, and over-consumption does not occur;

12. A review of Standard 1.2.9 Legibility Requirements will go ahead, but the insertion of an Editorial note is a practical, interim measure to clarify the legibility requirements of the Code for mandatory advisory statements;

13. FSANZ and the National Heart Foundation of Australia will collaborate in broadly based education activities that will significantly increase the visibility of information on plant sterols in the context of heart-healthy nutrition and dietary advice;

14. FSANZ will also prepare its own educational material on phytosterol-enriched foods suitable for wide distribution to professional organisations and the general public, linking to other sources of information on plant sterols;

15. Approval of the current applications is a conservative extension of use of plant sterols into foods types that are compatible with a healthy diet message; and

16. The development of policy guidance on the addition to food of non-vitamins and minerals and a new Standard for Health, Nutrition and Related Claims should not halt the progression of Applications A433, A434 and A508.

Summary Table

Issues addressed in the Second Review of Applications A433, A434 and A508 seeking to broaden the use of phytosterol esters and tall-oil phytosterols.

MINISTERIAL COUNCIL ISSUE	FSANZ RESPONSE
1. Protection of public health and safety.	• **Officials of jurisdictions contacted to seek clarification on concerns.** • **Formation of the Phytosterols Expert Advisory Group to consider safety issues holistically.** • **Further assessment of nutritional issues in the context of Australian data on beta-carotene levels.** • **Further assessment of effects of plant sterols used in conjunction with cholesterol-lowering medication.** • **Assessment of recently published literature on plant sterol-enriched foods and effects in children.** • **Further explanation of the potential benefits to consumers from a wider choice of phytosterol-enriched foods and clarification on the restrictions to breakfast cereals.** • **Consideration of several, recent post-market monitoring reports on phytosterol-enriched foods in Europe.** • **Revision of specifications for the tall oil phytosterols.**
2. Provision of adequate information to enable informed choice.	• **TNS social research commissioned to conduct a survey of consumers in New Zealand and Australia of phytosterol-enriched spreads to ascertain behaviour patterns and motivation.** • **Revision of the mandatory labelling statements for packaging of <u>all</u> phytosterol-enriched foods.** • **Established professional links with the National Heart Foundation of Australia to assist with the development and implementation of community education initiatives providing information relevant to the appropriate use of plant sterols, and dietary/nutritional advice in relation to heart disease.**
3. Policy issues.	• **Provided further explanation regarding the impact of the proposed health claims standard and the development of policy guidance for the addition to food of non-vitamins and minerals.**

Key changes as a result of the Second Review

PREVIOUS ASSESSMENT	ASSESSMENT AT SECOND REVIEW
) or no more than 0.9 g tall oil plant sterols in one serve of food.	*sterols (either vegetable oil or tall oil) per serve of food* • **The minimum amount is based on efficacy and the maximum amount is based on avoidance of consumer deception.** • **All plant sterols, whether derived from a vegetable oil or tall oil source, will be permitted within the same range, to avoid consumer confusion between the two types of phytosterols permitted in the FSC.** • **Dietary exposure estimates, including the use of phytosterol-ester enriched table spreads, show that mean daily consumption would be within 1-3 g.**
n as part of a diet low in saturated fats and high in fruits and vegetables.	*ied as part of a healthy diet* • **Plant sterols permitted only in foods that are compatible with a healthy diet i.e. low-fat milk, low-fat yoghurt and breakfast cereal with a compositional profile that is not attractive to children.** • **Advice to consume carotenoid-rich fruit and vegetables is not justified on the grounds that the reduction in serum beta-carotene is not indicative of any nutritional deficiency and is within natural variation.** • **Healthy diet message compatible with other public health messages in relation to diet and chronic disease.**
hildren and pregnant or lactating women unless under medical supervision.	*r the age of five years and pregnant or lactating women.* • **Many studies in hypercholesterolaemic children show the efficacy and safety of plant sterol-enriched foods. However, young children do not need to consume specific foods to achieve a cholesterol reduction.** • **Similarly, pregnant and lactating women do not need to lower serum cholesterol levels.**
n should seek medical advice on the use of this product in conjunction with their medication.	• **Clinical studies show that consumption of plant sterol-enriched foods can lead to a modest reduction in cholesterol levels, even in individuals on cholesterol-lowering medication, and is not a health concern.** • **There is no scientific evidence of adverse interactions of plant sterols in conjunction with cholesterol-lowering medication, particularly the statins, as they work by different physiological mechanisms.** • **Plant sterol-enriched foods may provide a more cost-effective means of reducing cholesterol in those who cannot achieve a reduction using prescribed medication alone.**

PREVIOUS ASSESSMENT	ASSESSMENT AT SECOND REVIEW
ide additional benefits when consumed in excess of three serves per day.	*en consumed in excess of three grams per day.* • **Consumers can more easily monitor their daily intake in grams of plant sterols across a range of foods.** • **Advises consumers that more than 3 g per day plant sterols do not provide any additional cholesterol-lowering benefit, thereby encouraging cost-effective use of the products.** • **There are no standardised serve sizes for these products, although manufacturers often indicate a recommended serving size on packaging.**
used when declaring the ingredient in the ingredient list , as prescribed in Standard 1.2.4	• **Manufacturers of phytosterol-enriched table spreads currently use the more generic term 'plant sterols'.** • **Consumers can readily monitor daily intake in grams of plant sterols by reference to the ingredient list.**
rol esters have been added may not be used as ingredients in other foods.	• **Manufacturers will not be permitted to use phytosterol-enriched foods in the preparation of other mixed foods.**
ols are listed in the Schedule to Standard 1.3.4 Identity and Purity.	• **New specifications for the tall oil phytosterols incorporate a minimum 97% level of purity, with a maximum of 3% minor sterols. The revised specifications also incorporate a reduction in the 'total heavy metals' component from a maximum of 10 ppm down to 2 ppm.**
ility Requirements	vs: *where prescribed information is placed other than on the outside of a package where it is readily accessible by a consumer prior to purchase, or during the life of the product, and not obscured by an outer covering. The requirements of this Standard will also not be met where prescribed information is printed in a small font so the statement cannot be read easily.* • **Intended only as an interim measure to reinforce the principles underpinning Standard 1.2.9, pending a systematic review of the effectiveness of the Standard.**

All drafting changes for Applications A433, A434 and A508 are at **Attachment 1**.

1. Introduction

In September 2005, the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) requested a Second Review of Applications A433, A434 and A508. These applications seek to broaden the range of foods to which phytosterols (plant sterols) may be added as follows:

Application A433	Addition of phytosterol esters* derived from vegetable oils to breakfast cereals
Application A434	Addition of phytosterol esters* derived from vegetable oils to low-fat milk and yoghurt
Application A508	Addition of phytosterols derived from tall oils** to low-fat milk

***Phytosterol esters** are plant sterols derived from edible vegetable oils which have been esterified with long-chain fatty acids from vegetable oil sources.
****Tall oil phytosterols** (non-esterified) are a by-product of the pulping process from coniferous trees.

Approval of all three applications involves variations to Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations, Standard 1.5.1 – Novel Foods, Standard 2.5.1 – Milk, and Standard 2.5.3 Fermented Milk Products of the *Australia New Zealand Food Standards Code* (the Code).

The purpose of the Second Review is to respond to the issues raised by the Ministerial Council, as outlined in Section 3. FSANZ has addressed these issues by seeking additional information from key stakeholders, undertaking further research and engaging external expertise. An extension of time was granted until 27 July 2006 to complete the review.

2. Objectives of review

The objective of the Second Review is to reconsider the draft variations notified to the Ministerial Council by FSANZ in July 2005 following completion of the First Review.

3. Grounds for the review

A Second Review was requested on the grounds that approval of the draft variations:

- does not protect public health and safety; and
- does not provide adequate information to enable informed choice.

The Ministerial Council provided additional comments concerning the grounds on which the Second Review is based. These comments have been broadly categorised in the following groups:

- Long term safety of phytosterols;
- Possible interactions with cholesterol-lowering medication;
- Nutritional effects;
- The effectiveness of labelling and advisory statements; and
- Consumer education and the role of health professionals.

Specific advice was also requested on the sterol composition of the tall oil phytosterols (TOPS) on the basis of changes to the specifications in the European Union.

4. Background

Currently, under Standard 1.5.1 - Novel Foods, phytosterol esters and tall oil phytosterols (plant sterols) are permitted for use only in edible oil spreads. As separate novel food ingredients, they are listed individually in the Table to clause 2 and are subject to specified conditions of use. Plant sterols must be declared in the ingredient list, and three advisory statements must be presented on packaging to advise consumers on how to use the products appropriately[21].

Consumption of plant sterols reduces absorption of dietary cholesterol leading to lower serum LDL-cholesterol levels. Foods containing added plant sterols are therefore targeted primarily to adult consumers with concerns about their cholesterol levels. Manufacturers seek to expand the range of phytosterol-enriched products primarily to broaden consumer choice.

In October 2004, the FSANZ Board approved the Final Assessment of Applications A433, A434 and A508. The FSANZ assessment focused on (i) the safety of phytosterol esters and tall oil phytosterols at proposed levels of use when used in breakfast cereal, low-fat milk and yoghurt, (ii) their efficacy in the relevant food matrices to ensure truth in labelling, and (iii) the suitability of the products to target consumers.

The optimal cholesterol-lowering effect is achieved when consumption is between 2-3 g plant sterols per day, irrespective of the type of sterols consumed. To ensure that target consumers were informed about this, an additional advisory statement was proposed to the effect that:

foods containing added plant sterols do not provide additional benefits when consumed in excess of three serves per day.

As an additional risk management measure, the conditions of use were also extended to the effect that:

foods containing added plant sterols must not be used as ingredients in other foods.

In December 2004, the Ministerial Council requested a First Review of the Applications on the grounds that there were remaining standards and policy issues. After consideration of these issues, in July 2005, the Board reaffirmed its approval of the draft variations recommended to the Ministerial Council.

4.1 Phytosterol-enriched foods in other countries

A variety of phytosterol-enriched foods are approved in Europe and the USA in the following categories:

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[21] It should be noted that although the permission for tall oil phytosterols exists in the Code, there are no tall oil products on the market. The two currently available brands of phytosterol-enriched table spreads (Logicol® and ProActive®) both contain phytosterol esters from vegetable oils.

(1) Fats and oils
(2) Dairy products
(3) Beverages
(4) Bakery products

Because of the complexity of the approval process for individual products in the European Union, FSANZ sought information from the food industry on the regulatory status and availability of phytosterol-enriched products in Europe. The information received is at **Attachment 2**. Milk and fermented milk products have been approved under the Novel Foods Regulation (EC No. 258/97) since 2004. Recently in 2006, the range of approved products was extended to rye bread.

4.2 Other applications

Some phytosterol-enriched products available in Europe contain the target amounts required for a cholesterol-lowering benefit in a single serve of food. For example, a single-shot of drinking yoghurt can contain two grams of plant sterols. Such products diversify the phytosterol-enriched foods market in general and, for some consumers, undoubtedly offer a simpler choice for obtaining the target amount of plant sterols in one meal event. FSANZ would consider any future applications for products that offer a suitable quantity of plant sterols in a single serve of food.

5. Issues in the Second Review

Formation of Expert Advisory Group

FSANZ formed a Phytosterols Expert Advisory Group, chaired by the Chief Medical Advisor Dr Bob Boyd, to broaden the technical input into the Second Review. The Group is comprised of invited members with identified expertise and knowledge on phytosterols from a variety of professional backgrounds. As well as researchers, academics and a clinician, representatives from organisations such as the Dietitians Association of Australia, the New Zealand Dietetics Association and the National Heart Foundation of Australia (NHF) were invited into the Group22.

The Group's purpose and function is to provide advice to FSANZ on the interpretation and evaluation of available scientific evidence relevant to consideration of the efficacy, safety and nutritional effects of phytosterol-enriched foods. Through representatives from health professional organisations, the Group also provided advice in relation to a number of consumer-related issues.

