FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

**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

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## 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**<br><br>**(i) novel foods;**<br><br>**(ii) health claims; and**<br><br>**(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.**<br>• **Applications cannot be delayed to await new policy guidelines.**<br><br>**Novel foods**<br>• Phytosterol-esters and tall-oil phytosterols already approved in the Code as novel foods.<br>• Current applications seek to broaden use to other foods.<br>• Existing guidelines require a pre-market safety assessment.<br>• Assessments consistent with existing policy guidelines for novel foods.<br><br>**Health claims**<br>• Currently not permitted.<br>• No previous or current assessment of a health claim for phytosterols. | • **FSANZ has addressed the standards issues only. Policy issues are discussed briefly:**<br>**Novel Foods**<br>• Existing policy guidelines endorsed in December 2003.<br>• Proposal P291 to review Standard 1.5.1 Novel Foods (at Draft Assesm'nt) will not change the existing policy.<br>• No impact on the assessment of the current Applications.<br>**Substances other than vitamins and minerals**<br>• FRSC sub-committee developing policy guidance on a broad range of substances.<br>• No delay of the current Applications is justified.<br>**Health claims**<br>• 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.**<br><br>**(i) Consumption of phytosterol-enriched foods can result in a decrease in serum β-carotene; and**<br><br>**(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**:<br>High-fibre breakfast cereal<br>• Restrictions on sugar content<br>• No breakfast cereal bars<br>Low-fat milk<br>• Maximum 1 litre container<br>• No flavourings<br>Low-fat yoghurt<br>• Maximum 200 g punnet size<br>**Current mandatory statements**:<br>• Diet should be low in saturated fats and high in fruit and vegetables;<br>• Not recommended for infants, children, pregnant or lactating women;<br>• Seek medical advice with cholesterol-lowering medications.<br>**Additional mandatory statement:**<br>• No additional benefits when consumed in excess of 3 serves/day.<br>**Additional condition of use:**<br>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.**<br><br>• Professor John W. Erdman (USA) agrees with FSANZ that lower β-carotene levels are not a nutritional concern.<br>• Professor Martijn Katan (The Netherlands) does not consider lower serum β-carotene levels as a safety concern.<br>• Professor John McNeil (FSANZ Fellow) does not consider that phytosterols are of particular nutritional concern for individuals with metabolic syndrome or diabetes.<br>• 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.<br>• Industry advertising, brochures, leaflets and consumer advice lines.<br>• Consumer familiarity with existing products. | • **Insertion of an Editorial Note** to reinforce the legibility and presentation requirements of the Code for mandatory statements.<br>• **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[1].

[1] 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[2];
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.

[2] 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[3] 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.

[3] 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 Adequate information to enable informed choice

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 -<br><br>1. the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables;<br><br>2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and<br><br>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 -<br><br>1. the product should be consumed as part of a diet low in saturated fats and high in fruit and vegetables;<br><br>2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision;<br><br>3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication; and<br><br>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.<br><br>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.<br><br>May only be added to food –<br><br>(1) according to Standards 1.3.4 and 2.4.2; and<br><br>(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.<br><br>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.<br><br>May only be added to edible oil spreads –<br><br>(1) according to Standard 2.4.2; and<br><br>(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.<br><br>May only be added to breakfast cereals, not including breakfast cereal bars, if –<br><br>(1) the total fibre content of the breakfast cereal is no less than 3 g/50 g serve;<br><br>(2) the breakfast cereal contains no more than 30g/100g of total sugars; and<br><br>(3) the total phytosterol ester added is no more than 26g/kg.<br><br>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.<br><br>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 –<br><br>1. the product should be consumed in moderation as part of a diet low in saturated fats and high in fruit and vegetables;<br><br>2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision; and<br><br>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 -<br><br>1. the product should be consumed as part of a diet low in saturated fats and high in fruit and vegetables;<br><br>2. the product is not recommended for infants, children and pregnant or lactating women unless under medical supervision;<br><br>3. consumers on cholesterol-lowering medication should seek medical advice on the use of this product in conjunction with their medication; and<br><br>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.<br><br>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.<br><br>May only be added to food -<br><br>(1) according to Standards 1.3.4 and 2.4.2; and<br><br>(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.<br><br>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.<br><br>May only be added to edible oil spreads –<br><br>(1) according to Standard 2.4.2; and<br><br>(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.<br><br>May only be added to milk in accordance with Standard 2.5.1.<br><br>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[4] (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 95$^{th}$ 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.

[4] 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 ($95^{th}$ 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[5] 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 95$^{th}$ 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.

[5] 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[6] (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.

[6] 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 95$^{th}$ 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

**John W. Erdman Jr., Ph.D.**
**Professor, and Nutrition Research Chair**
**Department of Food Science and Human Nutrition**
**University of Illinois at Urbana-Champaign**

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

**John J McNeil**
**Professor & Head**
**Department of Epidemiology & Preventive Medicine**
**Monash University**
**Central & Eastern Clinical School**
**The Alfred Hospital**
**Melbourne, Vic 3004**

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**
**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[7] 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;

[7] 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. |

***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.