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

## Supporting Document 1

Risk assessment report

Application A1065

Packaging Size for Phytosterol-enriched Milk

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# Executive Summary

This Application seeks permission to remove the size restriction on packages of milk containing phytosterols, phytostanols and their esters. This restriction was included as one part of a suite of risk mitigation measures aimed at encouraging appropriate use of phytosterol-enriched foods by target consumers and discouraging use by non-target consumers.

Given the comprehensive nature of previous scientific evaluations, the primary focus of this assessment is to review aspects of the scientific evidence, and consider any new information that has become available over recent years, particularly since the most recent assessment by FSANZ in 2010. This document also considers any potential risk to public health and safety from removing the volume-restriction risk management measure.

There is no new toxicological, clinical or epidemiological evidence indicating the need to change the previous safety assessments. Therefore the conclusion of previous safety assessment stands, that is, the consumption of phytosterol-enriched foods raises no safety concerns and a reference health standard is not warranted.

The previous risk assessments were based on national nutrition survey data (consumption data), and there was an assumption that consumers replaced all non-enriched products with enriched products. The volume of the package was not used to determine the dietary intake of phytosterols. Therefore, removing the package size restriction has no impact on previous dietary intake assessments, including nutritional assessment.

It is expected that removing the volume restriction from phytosterol-enriched milk is likely to increase the consumption of such milk by target and non-target populations (mainly children). However based on current usage data indicating most consumers fall within the target-population, any increased consumption in children is likely to be low and there is no evidence to suggest this will have an adverse health effect. Any increased consumption occurring in the target population is likely to be of additional benefit as there is evidence, that at least some of this population may not be receiving the minimum requirement due to incumbencies of the current volume restriction.

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# 1. Background

In November 2006, Standard 2.5.1 – Milk, was amended to permit the addition of phytosterols, phytostanols and their esters to milk.

The risk assessment on phytosterols proposed to be added to food concluded there were no public health or safety issues. Despite this, as phytosterol-enriched foods were relatively new in Australia and New Zealand (at the time of assessing the milk application the only other approval for the addition of phytosterols to food was for table spreads (Application A410), a cautious approach was proposed. This included requiring mandatory label advisory statements (as for other phytosterol-enriched foods) and a 1 litre volume restriction.

# 2. Introduction

The Applicant seeks permission to remove the size restriction on packages of milk containing phytosterols, phytostanols and their esters (referred to as phytosterol-enriched milk hereon in). There are no compositional or other changes requested as part of this Application.

Given the comprehensive nature of previous scientific evaluations, the primary focus of the safety assessment is to review aspects of the scientific evidence, and consider any new information that has become available over recent years, particularly since the most recent assessment by FSANZ in 2010. In addition the assessment covers any public health and safety consequences from removing the volume restriction risk management measure.

No new dietary intake estimation or nutritional assessment has been undertaken as part of this assessment because previous assessments assumed consumers replaced all non-enriched products with enriched products and there are no compositional changes. Therefore removing the package size restriction has no impact on these previous assessments.

# 3. Key risk assessment questions

For this application, the risk assessment questions were developed in the context of the section 18 objectives under the *Food Standards Australia New Zealand Act 1991*.

The following key questions are addressed in the risk assessment report:

1 a) Who is the target population?

b) Who are the non-target population groups?

2 a) What were the assessed health risks from consumption of phytosterols for the target and non-target sub-populations?

b) What assumptions and uncertainties were associated with the risk assessment? Have these assumptions and uncertainties changed since approval of the application with the volume restriction? If so how?

3 The 1 litre restriction was aimed at encouraging individual use (i.e. target consumer) and discouraging use by non-target population, e.g. by those in the same household.

a) What were the evidence/assumptions/uncertainties in relation to the risk of phytosterol enriched milk when consumed by non-target consumers? Has this altered? If so how?

b) What evidence/assumptions show that the volume restriction was successful in mitigating that risk? What are uncertainties around this?

4 What are the consequences of the volume restriction for:
a) target consumers?
b) non-target consumers?
c) manufacturers?

d) What were the evidence/assumptions/uncertainties in relation to these consequences for each identified group?