At a meeting in May 2006, the Phytosterol Expert Advisory Group discussed specific technical issues identified in the comments received from the Ministerial Council at Second Review. Through a consensus approach, the meeting was able to address a number of key concerns using the most recent scientific information and progressive thinking on the role of phytosterol-enriched foods in the context of a healthy diet.

[22] **Phytosterol Expert Advisory Group**: Dr Alex Chisholm, University of Otago (Dunedin, NZ); Dr Peter Clifton, CSIRO Human Nutrition; Ms Barbara Eden, National Heart Foundation of Australia; Ms Linda Hodge, Dietitians Association of Australia; Professor Paul Nestel, Baker Medical Research Institute; Dr Manny Noakes, CSIRO Human Nutrition; Professor Brian Priestly, Director, Australian Centre for Human Health Risk Assessment (Department of Epidemiology and Preventive Medicine, Monash University, Melbourne).

Wherever relevant, the deliberations and conclusions of the meeting have been used in addressing the following issues.

5.1 Protection of public health and safety

5.1.1 Long term safety of phytosterols at high levels of consumption

The Expert Advisory Group was not aware of more recent long term studies (greater than twelve months) on phytosterols, however considered that extrapolation from the results of the large number of published studies showing no safety concerns was appropriate.

Additional toxicological studies in animals were published between 2001-2004, and these had confirmed the absence of any adverse effects. Phytosterols are only poorly absorbed, and a number of potential toxicological effects had been examined and ruled out as a concern.

There are many studies examining safety in humans, and the effects on uptake of fat-soluble nutrients was the most significant finding, although these were variable in different studies. Low amounts of dietary phytosterols are currently being explored as anti-cancer agents, particularly for hormone-dependent cancers.

Studies on the effects of dietary phytosterols are available for both normocholesterolaemic and hypercholesterolaemic people. Previously, FSANZ has focused on studies using subjects with normal or mildly elevated cholesterol levels. Consideration of the studies using hypercholesterolaemic subjects, usually those in whom high cholesterol levels occur in families, broadens the available evidence as these tend to be longer term studies.

A 2004 Norwegian study examined the long-term compliance and changes in plasma lipids, plant sterols and carotenoids in children and parents with familial hypercholesterolaemia (FH) consuming phytosterol ester-enriched spread. The duration of the study was 6 months. A total of 37 children (7-13 y) and 20 parents (32-51 y) diagnosed with heterozygous FH were required to consume 20 g per day of phytosterol-enriched spread as part of their lipid lowering diet. The mean daily intake of phytosterols corresponded to 1.2 g in the children and 1.5 g in the parents. Most parents, but no children, used statins in addition to the dietary intervention. There was a reduction of approximately 11% in LDL cholesterol levels in both groups. The authors reported that lipid-adjusted serum alpha- and beta- carotene decreased by 17% and 11% respectively in the children at the end of the controlled phytosterol period. However, levels of both nutrients increased again during the follow-up period. Of note, serum alpha- and beta-carotene concentrations were unchanged in the parents. There were no adverse effects reported and the study concluded that long-term compliance of phytosterol consumption was associated with sustained efficacy in cholesterol reduction (Amundsen et al., 2004).

With respect to tall oil phytosterols (Application A508 only), FSANZ acknowledges that there have been no long term studies at higher levels of consumption, with studies limited to 28 days (3.6 g/day) or 8 weeks (1.8 g/day). However, given the higher proportion of stanols in the tall oil preparations, large studies examining the safety of plant stanol-enriched foods are relevant.

The Stresa Workshop23 whose findings were published in the Mayo Clinic Proceedings (Katan et al. 2003), is one of the most comprehensive reviews on the efficacy and safety of plant stanols and sterols. This review concluded that consuming 2 g per day of stanols and sterols lowers LDL cholesterol levels by 10%, and based on epidemiological data and trials with cholesterol-lowering drugs, long-term use likely will lower coronary heart disease risk by between 12% to 20% in the first 5 years, and by 20% over a lifetime. The Workshop further concluded:

> *Safety testing of [plant] sterols and stanols has exceeded that of ordinary foodstuffs that are eaten widely and generally recognised as safe; and*
> *Adverse health outcomes due to observed decreases in beta carotene levels in plasma are speculative and are of no major concern.*

With respect to the potential oestrogen-disrupting effects of phytosterols in foods, studies on tall oil phytosterols previously evaluated by FSANZ under Application A417[24], found no evidence of *in vitro* or *in vivo* oestrogenic activity in rats or humans. In addition, the former EU Scientific Committee on Food (SCF) Final Report (3 October 2002) stated that newly submitted studies provided sufficient reassurance of the absence of endocrine effects via the oral route (SCF, 2002). In addition, the Stresa Workshop report references several studies, including long-term and in vitro and in vivo studies, in reaching a conclusion that plant sterols do not bind to the oestrogen receptor and that there is no evidence of oestrogenic activity of stanols.

Based on the large number of safety/efficacy studies in humans and toxicological studies in animals, FSANZ concluded that there is no evidence to suggest that adverse effects would result from longer term consumption of phytosterols, from either tall oil or vegetable oil sources. On the contrary, phytosterols were well tolerated, efficacious in the food matrices under consideration (over and above a background low-fat diet) and raised no safety concerns in adults or children. High levels of consumption (up to 10 g per day) have been shown in clinical studies to be safe, providing a safe margin of exposure when compared to the expected level of consumption of 2-3 g per day.

5.1.1.1 Conclusion

Phytosterol-enriched foods are well studied in both adults and children and in situations of varying cholesterol status and there are no indications of adverse long-term effects. They have been available in the food supply for more than 10 years without raising safety concerns. Limitations on the level of consumption are recommended primarily because increasing intake beyond 3 g per day produces little additional reduction in LDL-cholesterol.

5.1.2 Beta carotene and diabetes

The Expert Group agreed that no causative link between lower serum beta-carotene levels and type 2 diabetes has been established. On the basis of current information, the biological meaning of the observations reported by Ford *et al* (2003) was not resolved.

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[23] The Stresa Workshop facilitated the combined deliberations of 32 scientific experts on the safety of sterols and stanols.
[24] Application A417 – An application assessed in 2000/2001 seeking permission to use non-esterified phytosterols from a tall oil source as a Novel Food ingredient in edible oil spreads.

The papers by Ford *et al* are analyses of the US Third National Health and Nutrition Examination Survey (NHANES). The NHANES are cross-sectional surveys conducted at regular intervals in the US and are similar to the 1995 Australian and 1997 New Zealand National Nutrition Surveys and the 1999-2000 Australian Diabetes, Obesity and Lifestyle (AusDiab) Study (Dunstan, Cameron). Serum carotenoids were measured in the Queensland participants of the AusDiab study and, like the results reported by Ford *et al*, analysis shows that those with diabetes have lower mean serum beta-carotene levels than those without diabetes (Coyne 2005).

In a cross-sectional survey, all factors are measured at the same time – i.e. diabetes presence and level of serum beta-carotene were measured in the same sample of blood – therefore it is not possible to know whether the diabetes led to the low serum beta-carotene levels or the low serum beta-carotene levels led to the diabetes. Either is theoretically possible: diabetes may increase the level of oxidants which might "use up" anti-oxidants leading to lower serum levels or alternatively, low serum beta-carotene levels may create an oxidative environment that may predispose to diabetes development. In a 10 year follow-up study, Wang *et al* found no prospective association between baseline plasma carotenoids and the risk of type 2 diabetes in middle-aged and older women (Wang *et al*, 2006).

The strongest way to examine these questions is to conduct a randomised controlled trial in which participants without diabetes are given beta-carotene or placebo and followed over time to determine whether the incidence of diabetes differs between the groups. Liu *et al* (1999) randomised 22,071 healthy US male doctors aged 40-84 years to 50 mg beta-carotene or placebo on alternate days. Over the next 12 years, the incidence of type 2 diabetes was the same in both groups (RR=0.98, 95%CI: 0.85-1.12).
Therefore it must be concluded that, in the studies of Ford and Coyne, serum beta-carotene levels act as a marker for some other factor that could be related to diabetes, but is not itself shown to be the causal agent.

Furthermore, a reduction in serum beta-carotene in the order of 20% should be put into perspective. In the Queensland AusDiab participants, mean serum beta-carotene levels ranged from 0.46 umol/L in men aged 25-43 years to 0.79 umol/L in men aged 75 years and older (i.e. young men have levels 42% lower than older men), and from 0.59 umol/L in women aged 25-34 years to 1.25 umol/L in women aged 75 years and older (i.e. young women have levels 53% lower than older women) (Coyne 2002). In other words, the age and sex-related range of mean serum beta-carotene levels across the Queensland population is much larger than the reduction seen in studies on plant sterols.

The Stresa Workshop (Katan *et al* 2003) also reports a similar conclusion with respect to other chronic diseases such as coronary heart disease and cancers. The Workshop concluded that a decrease in serum beta-carotene levels caused by plant sterols should be viewed in the context of other dietary factors that influence circulating levels. As well as dietary and seasonal factors, some lipid-lowering drugs cause decreases in serum beta-carotene levels beyond the expected decrease from the lower LDL-cholesterol levels. Several long-term trials (such as the Lipid Research Clinics Coronary Primary Prevention Trial) in which the health of subjects on certain cholesterol-lowering medication was followed for up to 10 years, found that significantly reduced beta-carotene levels were not associated with an increased incidence of coronary events or cancers.

5.1.2.1 Conclusion

A 25% reduction in serum beta-carotene levels is not considered significant in the context of fluctuations that occur naturally due to environmental factors. Furthermore, current reports of diabetes and low carotenoids do not constitute evidence that a reduction in serum beta-carotene in the order of 25% is causal with respect to disease outcomes. Rather, the available evidence indicates that a reduction of this magnitude in serum beta-carotene levels has no effect on vitamin A levels and cannot be directly associated with an adverse impact on nutritional status.

5.1.3 Possible interactions with cholesterol-lowering medications

There are several groups of drugs used to lower serum cholesterol levels, acting on different aspects of cholesterol metabolism. Sites of action, modes of action and side-effect profiles differ, however there are no reports in the literature of adverse interactions between phytosterol-enriched foods and cholesterol-lowering medications.

Two groups of drugs, the anion-exchange resins and the more recently introduced ezetimibe act, like the phytosterols, within the gut to inhibit the absorption of cholesterol. There is no evidence of hazard from combining these non-absorbed agents. Gastro-intestinal side-effects limit the use of the resins and these may possibly be increased if drugs are used in combination. The fibrate group act mainly by reducing serum triglycerides. Although there are precautionary statements about combining fibrates and statins, there are no recognised hazards from combining fibrates with drugs acting within the gut. The same would apply to phytosterols.

Statins (HMG Co-A reductase inhibitors) are overwhelmingly the most prescribed cholesterol lowering drugs. They act predominantly in the liver by blocking cholesterol synthesis. There is increasing evidence that “aggressive” cholesterol lowering treatment, such as combining optimum doses of statins with a drug working at another site, such as ezetimide, produces additional clinical benefits. There is no evidence that this combination treatment with statins increases side-effects or risks. Phytosterols and ezetimibe have similar actions, both blocking cholesterol absorption in the gut. Therefore it can be concluded that a phytosterol/statin combination is likely to be safe and effective.

Prolonged statin therapy is reported to cause increases in the levels of all plant sterols in the blood (cholesterol-adjusted), and small but significant increases in serum campesterol levels (unadjusted) (Tikkanen, 2005). However, the levels of plant sterols remain much lower than those observed in patients with sitosterolaemia (a rare metabolic disorder in which all naturally occurring plant sterols in the diet are hyperabsorbed). To put this into perspective, mean serum levels of plant sterols from consumption of phytosterol-enriched margarine represent only 5%-15% of the concentrations of plant sterols in the serum of patients with sitosterolaemia. A mechanism has been proposed to explain the increased absorption of plant sterols with concomitant statin use: a medication-induced reduction in biliary cholesterol leads to a diminished cholesterol pool in the intestine, which allows more plant sterols to become incorporated in mixed micelles, which in turn facilitates their uptake in enterocytes.