5 Based on the evidence, assumptions and uncertainties from question 4), what are the likely consequences of removing the volume restriction for:
a) target consumers ?
b) non-target consumers ?

This risk assessment report is structured to address the above questions in order.

## 3.1 Response to risk assessment question 1

*a) Who is the target population?*

Adults usually over 40 years of age who consider they may have elevated blood cholesterol levels and wish to control their cholesterol intake via their diet. Consumption of phytosterol-enriched food is not intended to replace medical treatment of elevated blood cholesterol.

*b) Who are the non-target population groups?*

Individuals without elevated blood cholesterol levels; pregnant and lactating women and children under 5 years of age, even where they have elevated blood cholesterol; individuals with cholesterol / phytosterol absorption disorders.

## 3.2 Response to risk assessment question 2

*a) What were the assessed health risks from consumption of phytosterols for the target and non-target sub-populations?*

None of the assessments performed to date by FSANZ have identified any potential public health or safety risks for the target and non-target consumers. Specific safety data in pregnant women, lactating women, and children under 5 years of age remain relatively limited in comparison to the extensive data available for the target population. Based however on knowledge of the mechanisms of phytosterol action, the now extensive experience of use of plant sterol enriched foods in the general population and an absence of effects in pregnant animals and their offspring, there is no basis for postulating a risk to these population subgroups.

Previous assessments concluded that the small number of people (approximately 45 cases worldwide) with cholesterol/ phytosterol absorption disorders should avoid consumption of phytosterols. Based on this advice the removal of the volume restriction has no impact on this sensitive sub-population.

ANZFA/FSANZ has previously assessed and characterised the risk from the consumption of foods containing added phytosterols, phytostanols and their fatty acid esters. These foods are edible oil spread (ANZFA 2000), breakfast cereal (FSANZ 2004a, 2005, 2006), low fat milk (FSANZ 2004b, 2004c, 2005, 2006), low fat yoghurt (FSANZ 2004b, 2005, 2006) and low fat cheese (FSANZ 2010a). FSANZ has also recently considered the safety equivalence of phytosterols, phytostanols and their fatty acid esters (FSANZ 2010b). Collectively, these risk assessments have considered all available information, including animal toxicity data and epidemiological data, relevant to the safety of phytosterols, phytostanols and their fatty acid esters. FSANZ concluded that consumption of phytosterol enriched foods raises no safety concerns and that a reference health standard is not warranted. This conclusion was also reached by regulatory agencies in Europe and the USA. However in 2008, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established an Acceptable Daily Intake (ADI) of 0-40 mg/kg bodyweight, based on findings from a 90 day rat study (WHO 2009). FSANZ re-evaluated this toxicological evidence and found no justification for establishing an ADI for phytosterols, phytostanols and their fatty acid esters (FSANZ 2010a). It was also concluded that a reduction in the absorption of beta-carotene with intake of phytosterols is expected, however this was considered to have no significant nutritional impact. Furthermore, phytosterols, phytostanols and their fatty acid esters were concluded to be equivalent in terms of their food safety properties (FSANZ 2010b).

The potential for phytosterol enriched foods to increase the risk of cardiovascular disease was specifically assessed by FSANZ. This issue merited evaluation because patients with a rare lipid disorder that results in hyperabsorption of dietary phytosterols develop early atherosclerosis and coronary heart disease (CHD). Some studies have investigated whether the modest increase in serum plant sterols, which occurs when phytosterol enriched foods are consumed by normal individuals, is associated with CHD risk. A comprehensive review of the literature did not indicate any population health risk arising from consumption of phytosterol enriched foods (FSANZ 2010a). Even with consumption of phytosterol enriched foods, the levels of phytosterols in the blood remain at less than 1% of total sterols. FSANZ concluded that added phytosterols are not present in sufficient amounts to be considered as an additional risk factor for CHD under normal circumstances.

A recently published randomised controlled trial reported an association between increased serum campesterol (one member of the phytosterol group) concentration and increased diameter of venules in the retina of subjects consuming phytosterol-enriched margarine. (Kelly et al 2011). Increased retinal venular diameter has been proposed as an indirect marker of CHD risk. In this study, three randomised groups of patients were studied at baseline and after 85-weeks. Group one (n = 11) consumed plant sterol enriched margarine (2.5 g phytosterols/day), the second (n = 8) plant stanol enriched margarine (2.5 g phytostanols/day), and the control group (n = 11) non-enriched margarine. All subjects were taking statins for the treatment of elevated blood cholesterol.

Kelly et al reported that no adverse effects were observed. There were no statistically significant differences in mean venular diameters for the plant sterol group, the plant stanol group or the control group when baseline measurements were compared to those after 85 weeks of treatment. However, when compared with the control group changes in cholesterol-standardised concentrations of the phytosterol campesterol correlated positively with changes in venular diameter.

This lead the authors to conclude that this finding may be related to the proposed effects of phytosterols on vascular function, however they did state that this finding requires confirmation and that more evidence is needed before it can be concluded that phytosterol consumption affects the microvasculature. FSANZ has reviewed the publication and notes that the reported association, while statistically significant ($p$ = 0.033), is unlikely to be physiologically relevant.

The scatterplot of change in venular diameter versus change in serum campesterol shows no convincing trend. For example, the subject with the greatest increase in serum campesterol exhibited only a small increase in venular diameter while a subject with an approximately 20-fold lower increase in serum campesterol exhibited an approximately six-fold larger increase in venular diameter. Moreover, two subjects with relatively large increases in serum campesterol exhibited *reductions* in mean venular diameter. Finally, in contrast to other studies, Kelly et al did not find any correlation between retinal venular diameter and other established CHD risk factors, possibly due to the low power of the study (only 8 to 11 subjects per group). However, it also remains possible that retinal venular diameter is not a valid marker of CHD risk. FSANZ concludes that this study does not warrant cause for concern with regard to the safety of phytosterol/stanol-enriched foods.

A recent review and meta-analysis was performed to investigate whether there is an association between serum phytosterol concentration and cardiovascular disease (CVD) (Genser et al 2012). The authors' systematically searched the databases MEDLINE, EMBASE and COCHRANE for studies published up to April 2010 that reported either risk ratios of CVD in relation to serum sterol concentrations or serum sterol concentrations in CVD cases and controls separately. Seventeen studies were identified involving a total of 11182 subjects. Genser et al concluded that their systematic review and meta-analysis did not reveal any evidence of an association between serum concentrations of phytosterols and risk of CVD.

FSANZ has not located any studies published since its previous risk assessment in 2010 that would indicate a potential for safety concerns in any population group consuming foods enriched with phytosterols, phytostanols and their fatty acid esters.

*b) What assumptions and uncertainties were associated with the earlier risk assessment?*
*Have these assumptions and uncertainties changed since approval of the application with the volume restriction? If so how?*

Several assumptions and uncertainties associated with previous FSANZ risk assessments of phytosterols relate to the assessment of dietary intake (FSANZ 2010a, 2010b). These assumptions and uncertainties remain as no dietary intake assessment was conducted for the present Application due to the absence of new data relevant to the dietary intake of phytosterols. Previous FSANZ estimates of intakes of phytosterols from a range of phytosterol-enriched foods showed that mean dietary intake would not exceed 1.9 g per day in any population group, assuming existing consumption patterns were maintained and there was complete replacement of regular foods with their phytosterol-enriched counterparts. The analysis also showed that in all population groups assessed, reduced fat milks contributed only 14-18% of total dietary intake of added phytosterols. Therefore any change in the consumption of phytosterol-enriched low fat milk due to the removal of the volume restriction is likely to have a relatively small impact on total dietary intake of added phytosterols.

FSANZ considers that there is now less uncertainty in the data supporting the safety of phytosterols in foods since the approval of the addition of phytosterols to reduced-fat milk in 2006. The nature of plant sterols together with their chemical and physical properties are well described in the scientific literature.

Detailed toxicity studies in animals are available. In addition, there are many published studies examining the safety, efficacy and nutritional effects in humans following consumption of phytosterol-enriched foods. Phytosterols have a history of safe use in the food supply of more than ten years. Areas of uncertainty continue to diminish as additional data supporting the safety of phytosterols accumulate in the published literature.

As stated in response to part (a) of this question, specific safety data in pregnant women, lactating women, and children less than 5 years of age remain relatively limited in comparison to the extensive data available for the target population. However, there is no basis for postulating a risk to these population subgroups.