Overall, the evidence indicates an additive cholesterol-lowering effect of plant sterols combined with statin therapy.

A trial conducted on patients using statins found an additional reduction of 10% in LDL levels with incorporation of stanol ester-enriched spread into the diet (Blair *et al*, 2000). The additional efficacy is reported to be greater than the effects usually achieved by doubling the statin dose (which normally provides an extra reduction in LDL-cholesterol levels in the order of 5%-7%).

5.1.3.1 Conclusion

Plant sterols can have an additional small cholesterol-lowering effect in people who are using cholesterol-lowering medications such as the statins. There are no reports in the literature of adverse effects from the consumption of phytosterol-enriched foods. Cholesterol-lowering medications are available on prescription only, and there are no reports of adverse interactions between plant sterols and cholesterol-lowering drugs. On the contrary, for those patients who have failed to respond adequately to medication, consumption of plant sterols may be a suitable (and more cost-effective) dietary intervention for further improving their cholesterol levels.

5.1.4 Specifications for tall oil phytosterols

The initial EU application for permission of tall oils was rejected because the purity of the nominated tall oil was 95%, with the remaining 5% of the sterols unknown. A later application reduced the levels of unknown sterol compounds to less than 1%.

The Applicant has provided FSANZ with revised specifications for tall oil phytosterols, incorporating a minimum purity level of 97%, with a maximum of 3% minor sterols. The revised specifications also incorporate a reduction in the 'total heavy metals' component from a maximum of 10 ppm to 2 ppm. These amendments have been included in revised drafting in the Schedule to Standard 1.3.4 Identity and Purity, at **Attachment 1**.

5.1.4.1 Conclusion

As there are no products containing tall oil phytosterols currently on the market in Australia and New Zealand, the revised specifications will not impact on any Australian or New Zealand manufacturers. Any tall oil products that enter the food supply in the future must comply with the new specifications.

5.1.5 Elevated serum cholesterol levels should be managed medically

Many studies have shown that the optimal cholesterol lowering effect from plant sterols is achieved when consumption is between 2-3 g per day. In approving a broader range of phytosterol-enriched foods, FSANZ has confined the permission to foods with a healthy compositional profile. Foods such as low-fat milk, low-fat yoghurt and high-fibre breakfast cereal are compatible with healthy eating patterns.

People with hypercholesterolaemia would be expected to be under medical supervision, however the preferred means of lowering a mildly elevated cholesterol level is through changes to the diet. Phytosterol-enriched foods are part of a package of dietary and lifestyle advice to help people self-manage their cholesterol levels. In addition, the food vehicle choices in these Applications are broadly compatible with current public health guidelines.

Some consumers with a slightly elevated cholesterol level may already be eating a 'healthy' diet. For these people, consumption of phytosterol-enriched foods involves a conservative dietary change that can assist them with achieving individual health-related goals or dietary preferences. The results of the consumer survey (see Section 5.3) indicate that consumers who are current users of phytosterol-enriched spreads are motivated by concern about their health, particularly cholesterol levels.

In terms of prescribed medications, patient compliance has always been an issue for clinicians. The availability of a broader range of phytosterol-enriched foods could not reasonably be considered to impact directly on this issue, given that people disregard medical advice for a variety of reasons. In addition, there would be a negligible cost benefit in choosing phytosterol-enriched foods over prescribed cholesterol-lowering medication.

5.1.5.1 Conclusion

Consumption of phytosterol-enriched low-fat milk, yoghurt and breakfast cereal has been shown to give small reductions in serum cholesterol levels irrespective of the background diet. Approval of these Applications therefore provides consumers with an additional range of appropriate dietary choices, over and above low saturated fat products, for addressing concerns about cholesterol levels.

5.1.6 Consumption of phytosterol-enriched products by non-target groups

FSANZ acknowledges that regular consumption of phytosterol-enriched foods is not generally appropriate for children, and pregnant or lactating women since there may be no necessity to lower blood cholesterol levels in these groups. Notwithstanding the absence of a health benefit, the modest reduction in cholesterol that may result from an increased intake of phytosterols by non-target groups is not likely to be physiologically or nutritionally significant.

Based on the findings of the consumer research undertaken by FSANZ (Section 5.3), and similar findings in the United Kingdom from a post-market consumer survey (ACNFP, 2006), FSANZ considers that the approval of a limited range of phytosterol-enriched foods would not be expected to significantly increase the likelihood of consumption by non-target groups for a number of reasons:

(i) Phytosterol-enriched foods are specialised, niche products, marketed to a limited consumer sector (adults with cholesterol concerns);
(ii) The evidence indicates that current users of phytosterol-enriched margarines choose the product for a health (cholesterol-lowering) benefit;
(iii) Post-market surveys in Europe, where additional phytosterol-enriched products are available, found they are used in moderation by the target group of consumers;
(iv) Lifestyle and dietary advice, including the use of phytosterol-enriched foods, is already available from dietitians, General Practitioners, and public health organisations such as the NHF;
(v) The food industry also provide advice on the suitability of products to consumer groups (via product information lines, promotional material and advertising);
(vi) Mandatory labelling on packaging advises against consumption by children and pregnant or lactating women; and

(vii) FSANZ is committed to preparing additional educational material that will be available for consumers on the website and distributed to health professionals.

5.1.6.1 Conclusion

Occasional consumption of phytosterol-enriched foods by non-target groups would not be a cause for concern. Consumer education strategies combined with appropriate risk management measures and consumer-specific marketing should ensure that the public has sufficient knowledge about phytosterol-enriched products to be able to make well-informed decisions on foods that are appropriate to their health needs.

5.1.7 Reduced beta carotene levels in individuals with a low fruit and vegetable intake.

A lower beta-carotene level would be of greater nutritional concern if consumption of phytosterols affected retinol (vitamin A) levels. However, a reduction in retinol has never been reported in studies on phytosterols, even with consumption up to 10 g per day.

People who have a high fruit and vegetable intake could have low serum beta-carotene if the fruit and vegetables they choose are apples, bananas, pears, nashi pears, cucumber, potatoes, inside leaves of iceberg lettuce, eggplant, corn, blueberries, dark grapes, strawberries or parsnip. Some of these foods have quite high levels of anthocyanins and other plant nutrients that are also antioxidants. Conversely, a low fruit and vegetable diet consisting of one carrot per day could result in a moderately high beta-carotene level.

5.1.7.1 Conclusion

Fruits and vegetables in the diet contribute a complexity of vitamins and other nutrients. Public health educators continue to promote the daily consumption of minimum quantities of fruits and vegetables as part of a healthy diet. Consumption of plant sterols is generally expected to lead to a reduction in LDL-cholesterol levels in the range of 5%-15%, a reduction which the National Health and Medical Research Council (NHMRC) equates to a significant reduction in cardiovascular disease risk. In this context, a moderate reduction in serum beta-carotene is not a health concern.

5.2 Labelling and consumer information

5.2.1 Advisory versus warning statements

FSANZ's labelling risk management framework for decision-making was developed during the review of the former Australian *Food Standards Code* and is outlined below:

High risk
Where the risk to public safety is potentially life threatening and it can reasonably be assumed that the general population or the specific target group is unaware of the potential safety risk, a prescribed labelling statement is needed to alert consumers of the risk. Warning Statements are required where the risk to public health and safety is high and awareness of the potential risk is low.

Medium risk
Advisory statements are provided where the general population or a sub group of the population are largely unaware of a potential, but non life threatening risk to public health and safety and need advice about that risk.

Low risk
Where a risk to public health and safety is determined to be low because the likelihood of an adverse event occurring is rare and the consequences minor, it should be sufficient to rely on general labelling provisions and existing food law to manage the risk. An education initiative could be used to raise awareness of and promote the use of general labelling information (FSANZ, 2002).

FSANZ has assessed the potential risk to public health and safety as low with respect to the consumption of phytosterol enriched products by non-target groups, and therefore a warning statement would be inappropriate.

Labelling is only one means of providing advice to consumers, recognising that its effectiveness as a source of information varies with the consumer and the nature of the food product. Despite these variables, advisory statements on phytosterol-enriched products provide the appropriate *level* of risk management advice in relation to the low risk to public health and safety posed by these foods.

5.2.1.1 Conclusion

A warning statement on phytosterol-enriched foods would be inconsistent with the existing framework and is not justified on public health and safety grounds.

5.2.2 Revision of advisory statements

Currently, the labelling of phytosterol-enriched table spreads must include three advisory statements. A fourth statement was proposed with the approval of these Applications. However, the Second Review triggered a re-evaluation of the purpose and effectiveness of the advisory statements as risk management tools. As a result of the review, FSANZ now proposes three new mandatory advisory statements for all phytosterol-enriched foods including the table spreads.

(i) Fruit and vegetable consumption

One of the current advisory statements required on phytosterol-enriched spreads requires words to the effect that *the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables*.

The Expert Advisory Group considered the effectiveness of this statement in correcting for the small reduction in beta-carotene observed with consumption of phytosterol-enriched foods. Given that there is no specific reference to *carotenoid* rich varieties, the wording of the statement could mislead consumers on the potential benefits of any additional fruits and vegetables when consuming plant sterols. Moreover, as *carotenoid* is not in common use as a term to describe particular nutrients, additional words to this effect would be likely to lead to some degree of consumer confusion.

FSANZ also considered that adding a list of carotenoid-rich fruits and vegetables to the labelling requirements would not meaningfully assist consumers to raise blood levels of beta-carotene because of a number of variables including seasonal variations, cooking and bioavailability. In addition, while a diet low in saturated fat is regarded as a healthy alternative, phytosterols have been studied in both a normal and low-fat background diet and are similarly effective in lowering cholesterol absorption.

Given the complexity of the additional message concerning consumption of carotenoid-rich fruit and vegetables necessary with phytosterol-enriched foods, FSANZ considers that consumer education on this issue could be undertaken more effectively through other types of educational approaches. FSANZ notes that a healthy diet message encouraging the consumption of fruits and vegetables is currently part of wider public health initiatives to lower the incidence of obesity and certain diseases in the population. In addition, organisations such as the NHF produce material for use by health professionals such as General Practitioners, cardiologists, clinical dietitians and nutritionists. FSANZ can also contribute to the education process by producing a fact sheet for the website and for public distribution, and provide links to information available on other websites.

To strengthen the capability of a consumer education initiative, FSANZ and the NHF have recently agreed to collaborate on the preparation of material providing information on (i) plant sterols in general, and (ii) the potential role of phytosterol-enriched foods in the diet for the purpose of lowering LDL-cholesterol levels, for both health professionals and the general public. As well as publications, the NHF supplements its educational role with other activities that directly link the distribution of information to its target audiences.

Providing information on phytosterol-enriched foods in addition to that provided on food labels should ensure that more consumers are able to access sufficient factual information to enable informed choice in the management of their diet.

5.2.2.1 Conclusion

While it is broadly consistent with public health messages, on the basis of more recent scientific evidence, the current statement on fruits and vegetables is superfluous and potentially misleading for consumers of phytosterol-enriched foods. A revised mandatory statement to the effect that ***when consuming plant sterol enriched foods, these should be consumed as part of a varied and healthy diet*** is considered to be more appropriate in the context of general dietary advice.

(ii) Non-target consumer groups

One of the current advisory statements required on phytosterol-enriched spreads requires words to the effect that *the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision.*

The Expert Advisory Group noted that while studies in pregnant women were not available, the effects of phytosterols in children with familial hypercholesterolaemia were well studied. While consumption by children with hypercholesterolaemia was without adverse physiological effects, it was generally agreed that children do not derive a benefit to the same extent as adults from a reduction in their cholesterol levels.

For this reason, it was therefore considered appropriate to compare the use of advisory statements currently required on packaging of foods such as low-fat milk and beverages made from soy or rice for the purpose of informing consumers that these foods are unsuitable for children under the age of two years.