## 3.3 Response to risk assessment question 3

*The 1 litre restriction was aimed at encouraging individual use (i.e. target consumer) and discouraging use by non-target population, e.g. by those in the same household.*

*a) What were the evidence/assumptions/uncertainties in relation to the risk of phytosterol enriched milk when consumed by non-target consumers? Has this altered? If so how?*

At the time of the approval of the addition of phytosterol to milk, research undertaken by FSANZ (FSANZ, 2006) and information available at the time from the United Kingdom from a post-market survey (ACNFP, 2006) showed that approval of a limited range of phytosterol-enriched foods would not be expected to significantly increase the likelihood of consumption by non-target groups. Support for this was as follows:

- Phytosterol-enriched foods were specialised, niche products, marketed to a limited consumer section (adults with cholesterol concerns).
- Users of phytosterol margarine (the only phytosterol-enriched product approved in Australia and New Zealand at the time of the assessment) choose the product for a health (cholesterol lowering) benefit.
- Phytosterol-enriched products were used in moderation by the target group of consumers.
- Advice on the appropriate use of phytosterol-enriched food was available from a variety of sources including dietitians, General Practitioners, public health organisations and the food industry. This advice was considered to ensure the public had sufficient knowledge about phytosterol-enriched products to make well-informed decisions on foods that are appropriate to their health needs.
- The presence of mandatory labelling on packages advising against consumption by children and pregnant and lactating women.

Despite the above evidence, there was still a level of uncertainty around the risk of phytosterol-enriched foods becoming staple foods for some households. This uncertainty arose mainly due to a) concern that the approval under consideration would be the first of many such approvals, which would lead to multiple phytosterol-based products being available to the consumers and b) as these products were relatively new to the Australian and New Zealand food market there had been insufficient time to assess whether the use pattern in Australia and New Zealand would mimic the safe use seen in Europe.

The concern that the approval of phytosterol-enriched milk would lead to a number of further requests to approve the use of phytosterols in food has not occurred. Consumer choice for such products, particularly in New Zealand (where currently phytosterol-enriched milk is not available) has remained relatively limited. The first approval of the use of phytosterol-enriched food was granted over ten years ago, since then there has been a history of safe use.
Since the approval of phytosterol-enriched milk FSANZ and other interested parties have extended the educational material available on appropriate use of phytosterol-enriched food.

In the last ten years there has been further segmentation of the milk market, resulting in an expansion of the product lines which now includes, for example, milks with varying fat and calcium content. Each of these milk varieties are targeted at particular sub-populations. It is now common for purchasers to make choices between different types of milk.

b) *What evidence/assumptions show that the volume restriction was successful in mitigating that risk? What are the uncertainties around these?*

It is not possible to assess what the impact of the volume restriction has had on the consumption of phytosterol-enriched milk by non-target consumers because it is part of a suite of risk management measures and there is no baseline to compare with.

The Applicant has provided evidence that current purchase of phytosterol-enriched milk in Australia (based on HeartActive milk, which is the only currently available fresh white phytosterol-enriched milk available in Australia), is mainly by the target group. Phytosterol-enriched milk is not currently marketed in New Zealand.

- 84.9% of purchasers are 35 years or older
- 70.1% of purchasers are 35 years and older and do not have children in their household
- 70.3% of purchasers are overweight compared with 59.1% for the total population
- 60% of consumers who purchased over a 12 month period, and 67% when looking at last 7 day purchases (Roy Morgan Single Source, April 09-March 11, cited by Applicant) are concerned about their cholesterol levels

In addition, information in the Application indicates most current purchasers of phytosterol-enriched milk tend to live in households without children aged under 16 years (Roy Morgan Single Source, April 09-March 11, cited by Applicant). Of households purchasing phytosterol-enriched milk in the last 12 months, 77% had no children aged under 16 years and the percentage rose to 82% when only purchase over the last 7 days was examined. These figures suggest that the current consumption of phytosterol-enriched milk by children, and particularly those aged under 5 years, will be low.

One hundred percent of current purchasers also purchase other milks (Roy Morgan Single Source, April 09-March 11, cited by Applicant), which suggests that a number of consumers are selective in their milk purchasing, choosing the milk most appropriate for various members of their household.