5.2.2.2 Conclusion

On the basis of available safety data, a revised mandatory statement to the effect that ***the product may not be suitable for children under the age of five years, and pregnant or lactating women*** is proposed for all phytosterol-enriched foods.

(iii) Efficacy of plant sterols

The Ministerial Council noted that the nature of the food vehicle appears to be a factor in the overall cholesterol-lowering effect of plant sterols. Milks are particularly effective (up to 15% reduction), while some studies show that yoghurts and breakfast cereal generally lead to reductions of 5%-8%. The Expert Group agreed that many other factors could also affect efficacy and there would be no advantage for consumers by making this information a mandatory labelling requirement for phytosterol-enriched foods.

There are insufficient data to show that different food matrices consistently produce a similar degree of efficacy. For example, the data for yoghurt vary considerably, with the literature reporting differing results (some papers show 5% reduction, while others report a 10% reduction), even when the same amounts of plant sterols are used. Other studies show phytosterols are effective in orange juice while some show no significant cholesterol-lowering effect. Phytosterols are generally more effective in a meal that contains fat. In addition, small variations in efficacy can arise due to the way in which the plant sterols are incorporated into the product (there are 5 patented processes), and even with batch-to-batch variation. This situation is not unique to phytosterol-enriched products and applies to any other nutrient or food component, where the benefits that are transferred to an individual may vary due to a combination of factors.

In general, the data do not support providing consumers with information to this level of detail for the following reasons:

- some variability between studies means that an unqualified statement could be misleading;
- this type of information is not provided for other foods (or drugs);
- there are variations between individuals due to metabolic profiles and lifestyle factors; and
- the NHF dietary advice is simply to eat a variety of (recommended) foods.

Rather than focus consumer attention on the food matrix, the Expert Advisory Group concluded that information on the minimum amount of plant sterols required to achieve a cholesterol-lowering effect would be more useful to consumers for allowing them to make informed choices. Based on a large number of published studies, the optimal cholesterol lowering benefits are achieved when consumption of plant sterols is around 2-3 g per day. Furthermore, there is no significant improvement in cholesterol reduction above approximately 3 g per day, and therefore higher levels of consumption are unnecessary.

In previous assessments, FSANZ used number of serves as a means to communicate to consumers on appropriate consumption levels. However, FSANZ acknowledges that determining the food serving sizes could be an issue for some consumers. There are no international standards for typical food portion sizes that are useful, on an allocation basis, for a strategy for phytosterol enrichment. To some extent, the Applicants are using self-appointed portion sizes which may not correlate closely with consumer behaviour.

Revised drafting is therefore proposed which provides for **a minimum of 0.8 g and a maximum of 1.0 g per quantity (average serving size) of food**. The minimum level ensures that intake of phytosterol-enriched foods (of any type) is more likely to reach the optimal amounts for a cholesterol-lowering effect. On the other hand, the maximum level should assist consumers to avoid higher intakes that provide no additional cholesterol-lowering benefits. This range is also in good compliance with the safety recommendations on the entire intake of phytosterols from multiple sources (see additional dietary exposure estimates at **Attachment 4**).

A mandatory labelling statement to the effect that ***plant sterols do not provide additional benefits when consumed in excess of 3 grams per day*** is also proposed. Expressing amounts in grams of plant sterols rather than serves of food should make individual monitoring of consumption easier on a daily basis.

5.2.2.3 Conclusion

Changes to the drafted permissions for plant sterols in low-fat milk, yoghurt and breakfast cereal should ensure that consumers have sufficient labelling information to allow them to use the products cost-effectively.

5.2.3 Labelling statements on efficacy of plant sterols

A health claim was not part of the assessment of these Applications. Nevertheless, it is pertinent to note that, as part of Proposal P293 – Nutrition, Health and Related Claims, FSANZ is proposing that specific conditions must be met before a general level health claim can be made in relation to biologically active substances (including phytosterols). Currently, these conditions are:

- only ‘contains’/‘source’ type descriptors are permitted;
- manufacturers will be required to substantiate the daily amount of the substance that will achieve the specific health effect;
- a serve of the food must contain at least 10% of the amount that must be consumed per day to achieve the specific health effect; and
- the claim must state the amount of the substance that is required to be consumed per day to achieve the health effect, in the context of a healthy diet including a variety of foods.

This Proposal is at Draft Assessment and subject to change.

5.2.3.1 Conclusion

Current labelling statements on table spreads are not regarded as health claims.

Any future application under a standard for nutrition, health and related claims would be required to meet the defined criteria and conditions for making a claim. Any high level claim will require pre-approval from FSANZ (see section 5.4.1 below).

5.2.4 Presentation and legibility of mandatory advisory statements

The size and legibility requirements of advisory statements on packaging are not explicitly defined in the Code. FSANZ acknowledges that the legibility of labelling statements can vary with products and is therefore open to interpretation. An Editorial Note to Standard 1.2.9 Legibility Requirements which clarifies for manufacturers what is expected in terms of placement and legibility of prescribed information is not legally binding.

FSANZ has previously agreed to review Standard 1.2.9 and a new Proposal is currently at the scoping stage. The purpose of the review will be to evaluate the effectiveness of the Standard for general labelling information requirements. However, the insertion of an Editorial Note is seen as an appropriate interim measure until the review of Standard 1.2.9 is completed.

FSANZ has noted that industry is conscious of this issue and has made efforts to improve the presentation and legibility of labelling information on existing phytosterol-enriched products. For example, mandatory advisory statements are no longer being presented on a removable outer cardboard sleeve, thereby improving consumer access to the information.

5.2.4.1 Conclusion

An Editorial Note is regarded as a practical, short term measure to reinforce the principles underpinning the Standard, pending a more comprehensive review.

5.3 Consumer knowledge and behaviour

FSANZ has previously claimed that consumers have some knowledge of phytosterol-enriched foods through the market availability of two brands of table spreads since 2001. From advertising and other marketing strategies as well as information on various websites, health professionals are also aware of the products, although it is unclear to what extent their awareness is translated to consumers.

A number of key consumer issues were raised in the Second Review request. These include:

- ***Target audience:*** including the possibility that those outside the target group of consumers will be primary consumers, such as children or pregnant or lactating women;

- ***Consumption levels:*** including frequency and quantity of enriched product and the potential for consumption in excess of recommended amounts;

- ***Understanding and comprehension:*** including the interpretation of serving sizes and label information; and

- ***Dietary and lifestyle behaviours:*** including possible changes to diet and exercise, such as an increased consumption of cholesterol/saturated fats or a reduction in the level of exercise.

There is a lack of data concerning the responses of consumers to plant sterol-enriched products in Australia and New Zealand. However there are a number of international studies that show consistent results with respect to key issues of concern. FSANZ is confident that conclusions can be drawn about how Australian and New Zealand consumers are likely to react to these products. In addition to the existing literature FSANZ commissioned a survey of Australian and New Zealand consumers of plant sterol-enriched spreads.

This section provides a summary of the findings relevant to the four key issues identified above. A detailed discussion of the findings is at **Attachment 3**.

5.3.1 Target audience

5.3.1.1 Plant sterol enriched products appear to occupy a small niche market.

Plant sterol enriched products are likely to be a niche product in Australia and New Zealand appealing to a small, but highly differentiable market segment. Existing Australian market data confirm that plant sterol enriched spreads are a small proportion of the overall spread market accounting for 3.7% by volume of the total Australian spread market (data supplied by industry).

5.3.1.2 Most users of plant sterol enriched products are older adults.

There are no Australian data that provide a measure of the number of individuals who use plant sterol enriched spreads. International studies carried out in the European Union and United States confirm that plant sterol enriched spreads are used by a minority of adults, less than 5% (Anttolainen *et al.* 2001; Simojoki *et al.* 2005; 2004 Gallop Study of Cholesterol Lowering Options provided by Goodman Fielder). Those who used the products were older, with 75 to 95% of purchasers being over 45 years old (SCF 2002).

5.3.1.3 Most purchasers of plant sterol enriched products do not have children in the household.

Plant sterol enriched products are generally recommended for use by adults and the potential that children may incidentally consume these products was raised in the second review. European research found that 79%-91% of households that had purchased plant sterol enriched spreads had no children (SCF 2002).

5.3.1.4 Purchasers are motivated by concern about their health, particularly cholesterol.

The FSANZ survey found health related concerns were the primary motivation for the largest group of enriched spread users followed by convenience. Of these the majority highlighted cholesterol as the major issue. Seven percent of enriched spread users reported their primary motivation for using enriched spread as ‘someone else in my household prefers it so I use it too’.

From a large nation-wide study in Finland on the use of plant stanol enriched spread the researchers concluded:

Users of plant stanol ester margarines are a self-selected group of persons who have taken an active interest in their health. They use plant stanol ester margarines as part of a generally healthy life-style and diet. Nevertheless, they commonly have a history of cardiovascular disease or are at risk to have it. Thus plant stanol ester margarine seems to be used by persons for whom it was designed and in a way it was meant: as part of efforts for cardiovascular disease risk reduction (Simojoki et al. 2005).

5.3.2 Consumption levels

5.3.2.1 <u>There is no evidence that consumers of plant sterol enriched products consume too much – the reverse appears to be true.</u>

The FSANZ survey found that adults who used plant sterol enriched spreads used them differently to those who did not use sterol enriched spreads. They tended to use less spread on bread and toast. This is consistent with a health based motivation that may be linked to reduction in fat intake more generally. Based on reported levels and frequency of plant sterol enriched spread use, it is likely that a proportion of consumers will not receive enough plant sterols through their current consumption of enriched spreads on bread and toast.

These results indicate current intakes of plant sterols from enriched spreads are below the optimal intake recommended for cholesterol reduction. As this could be due to the nature of the food vehicle itself, the availability of additional plant sterol-enriched products will increase the range of choice for consumers. Several post-market monitoring reports from European countries indicate however that increased product availability is not linked to excess consumption of plant sterols. Recent data collected in the UK across the major phytosterol-enriched products provide additional evidence that products are more likely to be under-consumed (ACNFP 2006; Bradford 2006, unpublished data).

5.3.3 Understanding and comprehension

5.3.1.1 <u>Consumers have mixed understandings of the role of these products and labelling information.</u>

Concerns about consumers' understanding of target audience, purpose and recommended serving size have been raised. The FSANZ survey suggested that consumers were mixed in their levels of understanding and comprehension with respect to these issues. They indicate some areas of limited understanding, particularly with regards to the suitability of plant sterol enriched products for children and consumers considered they had insufficient serve size information.

5.3.4 Dietary and lifestyle behaviours

A key concern raised in the second review request is the extent to which the consumption of plant sterol enriched products will lead to changes in dietary or lifestyle behaviours that are contrary to the National Dietary Guidelines or recommended exercise regimens. The contention is that consumers of plant sterol enriched products may gain a benefit from consumption of these products and consequently be less concerned about their health and accordingly be less inclined to adopt appropriate diet and lifestyle behaviours. For example consumers may eat more saturated fats as they believe their consumption of plant sterol enriched products will counteract their indulgence.

As there was no evidence to support or refute this contention the FSANZ survey specifically sought to collect data in order to better understand the motivations and likely behaviours of people in response to plant sterol enriched foods.

5.3.4.1 Consumers do not see plant sterol enriched spreads as a 'silver bullet' that will absolve them of further responsibility for health conscious behaviour.

The FSANZ survey found no significant differences between users and non-users of plant sterol enriched spreads in the level of exercise they carried out. In terms of diet there was a demographic distinction with younger users of enriched spreads having a 'better diet' than those who didn't use enriched spreads. There was no significant differences in diet between enriched-spread users and non-users in consumers of age 35 years and older. There was a minority of enriched spread users who reported that their diet and exercise had improved since using plant sterol enriched spreads. Overall, consumption of plant sterol enriched spread was not linked to either better or worse diet and exercise measures, although a minority of consumers considered they had improved diet and exercise levels.

The diet and the exercise findings highlight that those who consume plant sterol enriched spreads do not have significantly worse diets and exercise levels than those who do not use plant sterol spreads. This evidence does not support the contention that use of plant sterol enriched spreads are associated with less healthy diet and lifestyle choices. While the evidence does not suggest that those who consume plant sterol enriched spreads make healthier diet and lifestyle choices than those who do not consume these spreads, self-assessments of enriched spread users suggest there have been some improvements in diet and exercise for some individuals.

5.4 Policy considerations

FSANZ has previously stated that there are no provisions in the FSANZ Act for deferral of the assessment of an application on the grounds that it intersects with policy issues under consideration by FRSC, or pending finalisation of a new standard. Assessment of the current Applications has therefore progressed under the existing policy for Novel Foods, which calls for a pre-market safety assessment.

5.4.1 Health claims

Approval of these Applications to add phytosterols to breakfast cereal, low-fat milk and yoghurt **does not** constitute approval for a health claim in relation to these products. Assessment of a health claim would require examining data and information on phytosterols from a different perspective. Any future requests by manufacturers for assessment of a health claim would need to be submitted under the health claims standard, which is yet to be completed.

Proposal P293 Nutrition, Health and Related Claims is currently at the Preliminary Final Assessment stage but is not expected to be finalised until 2007. Claims which reference a biomarker or serious disease will be regulated as a high level claim and will be required to undergo pre-approval by FSANZ. However, general level claims which do not reference a serious disease or condition will be generally permitted provided they can be substantiated and provided they comply with any criteria or conditions specified in the Standard.

As serum cholesterol is proposed as a biomarker for serious disease, under the proposed regime, any claim that references serum cholesterol would be regulated as a high level claim. However, a claim that references dietary cholesterol, which is not a biomarker for a serious disease, would be regulated as a general level claim.

Until the new Standard is finalised, manufacturers must comply with the current requirements in the Transitional Standard for Health Claims, Standard 1.1A.2 in the Code. This Standard sets out the following restrictions on the use of health claims in food labels or in advertising:

- The label on or attached to a package containing, or an advertisement for, food shall not contain a claim or statement that the food is a slimming food nor has intrinsic weight reducing properties.

- Any label on or attached to a package containing, or any advertisement for, food shall not include a claim for therapeutic or prophylactic action or a claim described by words of similar import.

- Any label on or attached to a package containing or an advertisement for a food shall not include the word 'health' or any word or words of similar import as a part of or in conjunction with the name of the food.

- Any label on or attached to a package containing or any advertisement for food shall not contain any word, statement, claim, express or implied, or design that directly or by implication could be interpreted as advice of a medical nature from any person.

- The label on or attached to a package containing or any advertisement for food shall not contain the name of or a reference to any disease or physiological condition.

A failure to comply with these requirements when making any voluntary statement about a food constitutes a breach of the Code.

5.4.2 Other policy issues

The Policy Guideline on the Addition to Food of Substances other than Vitamins and Minerals is currently being developed by the FRSC. The scope of the policy is yet to be agreed but the initial scope included all substances that can potentially be added to food for a technological purpose, with the exception of vitamins and minerals. Therefore, foods or food ingredients such as phytosterols that have already been considered by FSANZ as novel foods may be included. There is a clear interface of this process with a review of the Novel Foods Standard.

Nevertheless, there is currently a clear mechanism for dealing with novel food applications under Standard 1.5.1 – Novel Foods. FSANZ considers that progression of Applications A433, A434 and A508 is consistent with the <u>existing</u> policy for novel foods and the transitional health claims standard and should not depend on the outcome of any review process that is not yet completed.

5.5 Nutrient criteria

Given that plant sterols lower LDL-cholesterol levels, it is appropriate that they be permitted in foods that are consistent with a healthy diet. Similarly, the products should not promote consumption patterns that are inconsistent with dietary advice to reduce cholesterol.
The nutrient criteria proposed for breakfast cereal was based on an existing range of products targeted specifically to adult consumers.

The primary purpose of imposing specific nutrient criteria on the phytosterol-enriched breakfast cereals[25] was to focus on those properties of the food that are considered to have a greater impact on the target consumer group, and at the same time be less attractive to children. The fibre and maximum sugar requirements proposed were modelled on a muesli-style product containing added fruit that was considered to be more compatible with adult preferences. On the basis of evidence gathered at that time, these requirements could not be met by breakfast cereal products that are typically marketed to children.

A small survey of the available range of breakfast cereals conducted by FSANZ showed a clear demarcation between 'high sugar' breakfast cereals and those of a more moderate type when assessed on the basis of the content of *added sugar*. Those breakfast cereals that have a total sugars content above 30g/100g use added sugar only (i.e. primarily sucrose) to achieve this level. For cereals with a range between 10-30g/100g of total sugars, the main contributor to total sugars is through the addition of fruit (as found in muesli style cereals), not refined sugar. As such, breakfast cereals typically contain either 0-10g/100g or 30+ g/100g of added sugars.

Sugar content across the range of breakfast cereals

Breakfast cereal category	Total sugars content (g/100 g)	Estimated added sugar content (% total sugar content)
Low/moderate in added sugar	1.5-11	0-11
Muesli style or those with added fruit	15-30	0-10
High in added sugar	31-53	31-53

Thus, the selected criteria were not specifically intended to classify a breakfast cereal into a 'healthy' category in terms of general nutrition advice. Moreover, regulating the use of phytosterols according to dietary ideals for sugar, fat and salt intake would introduce an inappropriate level of control that could not be justified on the basis of the safety evidence and the proposed levels of use.

8. Review Options

Three options were considered in this Review:

1. re-affirm the draft variations to Standard 1.2.3 – Mandatory Warning and Advisory Statements and Declarations, Standard 1.2.9 – Legibility Requirements, Standard 1.3.1 – Food Additives, Standard 1.3.4 – Identity and Purity, Standard 1.5.1 – Novel Foods, Standard 2.5.1 – Milk, and Standard 2.5.3 – Fermented Milk Products of the Code approved at Final Assessment and First Review; or

[25] Application A433 only

2. re-affirm approval of the draft variations to the Code as listed above, subject to specified amendments as a result of the Second Review; or

3. withdraw approval of the previous draft variations to the Code as listed above.

Summary of specified amendments under Option 2:

1. A minimum of 0.8 g and a maximum of 1.0 g phytosterols per serve (one serve taken to be 250 ml low-fat milk, one punnet of yoghurt up to 200 g, 45 g cereal);

2. Three mandatory advisory statements:

(i) when consuming this product, it should be consumed as part of a healthy diet;
(ii) this product may not be suitable for children under the age of five years, and pregnant or lactating women; and
(iii) plant sterols do not provide additional benefits when consumed in excess of 3 grams per day.

3. Deleted the following advisory statement: consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication.

4. Existing specifications for the tall oil phytosterols replaced with new specifications relating to the purity of the sterol components and reduced levels of heavy metals.

5. Additional wording in the Editorial note inserted at First Review to Standard 1.2.9 – Legibility Requirements, to read (in part):

The requirements of this standard will not be met where prescribed information is placed other than on the outside of a package where it is readily accessible by a consumer prior to purchase, <u>and during the life of the product</u>, and not obscured by an outer covering.

9. Conclusion and recommendation

The Second Review concludes that the preferred review option is Option 2. This re-affirms the approval for the addition of phytosterol esters in breakfast cereal, low-fat milk and low-fat yoghurt and tall oil phytosterols in low-fat milk according to the draft variation to Standards 1.2.3, 1.2.9, 1.3.1, 1.3.4, 1.5.1, 2.5.1 and 2.5.3 of the Code, as detailed in **<u>Attachment 1</u>**.

ATTACHMENTS

6. Draft variations to the *Australia New Zealand Food Standards Code*.
7. Approvals of phytosterol-enriched food products in Europe.
8. Social research on use of phytosterol-enriched spreads in New Zealand and Australia.
9. Report on additional dietary exposure estimates.
10. References

ATTACHMENT 1

Draft Variations to the *Australia New Zealand Food Standards Code*

APPLICATION A433

To commence: On gazettal

[1] ***Standard 1.2.3*** *of the Australia New Zealand Food Standards Code is varied by omitting from the* Table to clause 2 –

Food regulated in Standard 2.4.2 containing phytosterol esters	Statements to the effect that – 1. the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables; 2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and 3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication.

substituting –

Foods containing added phytosterol esters	Statements to the effect that - 1. when consuming this product, it should be consumed as part of a healthy diet; 2. this product may not be suitable for children under the age of five years and pregnant or lactating women; and 3. plant sterols do not provide additional benefits when consumed in excess of three grams per day.

[2] ***Standard 1.2.9*** *of the Australia New Zealand Food Standards Code is varied by inserting after subclause 2(1) –*

Editorial note:
The requirements of this Standard will not be met where prescribed information is placed other than on the outside of a package where it is readily accessible by a consumer prior to purchase, and during the life of the product, and not obscured by an outer covering. The requirements of this Standard will also not be met where prescribed information is printed in a small font so the statement cannot be read easily.

Within 24 months of the gazettal of this editorial note, Standard 1.2.9 Legibility Requirements will be reviewed.

[3] ***Standard 1.5.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[3.1] *omitting from the* Table to clause 2 –

Phytosterol esters	The requirements in clause 2 of Standard 1.2.3. The name 'phytosterol esters' or 'plant sterol esters' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to food – (1) according to Standards 1.3.4 and 2.4.2; and (2) where the total saturated and trans fatty acids present in the food is no more than 28% of the total fatty acid content of the food.

substituting –

Phytosterol esters	The requirements in clause 2 of Standard 1.2.3. The name 'phytosterol esters' or 'plant sterol esters' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to edible oil spreads – (1) according to Standard 2.4.2; and (2) where the total saturated and trans fatty acids present in the food are no more than 28% of the total fatty acid content of the food. May only be added to breakfast cereals, not including breakfast cereal bars, if – (1) the total fibre content of the breakfast cereal is no less than 3 g/50 g serve; (2) the breakfast cereal contains no more than 30g/100g of total sugars; and (3) the total phytosterol ester added is no less than 26g/kg and no more than 32g/kg. Foods to which phytosterol esters have been added may not be used as ingredients in other foods.

[3.2] *omitting* from the Editorial note *after the* Table to clause 2 –

The Table to Clause 2 contains conditions relating to novel foods. Nothing contained in this Code permits the mixing of phytosterol esters and tall oil phytosterols.
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APPLICATION A434

To commence: On gazettal

[1] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in* Schedule 1*, after* item 1.1.2 –

1.1.3 Liquid milk to which phytosterol esters have been added

401	Sodium alginate	2	g/kg
407	Carrageenan	2	g/kg
412	Guar gum	2	g/kg
471	Mono- and diglycerides of fatty acids	2	g/kg

[2] ***Standard 1.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in* Column 2 *of the* Table to clause 2 *corresponding to the entry for Phytosterol esters –*

May only be added to milk in accordance with Standard 2.5.1. May only be added to yoghurt in accordance with Standard 2.5.3.

[3] ***Standard 2.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting after the* Editorial note *to clause 4 –*

5 Phytosterol Esters

Phytosterol esters may only be added to milk –

(a) such that the milk contains no more than 1.5 g total fat per 100 g; and
(b) that is supplied in a package, the labelled volume of which is no more than 1 litre; and
(c) where the total phytosterol ester added is no less than 5.2 g/litre of milk and no more than 6.4g/litre of milk.

[4] ***Standard 2.5.3*** *of the Australia New Zealand Food Standards Code is varied by inserting after the* Editorial note *to clause 3 –*

4 Phytosterol Esters

Phytosterol esters may only be added to yoghurt –

(a) such that the yoghurt contains no more than 1.5 g total fat per 100 g; and
(b) that is supplied in a package, the capacity of which is no more than 200 g; and
(c) where the total phytosterol ester added is no less than 1.3 g and no more than 1.6g.