Phytosterol-enriched foods are widely available in Europe and the USA. Neither of these jurisdictions have a similar volume restriction to that required in the Code. Even in the absence of the volume restriction, EFSA has reported that phytosterol intake was generally below the minimum dose required to significantly lower blood cholesterol and there was little over consumption (EFSA, 2008).

Europe requires labelling similar to that required by the Code, whereas the USA does not require any cautionary or advisory statements regarding target-consumers. In addition, in the US there is no requirement to stipulate a maximum daily intake of phytosterols.

The information from Europe and the US indicate that the absence of a volume restriction does not lead to adverse health effects from consumption of phytosterol-enriched foods, including milk.

## 3.4 Response to risk assessment question 4

*a) What are the consequences of the volume restriction for target consumers?*

The Applicant has provided some evidence that the current regulation has created a situation of inconvenience for target consumers. A total of 164 customer inquiries on phytosterol-enriched milk, were received by the Applicant in the period July 2010 to April 2011. Twenty-four of these (14.6%) were requesting larger pack sizes for phytosterol-enriched milk (p.8 of Application). These enquiries from within Australia suggest there is consumer demand for larger pack sizes, and suggest unmet consumer need.

In addition, the Applicant has stated that the majority of other consumer enquires on phytosterol-enriched milk were asking where the product could be purchased (ibid). Both types of enquiry suggest that informed consumers want more convenient access to phytosterol-enriched milk.

FSANZ notes that consumers following advice on recommended daily amounts of 2 to 3g of phytosterols (http://www.foodstandards.gov.au/scienceandeducation/factsheets/factsheets/plantsterols2011.cfm) combined with the Code requirement for phytosterol-enriched milk to contain no less than 3 g/L and no more than 4 g/L of plant sterol equivalents (Standard 2.5.1 – Milk, clause 5 (c)) need to drink two to four 250 mL servings of phytosterol-enriched milk per day. This in turn leads to the need to either purchase 1 litre packs every one to two days or bulk buy packs. Although there is a restriction on the pack size, there is no restriction on the number of packs which can be purchased and therefore it is likely that at least some consumers already purchase multiple litre packs as part of their regular grocery shop.

As a result of either having to buy phytosterol-enriched milk on multiple occasions in a week or to find storage for bulk purchase of litre packs target populations may not, on a daily basis, be achieving a health benefit. Evidence from Europe, where there is not a similar volume restriction, (although the common pack size for phytosterol-enriched milk is 1 litre) and there is a wider choice of phytosterol-enriched foods, indicates that target consumers still are not consuming enough phytosterols to gain the proposed benefits.

*b) What are the consequences of the volume restriction for non-target consumers?*

As a result of the volume restriction being part of a suite of risk management measures and the absence of a baseline to compare with it is not clear what effect, if any, the volume restriction has had on non-target consumers.

Based on information regarding current purchasers of phytosterol-enriched milk, reported in section 3.3 (b) of this document, consumption by children, particularly those aged under 5 years, will be low.

Information relating to the consumption of phytosterol-enriched milk by pregnant or lactating women was not available in the Application or from other sources.

FSANZ has reviewed two recently published studies (Sioen et al 2011 and Hearty et al 2008) on patterns of phytosterol consumption in Belgium and Ireland. These studies showed there is consumption of phytosterol-enriched foods by non-target populations, including children 2.5–7 years of age, some of which is non-accidental. The Hearty study also showed that intake of phytosterols came from a combination of phytosterol-enriched foods, not just milk.

Both studies provided some general information on consumption of phytosterol-enriched foods in the absence of volume restriction. However, due to a combination of the Sioen study not including phytosterol-enriched milk (this product was not available in Belgium at the time of the study) and some deficiencies in study design and interpretation, FSANZ considers neither study provides specific information to assist our risk management determinations.

*c) What are the consequences of the volume restriction for manufacturers?*

The Applicant states that only 12% of general milk sales in Australia are in 1 litre pack sizes, while 87.4% of sales are for packs greater than 1 litre. The consequences therefore are potential disadvantage in sale, and environmental inefficiency from increased use of plastic.

*d) What are the evidence/assumptions/uncertainties in relation to these consequences for each identified group?*

At the time of the approval of the addition of phytosterol to milk there was little information available on the effects of consuming phytosterol-enriched foods, including among non-target consumers. FSANZ therefore adopted a suite of risk management measures which aimed to provide sufficient information for consumers to make an informed choice and discourage consumption by non-target groups. The volume restriction was particularly targeted at encouraging use by target users and discouraging use by non-target consumers.

The initial Application requesting permission to add phytosterols to milk did not mention a potential volume restriction; this was first recommended as an outcome of the first assessment report. At the public consultation stages for the Application, industry (including manufacturers) did not raise any objections to the proposed restriction.

## 3.5 Response to risk assessment question 5

*5 Based on the evidence, assumptions and uncertainties from question 4, what are the likely consequences of removing the volume restriction for:*

*a) Target consumers*

FSANZ considers that consumption of the phytosterol-enriched milk is likely to increase if the pack size restriction is lifted. Firstly, current consumers may purchase more product and increase their intake from current levels. Secondly, some target consumers who currently do not consume the product will start to purchase and consume the product, due to reduced pricing relative to the 1litre pack size and due to increased availability, also due to the pack size. A net consequence of a more convenient supply is that consumers are more likely to consume 2-3g of phytosterols daily and therefore achieve the health benefit.

*b) Non-target consumers?*

There is also likely to be some increased consumption by the non-target group, particularly children in households that currently purchase the product and where there is only one target consumer. As a worse-case, some of these households may opt to purchase just one type of milk – the phytosterol-enriched one, (although this is not supported by information in the Application). From an affordability perspective, the move to purchasing one type of milk is unlikely to have economically detrimental effects on these households, as current consumers tend to live in households with a medium-to-high income (Roy Morgan Single Source, April 09-March 11, cited by Applicant) and therefore have disposable income. In the situation where all milk purchases become the more expensive phytosterol-enriched milk, the economic impact in these households will be mainly or exclusively on disposable income.

Households which contain a mixture of target and non-target consumers may see a rise in consumption by non-target consumers. There are two most likely mechanisms by which this will occur. First, in some cases the main grocery buyer may start purchasing only one type of milk – the phytosterol-enriched one. While the phytosterol-enriched milk is likely not to be viewed as a staple, the larger pack size may mean that some grocery buyers will purchase just the one type of milk for reasons of convenience. This would be a consciously-decided outcome, and likely to be limited to households where the increased cost will have little impact on discretionary income.

Second, where the phytosterol-enriched milk is situated in a refrigerator with non-enriched milk in same sized packaging, there is likely to be some unintentional consumption by the non-target group when the packaging labels are not checked as there is no longer a pack-size visual cue for the special nature of the phytosterol-enriched milk. This unintentional consumption is unlikely to occur with young children, as phytosterol-enriched milk tends to be purchased by consumers in child-free households (Roy Morgan Single Source, April 2009–March 2011, cited by Applicant) and young children do not tend to pour their own drinks.

Finally, there is the possibility of increased use by households that contain only non-target consumers. These are unlikely to be households with lower incomes, as phytosterol-enriched milk is currently typically purchased by households with medium to high incomes, and the price premium that will occur with the milk being in a larger package will continue to discourage use by this consumer group, particularly those in lower income groups.

## 3.6 Conclusions

- None of the assessments performed to date by FSANZ have identified any potential public health risks in target or non-target populations.
- Based on knowledge of the mechanisms of phytosterol action, the now extensive experience of use of plant sterol-enriched foods in the general population and an absence of effects in pregnant animals and their offspring, there is no basis for postulating a risk to pregnant or lactating women.
- The majority of current purchasers of phytosterol-enriched milk, in Australia, fall within the target population i.e. are over 35 years of age; are overweight; are concerned about their blood cholesterol levels.
- A large proportion (approximately 80%) of Australian households buying fresh white phytosterol-enriched milk does not have children in the household. This suggests consumption of phytosterol-enriched milk by children below 5 years of age is likely to be low and the removal of the volume restriction is likely to have little impact on the consumption of this sub-population.
- The volume restriction to 1 litre is an inconvenience for consumers.
- There is no evidence of a risk in Europe or the US where there are no pack size restrictions.

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