APPLICATION A508

To commence: On gazettal

[1] ***Standard 1.2.3*** *of the Australia New Zealand Food Standards Code is varied by omitting from the* Table to clause 2 –

Food regulated in Standard 2.4.2 containing tall oil phytosterols	Statements to the effect that – 1. the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables; 2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and 3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication.

substituting –

Foods containing added tall oil phytosterols	Statements to the effect that - 1. when consuming this product, it should be consumed as part of a healthy diet; 2. this product may not be suitable for children under 5 years and pregnant or lactating women; and 3. plant sterols do not provide additional benefits when consumed in excess of three grams per day.

[2] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by inserting in* Schedule 1 *after* item 1.1.2 –

1.1.4 Liquid milk to which tall oil phytosterols have been added

460	Microcrystalline cellulose	5	g/kg

[3] ***Standard 1.5.1*** *of the Australia New Zealand Food Standards Code is varied by omitting from the* Table to clause 2 –

Tall oil phytosterols	The requirements in clause 2 of Standard 1.2.3. The name 'tall oil phytosterols' or 'plant sterols' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to food - (1) according to Standards 1.3.4 and 2.4.2; and (2) where the total saturated and trans fatty acids present in the food is no more than 28% of the total fatty acid content of the food.

substituting –

Tall oil phytosterols	The requirements in clause 2 of Standard 1.2.3. The name 'tall oil phytosterols' or 'plant sterols' must be used when declaring the ingredient in the ingredient list, as prescribed in Standard 1.2.4. May only be added to edible oil spreads – (1) according to Standard 2.4.2; and (2) where the total saturated and trans fatty acids present in the food is no more than 28% of the total fatty acid content of the food. May only be added to milk in accordance with Standard 2.5.1. Foods to which tall oil phytosterols have been added may not be used as ingredients in other foods.

[4] ***Standard 2.5.1*** *of the Australia New Zealand Food Standards Code is varied by inserting after the* Editorial note *to clause 4 –*

6 Tall oil phytosterols

Tall oil phytosterols may only be added to milk –

(a) such that the milk contains no more than 1.5 g total fat per 100 g; and
(b) that is supplied in a package, the labelled volume of which is no more than 1 litre; and
(c) where the total tall oil phytosterol added is no less than 3.2 g/litre of milk and no more than 4.0 g/litre of milk.

[5] ***Standard 1.3.4*** *of the Australia New Zealand Food Standards Code is varied by omitting from the* Schedule *–*

Specification for tall oil phytosterols derived from tall oils

Tall oil phytosterols (non-esterified) are derived from tall oil soap, a by-product of the pulping process and then purified.

Total Phytosterol/phytostanol content (%)	min. 95
Loss on drying (water (%))	max. 5.0
Solvents (%)	max. 0.5
Residue on ignition (%)	max. 0.1
Total Heavy metals (ppm)	max. 10
Cadmium (ppm)	max. 1.0
Mercury (ppm)	max. 1.0
Arsenic (ppm)	max. 2.0
Lead (ppm)	max. 0.25
Total aerobic count (CFU/g)	max. 10,000

Combined moulds and yeasts (CFU/g)	max. 100
Coliforms	Negative to test
E. coli	Negative to test
Salmonella	Negative to test

Major Sterol profile (%) as below –

Campesterol	min. 4.0	max. 25.0
Campestanol	min. 0.0	max. 14.0
β-Sitosterol	min. 36.0	max. 79.0
β-Sitostanol	min. 6.0	max. 34

substituting –

Specification for tall oil phytosterols derived from tall oils

Tall oil phytosterols (non-esterified) are derived from tall oil soap, a by-product of the pulping process and then purified.

Total Phytosterol/phytostanol content (%)	min. 97
Loss on drying (water (%))	max. 4.0
Solvents (%)	max. 0.5
Residue on ignition (%)	max. 0.1
Total Heavy metals (ppm)	max. 2
Cadmium (ppm)	max. 0.1
Mercury (ppm)	max. 0.1
Arsenic (ppm)	max. 0.1
Lead (ppm)	max. 0.1
Total aerobic count (CFU/g)	max. 10,000
Combined moulds and yeasts (CFU/g)	max. 100
Coliforms	Negative to test
E. coli	Negative to test
Salmonella	Negative to test

Major Sterol profile (%) as below –

Campesterol	min. 4.0	max. 25.0
Campestanol	min. 0.0	max. 14.0
β-Sitosterol	min. 36.0	max. 79.0
β-Sitostanol	min. 6.0	max. 34

Minor sterols (%)	max. 3.0

ATTACHMENT 2

European Union (EU) Regulation and the marketing of phytosterol/phytostanol containing food products in the EU[26]

In the European Union (comprised of 25 countries[27]) the use of phytosterols in foods is regulated under Regulation (EC) No. 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients.

Novel foods are foods and food ingredients that have not been used for human consumption to a significant degree within the Community before 15 May 1997. Regulation EC No. 258/97 lays out detailed rules for the authorisation of novel foods and novel food ingredients[28].

Before a novel food or food ingredient can be placed on the market, it must go through an applicant specific authorisation procedure. This involves a safety assessment. Decisions about authorisation prior to marketing are made by the European Commission (EC) and experts in the 25 Member States. Additional scientific input is provided, if requested, by the European Food Safety Authority[29].

To date the EC has granted eight applicant specific approvals (see Table 1):

Table 1: EC Approvals

Commission Decision	Applicant	Approved Food Formats
2000/500/EC	Unilever	yellow fat spreads
2004/333/EC	Archer Daniels Midland Company (ADM)	yellow fat spreads, salad dressing, milk type products, fermented milk type products, soya drinks, cheese type products
2004/334/EC	Pharmaconsult Oy Ltd.	yellow fat spreads, milk type products, yoghurt type products, spicy sauces
2004/335/EC	Unilever	milk type products, yoghurt type products
2004/336/EC:	Teriaka Ltd.	yellow fat spreads, milk based fruit drinks, yoghurt type products and cheese type products
2004/845/EC	Novartis (now Forbes Medi-Tech Inc.)	milk based beverages
2006/58/EC	Pharmaconsult Oy Ltd.	rye bread
2006/59/EC	Karl Fazer Ltd.	rye bread

NOTE: Approvals have been granted for phytosterols and phytostanols that are extracted from plants (vegetable and tall oil) and may be presented as free sterols and stanols or esterified with food grade fatty acids.

[26] Author: Tiina Mutru, Regulatory Affairs Manager, Unilever, United Kingdom. Date: June 2006

[27] Austria, Belgium, Czech Republic, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, the Netherlands, UK.

[28] Note that plant stanols are not covered by this Regulation as yellow fat spreads containing stanol esters were launched in Finland prior to 15 May 1997. The European Commission (EC) decided that neither the spread nor the ingredient was covered by Regulation EC No. 258/97.

[29] European Union scientific body charged with providing independent and objective advice on food safety issues associated with the food chain.

The approved food formats, with added phytosterols, can be marketed in any of the 25 European Union countries.

Novel foods or novel food ingredients may follow a simplified procedure, only requiring a notification from the company, when they are considered by a national food assessment body as "substantially equivalent" to existing foods or food ingredients (as regards their composition, nutritional value, metabolism, intended use and the level of undesirable substances contained therein). Table 2 provides a summary of all the notifications that applicant companies (includes ingredient suppliers and food manufacturers) have submitted to the EC for the marketing of phytosterol ingredients that are considered to meet the criteria set out above.

Table 2: Notifications under Article 5 of the Novel Foods Regulation (EC) No. 258/97 specific to phytosterol ingredients[30]

Notifier	Food Format	Date of Notification
Corporacion Alimentaria Peffasanta SA (Spain)	milk type and fermented milk type products	7 June 2004
Teriaka Ltd. (Finland)	milk type products, soya drinks	1 July 2004
Novandie (France)	yoghurt type products	22 July 2004
Cognis (Germany)	milk type products, yoghurt type products, yellow fats spreads	23 July 2004
Danone (France)	yoghurt	29 July 2004
Dairygold (Ireland)	yellow fat spreads	30 August 2004
Lactogal Produtos Alimentares S.A. (Portugal)	milk and yoghurt type products	30 September 2004
Teriaka Lts. (Finland)	fermented milk type products	4 October 2004
Cargill (USA)	yellow fat spreads	24 October
Danone Vitapole (France)	fermented milk type products	23 November 2004
Cognis (Germany)	yellow fat spreads, salad dressings (including mayonnaise), milk type products, spicy sauces, milk based fruit drinks	20 April 2005
Forbes Medi-Tech Inc. (Canada)	yellow fat spreads, salad dressings, fermented milk type products, soya drinks, cheese type products, yoghurt type products spicy sauces, milk based fruit drinks (for plant sterol esters)	22 April 2005
Forbes Medi-Tech Inc (Canada)	yellow fat spreads, salad dressings, fermented milk type products, soya drinks, cheese type products, yoghurt type products spicy sauces, milk based fruit drinks (for Reducol™ sterols)	22 April 2005
Juustoporti Oy (Finland)	yoghurt type products	10 May 2005
Estavayer Lait (Switzerland)	milk type and yoghurt type products	11 May 2005
Forbes Medi-Tech Inc. (Canada)	yellow fat spreads, salad dressings, fermented milk type products, soya drinks, cheese type products, yoghurt type products spicy sauces, milk based fruit drinks (for Phyto-S-Sterols™)	20 May 2005
Novandie (France)	yoghurt type products and other diary products	27 May 2005

[30] Compiled using the following sources: The European Commission (DG Sanco), the UK Food Standards Agency Advisory Committee on Novel Foods and Processes (ACNFP), and the Finnish Food Safety Authority (Evira). Date of last information 8 May, 2006.

Notifier	Food Format	Date of Notification
MIFA AG (Switzerland)	yellow fat spreads	30 May 2005
Distribuigao Alimentar SA (Portugal)	milk based beverages	17 June 2005
Robert Wiseman & Sons Ltd.	milk based beverages	27 June 2005
Kerry Foods (Ireland)	yellow fat spreads	5 July 2005
Homann Feinkost GmbH & Co (Germany)	salad dressings and mayonnaises	5 July 2005
Walter Rau Lebensmittel-werke GmbH & Co	yellow fat spreads	13 July 2005
Fayrefield Foods Ltd.	yellow fat spreads	13 July 2005
Lacteas Garcia Baquero, SA (Spain)	cheese type products	22 July 2005
Granarolo S.p.a. (Italy)	fermented mil (yoghurt) type products	5 August 2005
SkUnemejerier (Sweden)	yoghurt type products	26 August 2005
Nom AG (Austria)	milk type products	2 September 2005
Degussa Food Ingredients GmbH (Germany)	yellow fat spreads, salad dressings; fermented milk type products, soya drinks; cheese type products; yoghurt type products, spicy sauces, milk based fruit drinks,	27 September 2005
Triple Crown AB (Sweden)	yoghurt type products and milk type products	11 November 2005
Westland Kaasspecialiteiten (The Netherlands)	cheese type products	12 January 2006
Prima Pharm (The Netherlands)	yellow fat spreads	16 January 2006
Poligono Industrial Torrehierro (Spain)	yellow fat spreads, yoghurt type products, milk type products	30 January 2006
Glanbia (Ireland)	yoghurt type products	7 February 2006
Dragsbark (Denmark)	yellow fat spreads	23 March 2006
Tucano Vertriebs GmbH & Co. (Germany)	soya drinks	13 March 2006

The following plant sterol/stanol containing food products are currently being marketed in the United Kingdom:

Food Company/Retailer	Product format
Unilever (Flora pro.activ)	· spreads (different variants i.e. low fat, light, olive) · yoghurts · milk · yoghurt drinks (1-a-day)
McNeil Nutritional Ltd. (Benecol)	· spreads (different variants light, olive) · cream cheese · yoghurt (1-a-day & range concept) · yoghurt drinks (1-a-day) · orange juice
Fayrefield Foods	· cheese
Danone (Danacol)	· mini-drinks (1-a-day)

Food Company/Retailer	Product format
Tesco (own range)	· spreads · yoghurts · milk · yoghurt drinks (1-a-day)
Asda (own range)	· yoghurt drinks (1-a-day)

NOTE: Products containing phytosterols/phytostanols should be presented in either single portions containing a maximum 3g of phytosterols/phytostanols (i.e. 1-a-day concept) or three portions containing maximum 1 g (10).

References:

1. Regulation (Ec) No 258/97 Of The European Parliament And Of The Council of 27 January 1997 concerning novel foods and novel food ingredients.

2. European Commission (2000). Commission Decision 2000/500/EC of 24 July 2000 on authorising the placing on the market of “yellow fat spreads with added phytosterol esters” as a novel food or novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Communities, 08.08.2000, L200/59.

3. European Commission (2004). Commission Decision 2004/333/EC of 31 March 2004 authorising the placing on the market of yellow fat spreads, salad dressings, milk type products, fermented milk type products, soya drinks and cheese type products with added phytosterols/phytostanols as novel foods or novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Union, 14.04.2004, L105/40.

4. European Commission (2004). Commission Decision 2004/334/EC of 31 March 2004 authorising the placing on the market of yellow fat spreads, milk type products, yoghurt type products, and spicy sauces with added phytosterols/phytostanols as novel foods or novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Union, 14.04.2004, L105/43.

5. European Commission (2004). Commission Decision 2004/335/EC of 31 March 2004 on authorising the placing on the market of milk type products and yoghurt type products with added phytosterol esters” as a novel food or novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Union, 14.04.2004, L105/46.

6. European Commission (2004). Commission Decision 2004/336/EC of 31 March 2004 authorising the placing on the market of yellow fat spreads, milk based fruit drinks, yoghurt type products and cheese type products with added phytosterols/phytostanols as novel foods or novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Union, 14.04.2004, L105/49.

7. European Commission (2004). Commission Decision 2004/845/EC of 12 November 2004 on authorising the placing on the market of milk based beverages with added phytosterols/phytostanols as novel foods or novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Union, 11.12.2004, L336/14.

8. European Commission (2006). Commission Decision 2006/58/EC of 24 January 2006 authorising the placing on the market of rye bread with added phytosterols/phytostanols as novel foods or novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Union, 3.2.2006, L31/18.

9. European Commission (2006). Commission Decision 2006/59/EC of 24 January 2006 authorising the placing on the market of rye bread with added phytosterols/phytostanols as novel foods or novel food ingredients under Regulation (EC) No 258/97 of the European Parliament and of the Council. Official Journal of the European Union, 3.2.2006, L31/21.

10. Commission Regulation (EC) No. 608/2004 (of 31 March 2004) concerning the labelling of foods and food ingredients with added phytosterols, phytosterol esters, phytostanols and/or phytostanol esters. Official Journal of the European Union, 1.4.2004, L97/44.

ATTACHMENT 3

Consumer aspects of plant sterol enriched foods

FSANZ used a number of international studies to understand how consumers view and use these products, including research we commissioned. The 4 key findings were

- Plant sterol enriched products occupy a niche market of highly differentiated consumers.
- Consumers are an older section of the population and use is motivated by health concerns.
- Under consumption of plant sterol enriched products in the target audience is a greater issue than over consumption.
- Consumers of these products do not view them as 'magic bullets' that will resolve them of further responsibility for healthy behaviour.

A number of key consumer issues were raised in the Second Review request. These include:

- ***Target audience:*** including the possibility that those outside the target group of consumers will be primary consumers, such as children or pregnant or lactating women;
- ***Consumption levels:*** including frequency and quantity of enriched product and the potential for consumption in excess of recommended amounts;
- ***Understanding and comprehension:*** including the interpretation of serving sizes and label information; and
- ***Dietary and lifestyle behaviours:*** including possible changes to diet and exercise, such as an increased consumption of cholesterol/saturated fats or a reduction in the level of exercise.

There is a lack of data concerning the responses of consumers to plant sterol enriched products in Australian and New Zealand. However there are a number of international studies that show consistent results with respect to key issues of concern. FSANZ is confident that some conclusions can be drawn about how Australian and New Zealand consumers are likely to react to these products.

In addition to drawing on relevant consumer research and published scientific literature FSANZ requested the applicants to provide any additional data. Some of these data were provided on a commercial in confidence basis. An important source of data on plant sterol consumption levels and demographics of consumers was a post launch monitoring study of plant sterol enriched spreads in the European Union (SCF 2002).

FSANZ commissioned a survey of adult Australian and New Zealand consumers to provide additional data. Noting that the only allowable plant sterol products currently available for purchase in Australia and New Zealand are spreads, a random sample of users of this group of products were used as a proxy for the potential users of a broadened range of plant sterol enriched products. A random sample of users of non-plant sterol enriched spreads was used as a control group to test for differences between the two groups of spread users. The survey collected data using an on-line panel of adult consumers administered by TNS Social Research. The on-line approach used to collect data is likely to deliver a sample younger than the general population.

Target Audience

Plant sterol enriched products appear to occupy a small niche market.

Plant sterol enriched products are likely to be a niche product in Australia and New Zealand appealing to a small, but highly differentiable market segment. Existing Australian market data confirms that plant sterol enriched spreads are a small proportion of the overall spread market. In the 12 months to late September 2005, enriched spreads accounted for 3.7% by volume of the total Australian spread market (data supplied by Goodman Fielder). This is higher than equivalent market shares in the European Union at 1-1.5% and the United States at approximately 0.5% (data supplied by Goodman Fielder).

Most users of plant sterol enriched products are older adults.

There are no Australian data that provide a measure of the number of individuals who use plant sterol enriched spreads. Such data would require a very large random survey of the population to achieve a satisfactory sample of users given their low prevalence[31]. However international studies carried out in the European Union confirm that plant sterol enriched spreads are used by a minority of adults. Finnish studies found 4.5% to 4.7% of adults older than 35 used enriched spreads (Anttolainen *et al.* 2001; Simojoki *et al.* 2005). The Finnish studies excluded individuals under 35 as they were very uncommon users of enriched spreads (less than 0.07% of 24-35 year olds used plant sterol enriched spreads (Anttolainen *et al.* 2001)). In the United States approximately 2% of the general population consume plant sterol enriched foods or beverages (2004 Gallop Study of Cholesterol Lowering Options provided by Goodman Fielder).

Consumer research has consistently found a range of psycho-social and demographic variables influence health-related attitudes and behaviours to food (e.g. Childs and Poryzees 1998; Worsley and Scott 2000; Cox and Anderson 2004; Ikeda 2005). Accordingly the use of plant sterol enriched products is not uniform across socio-demographic groups. International research has generally found that the proportion of enriched product users increases with increasing age. In Finnish research using 1997-1998 data sets the mean age of enriched spread users was 59 years (Anttolainen *et al.* 2001). More recent research puts the highest incidence of Finnish enriched spread use at 9% for those aged 65-74. At the next decadal cohort older (75-84), and younger (55-64), 6% of each used enriched spreads (Simojoki *et al.* 2005). In Europe between 75 and 95% of purchasers were over 45 years of age (SCF 2002).

[31] At 3.7% market share a sample of at least 8,000 consumers would be required to deliver a sample of at least 300 enriched spread users.

The FSANZ survey found 50% of users were over 35 years. There was no significant difference in the age of users of enriched spreads and those who do not use enriched spreads. The age of users in this survey however may be an underestimate as the on-line methodology would be likely to generate a positive bias for younger respondents. The Finnish studies were carried out using mail-out methods and the data from the EU were collected using in-household techniques which are likely to reduce any age bias due to methodology.

Most purchasers of plant sterol enriched products do not have children in the household.

Plant sterol enriched products are primarily targeted to adults. The potential that children may incidentally consume these products was raised in the second review request. European research found that 79%-91% of households that had purchased plant sterol enriched spreads had no children (SCF 2002).

Purchasers are motivated by concern about their health, particularly cholesterol.

Health concerns are one category of motive that may influence food choice decisions, others include cost, convenience, familiarity and sensory appeal (Steptoe et al. 1995). In the FSANZ survey, plant sterol enriched spread users were asked what their primary motivations are for purchasing an enriched spread. Health related concerns were the primary motivation for the largest group of enriched spread users followed by convenience (Table 1). This is an expected finding with the majority of individuals motivated by health related issues with cholesterol being the major issue. Seven percent of enriched spread users reported their primary motivation for using enriched spread as 'someone else in my household prefers it so I use it too'.

Table 1: Motivations for using an enriched spread

Motivation	Proportion of enriched spread users
Health-related (total)	***68***
To lower cholesterol levels	30
To prevent me getting high cholesterol problems	20
To improve my health	13
Doctor/Health professional advised me to use it	5
Convenience (total)	***12***
Someone else in my household prefers it so I use it too	7
Pack size	4
It's the brand that's available at my local shop	1
Sensory appeal (total)	***9***
Flavour/taste	5
I like the texture/it spreads easily	4
Familiarity and Naturalness (total)	***9***
It contains natural ingredients	5
It's my usual brand	3
It contains the ingredients I prefer	1
Others (total)	***2***

Consumption levels

There is no evidence that consumers of plant sterol enriched products consume too much – the reverse appears to be true.

The FSANZ survey found that adults who used plant sterol enriched spreads used them differently to those who did not use sterol enriched spreads. While nearly all consumers of both plant sterol enriched and non-enriched spreads used them for spreading on bread and toast (98% and 97% respectively), the consumers of enriched spreads were less likely to use the spread in cooking and baking than the consumers of non-enriched spread (53% and 78% respectively). Similar proportions of each group used their spread at least daily (Table 2). Those who used enriched spreads were more likely to use less on their bread and toast than those who did not use enriched spreads. The majority of enriched spread users (73%) used less than 2 teaspoons on average for spreading on bread and toast, while the majority (87%) of other spread users used more than 2 teaspoons (Table 3). Such a finding is consistent with a health based motivation that may be linked to reduction in fat intake more generally.

Table 2: Frequency of spread use on bread and toast

Frequency of use	Enriched spread users (%)	Other spread users (%)
More than once a day	44	53
Around once a day	35	19
Around 2-3 times a week	17	26
Less than 2 times a week	4	2

Table 3: Quantity of spread used on bread and toast

Quantity of spread used	Enriched spread users (%)	Other spread users (%)
Less than 1 teaspoon	32	5
1 to less than 2 teaspoons	41	7
2-6 teaspoons	25	45
More than 6 teaspoons	3	42

Based on reported levels and frequency of plant sterol enriched spread use, it is likely that a proportion of consumers will not receive enough plant sterol through their current consumption of enriched spreads on bread and toast.

Data collected from the European Union covering the breadth of plant sterol enriched products available (including spreads, milks, yoghurts and drinking yoghurts) found the median intake of plant sterols/stanols ranged from 0.11 gram/day in Spain to a high of 0.45 gram/day in the Netherlands. At the 95th percentile the intake ranged from 0.67 gram/day in Spain to a high of 2.9 gram/day in the Netherlands (Bradford 2006, unpublished data). The United Kingdom, arguably the EU country most similar to Australia and New Zealand, had a median intake of 0.31 gram/day and 95th percentile intake of 2.36 gram/day.

The evidence indicates that current intakes of plant sterols only from enriched spreads are below the optimal intake recommended for cholesterol reduction. As this could be due to the nature of the food vehicle, the availability of additional plant sterol-enriched products will increase the range of choice for consumers. Post-market monitoring in other countries, where additional enriched products have been available for some time, suggests however that increased product availability is not linked to excess consumption of plant sterols.

Recent data collected in the UK across the major phytosterol-enriched products provide additional evidence that products are more likely to be under-consumed (ACNFP 2006; Bradford 2006, unpublished report).

Understanding and comprehension

Consumers have mixed understandings of the role of these products and labelling information.

Concerns about consumers' understanding of target audience, purpose and recommended serving size were raised in the second review request from the Ministerial Council. The FSANZ survey suggested that consumers were mixed in their levels of understanding and comprehension with respect to these issues. Forty-eight percent of enriched spread consumers were aware of the terms 'plant sterol' or 'phytosterol'. Fifty-eight percent perceived the main benefit of plant sterols to reduce cholesterol level and 25% were not sure of the main benefit. There were some age differences in the perceived benefits of plant sterols, with fewer younger people (less than 35 years old) identifying cholesterol reduction as the main benefit and more of them responding that they were unsure.

Table 4 indicates the main sources of information about plant sterols for users of enriched spreads. Articles and advertising were the most common sources of information, though doctors and other health professionals, supermarket and peer networks are also important sources of information. Data from the US indicate that health professionals were a more important source of information than advertising and print media for adults (2004 Gallop Study of Cholesterol Lowering Options provided by Goodman Fielder).

Table 4: Sources of information about plant sterols

Main sources of information	Proportion of enriched spread users (%)
Articles in newspapers, mags., TV	62
Advertising	58
Doctor/health professional	42
Supermarket	36
Family/friend recommended product	30
Manufacturers website	12

In addition to these sources of information, consumers also gain information from the packaging and labels. The survey tested enriched spread users' knowledge of the products with respect to plant sterols in a broader dietary context, serve sizes and target audience (Table 5). The findings indicate some areas of limited understanding, particularly with regards to the suitability of plant sterol enriched products for children. There was some awareness of appropriate serve size with the majority of consumers aware that extra serves would not deliver extra benefits, though recognising that eating extra serves was not harmful. Nonetheless, only 36% considered they had sufficient serve size information.

Plant sterol enriched margarines were not perceived as a 'magic bullet' with 89% of consumers recognising they still need to be concerned about other fats in their diet despite the use of plant sterol enriched spreads.

Table 5: Knowledge about plant sterol enriched products

Statement	Desirable response	Proportion
Diet-related statements		
If I use plant sterol margarines, I don't have to worry about the other fats in my diet	False	89%
If I currently have health problems, I should check with my doctor before using this product	True	56%
I should eat extra fruit and vegetables if I eat plant sterol margarine	True	38%
Serve size statements		
The more of this product I eat, the better it is for me	False	66%
Extra serves might be bad for my health	False	53%
I have enough information to decide how much plant sterol margarine I should consume each day	True	36%
Target audience statements		
Everybody can eat plant sterol margarine	False	38%
Plant sterol margarines are not suitable for children	True	26%

Dietary and lifestyle behaviours

A key concern raised in the second review request is the extent to which the consumption of plant sterol enriched products will lead to changes in dietary or lifestyle behaviours that are contrary to the National Dietary Guidelines or recommended exercise regimens. The contention is that consumers of plant sterol enriched products may gain a benefit from consumption of these products and consequently be less concerned about their health and accordingly be less inclined to adopt appropriate diet and lifestyle behaviours. For example consumers may eat more saturated fats as they believe their consumption of plant sterol enriched products will counteract their indulgence. As there was no evidence to support or refute this contention the FSANZ survey specifically sought to collect data in order to better understand the motivations and likely behaviours of people in response to plant sterol enriched foods.

Consumers do not see plant sterol enriched spreads as a 'silver bullet' that will absolve them of further responsibility for healthy behaviour.

An experimental study designed to identify the existence or not of causal links was outside the scope of the FSANZ survey, rather a quasi-experimental design was used in order to identify associations between enriched spread use or not on the one hand and diet and exercise behaviours on the other (Table 6). The test group was those who used plant sterol enriched spreads and the control group was those who did not use plant sterol enriched spreads. Two types of measures were used: 1) objective self-reported measures of diet and exercise derived from the Australian National Health Survey (ABS 2006); and 2) subjective self-reported measures of perceived impacts of plant sterol margarine consumption on diet and exercise.

If there was an association between plant sterol enriched spread use and diet or exercise then there would be a significant difference in the responses of the test and control groups for each of these measures. Additionally, if users are aware of any diet or exercise changes that *they* attribute to use of enriched spread this will be picked up in the subjective measures.

Table 6: Survey design to test for impact on diet and exercise behaviour

Measures	Test group	Control group
Objective measure of diet	✓	✓
Subjective measure of impact on diet	✓	×
Objective measure of exercise	✓	✓
Subjective measure of impact on exercise	✓	×

Consumers of plant sterol enriched spreads do not exercise less or eat worse than non-consumers.

In summary the survey found no significant differences between the test and control groups in the level of exercise they carried out. In terms of diet there was a demographic distinction with younger users of enriched spreads having a better diet than those who didn't use enriched spreads. There was no significant differences in diet between test and control groups of those 35 years and older. There were a minority of enriched spread users who reported that their diet and exercise had improved since using plant sterol enriched spreads. Consumption of plant sterol enriched spread was not linked to either better or worse diet and exercise measures, though a minority of consumers considered they had improved diet and exercise levels.

Diet was measured through the usual daily intake of fruit and vegetables. Individuals who had consumed 2 or more serves of fruit and 4 or more serves of vegetable a day were considered to have met their dietary intake of fruit and vegetables. A minority of both consumers and non-consumers of plant sterol enriched spreads surveyed satisfied this requirement. There were no significant differences in the proportion who satisfied this requirement between enriched and other spread users who were over 35 years of age. There was a slight age difference with younger (less than 35) enriched spread users being more likely to meet the fruit and vegetable requirements than younger people who did not use enriched spreads.

In terms of subjective impact on diet 55% reported their diet had stayed about the same since using enriched spreads and 43% reported it had improved (Table 6). Additionally 89% of respondents who used plant sterol enriched margarines noted considered the statement *If I use plant sterol margarines, I don't have to worry about the other fats in my diet* to be false. The consumption of plant sterol enriched spread may, at worst, be associated with no poorer diet than non-consumption of enriched spreads, and at best, be associated with a better diet for those under 35 years.

Exercise was measured adopting the approach of the National Health Survey (ABS 2006) which categorises individual's level of exercise into one of four 1 of 4 exercise level categories (sedentary, low, moderate, high) based on exercise time and intensity. Approximately 50% of respondents had low levels of exercise. There were no significant differences between plant sterol enriched spread users and other spread users in the level of exercise performed.

In terms of subjective impact on exercise levels, 71% reported their level of exercise had stayed about the same since using enriched spreads and 26% reported it had increased (Table 7). The consumption of plant sterol enriched spread may, at worst, be associated with no lesser levels of exercise than non-consumption of enriched spreads.

Table 7: Changes in diet and exercise levels since using plant sterol enriched spreads

Exercise/diet changes since using enriched spread	Exercise (%)	Diet (%)
Exercise increased a lot / Diet much healthier	8	11
Exercise increased a little / Diet somewhat healthier	18	32
Stayed about the same	71	55
Exercise decreased a little / Diet somewhat less healthy	1	1
Exercise decreased a lot / Diet much less healthy	2	0

The diet and the exercise findings highlight that those who consume plant sterol enriched spreads do not have significantly worse diets and exercise levels than those who do not use plant sterol spreads. This evidence does not support the contention that use of plant sterol enriched spreads are associated with less healthy diet and lifestyle choices. While the evidence does not suggest that those who consume plant sterol enriched spreads make healthier diet and lifestyle choices than those who do not consume these spreads, self-assessments of enriched spread users suggest there have been some improvements in diet and exercise for some individuals.

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ATTACHMENT 4

Phytosterols Dietary Exposure Assessment Report for the Second Review

Previous phytosterol exposure estimates

For applications A433, A434 and A508, estimates of dietary exposure were conducted assuming the concentration of free phytosterols was 0.8 g/serve (except for reduced and low fat milk in A508 which was assumed to contain 0.9 g/serve). Estimated exposures to free phytosterols from these three applications (and a combination of A433 and A434 which were assessed concurrently) were up to between 1.7 g/d and 1.9 g/d for mean consumers of free phytosterols and up to between 4.4 g/d and 4.8 g/day for 95th percentile consumers of free phytosterols across all of the population groups assessed.

Table 1 shows a summary of the dietary exposure assessments and results for A433, A434, A433 + A434 and A508.

Table 1: Summary of dietary exposure assessments previously reported at Final Assessment

	Application			
	A433 **Phytosterol esters in breakfast cereals**	**A434** **Phytosterol esters in low fat milk and yoghurt**	**A433 + A434**	**A508** **Tall oil Phytosterols in low fat milk**
Concentrations used*	0.8g/serve table spreads 0.8g/serve breakfast cereals	0.8g/serve table spreads 0.8g/serve reduced fat milk 0.8g/serve reduced fat yoghurt	0.8g/serve table spreads 0.8g/serve breakfast cereals 0.8g/serve reduced fat milk 0.8g/serve reduced fat yoghurt	0.8g/serve table spreads 0.9g/serve reduced fat milk
Population groups assessed	Australia: 2 years+, 40-64 years, 65 years+, 2-12 years, females 16-44 years New Zealand: 15 years+, 40-64 years, 65 years+, females 16-44 years			
Mean exposure*#	≤ 1.7 g/d	≤1.9 g/d	≤ 1.9 g/d	≤ 1.9g/day
95th percentile exposure*#	≤ 4.4 g/d	≤ 4.7 g/d	≤ 4.7 g/d	≤ 4.8g/day

* As free phytosterols.
\# Less than or equal to the value presented across all of the population groups assessed.

Additional assessment

An additional assessment has been conducted by FSANZ to determine the estimated exposure to phytosterols should the concentration in the foods assessed previously in other applications be equal to 1.0 g/serve as free phytosterols. All food groups, population groups, food consumption data, serve sizes and methodologies remained the same as in previous assessments. This additional assessment was not conducted for A433 and A434 combined, however, it can be seen from Table 1 that estimated exposures for this scenario were similar to when the applications were assessed separately.

As expected, assuming foods contain 1.0 g free phytosterols per serve, the estimated exposures were slightly higher compared to previous estimates using a lower concentration. Estimated exposures were up to between 2.1 g/day and 2.4 g/day for mean consumers of free phytosterols and up to between 5.5 g/day and 5.9 g/day for 95th percentile consumers for free phytosterols across all of the population groups assessed. A summary of these results are shown in Table 2.

The target group of 40-64 years had the highest levels of exposure. Children aged 2-12 years (Australia only) and females of child bearing age (16-44 years) had lower exposures than the target group. (See Table 3 for further details on exposure for each population sub-group assessed).

Table 2: Summary of estimated dietary exposure to free phytosterols assuming a concentration of 1.0 gram of free phytosterols per serve

	Estimated dietary exposure for consumers of phytosterols*# (grams/day)	
Application	**Mean**	**95th percentile**
A433	≤ 2.1	≤ 5.5
A434	≤ 2.4	≤ 5.9
A508	≤ 2.3	≤ 5.8

* As free phytosterols.
# Less than or equal to the value presented across all of the population groups assessed.

Table 3: Estimated dietary exposure to free phytosterols assuming a concentration of 1.0 gram of free phytosterols per serve for various population groups assessed

			Estimated exposure (g/day)*	
Application	**Country**	**Population group**	**Mean**	**95th percentile**
A433	Australia	2 years+	1.8	5.0
		40-64 years	1.9	5.1
		65 years+	1.9	5.0
		2-12 years	1.4	3.5
		Females 16-44 years	1.6	4.1
	New Zealand	15 years+	2.0	5.4
		40-64 years	2.1	5.5
		65 years+	2.0	4.8
		Females 16-44 years	1.7	4.3

Application	Country	Population group	Estimated exposure (g/day)*	
			Mean	95th percentile
A434	Australia	2 years+	2.0	5.3
		40-64 years	2.1	5.4
		65 years+	2.2	5.4
		2-12 years	1.6	4.3
		Females 16-44 years	1.8	4.4
	New Zealand	15 years+	2.2	5.7
		40-64 years	2.4	5.9
		65 years+	2.3	5.3
		Females 16-44 years	1.9	4.6
A508	Australia	2 years+	2.0	5.2
		40-64 years	2.1	5.3
		65 years+	2.1	5.3
		2-12 years	1.5	4.2
		Females 16-44 years	1.7	4.3
	New Zealand	15 years+	2.2	5.6
		40-64 years	2.3	5.8
		65 years+	2.2	5.2
		Females 16-44 years	1.8	4.6

* As free phytosterols.

ATTACHMENT 5

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